Development of digital learning materials for renewable pharmaceutical practice-oriented skills in English and Hungarian. Preparing university lecturers for educational challenges of the 21st century.

Pharmacognosy 2

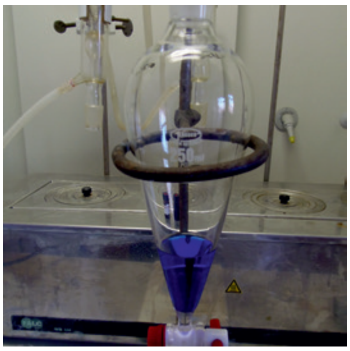
Dr. Györgyi Horváth, Prof. Dr. Péter Molnár, Dr. Tímea Bencsik

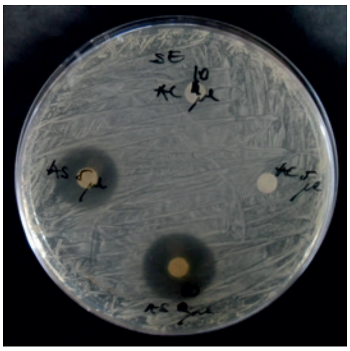
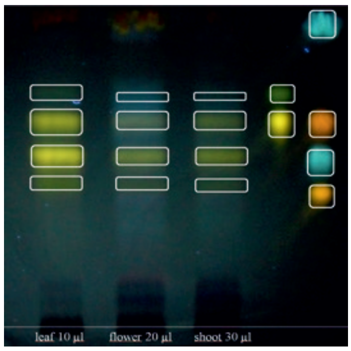


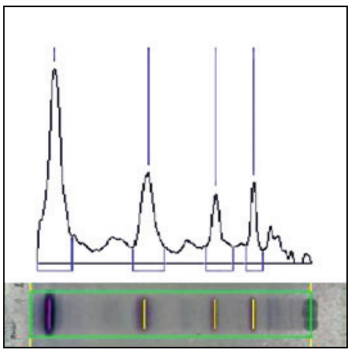
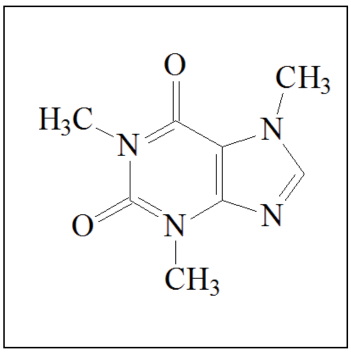








NEW SZÉCHENYI PLAN

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Content

Introduction

Short description of the digital learning material:
Pharmacognosy covers general aspects of medicinal plants (such as industrial applications, research, cultivation and cultivars, gene technology, critical evaluation of holistic medicine and homeopathy, possibilities of phytotherapy) and discusses the chemical composition and other qualitative characteristics, as well as the most important areas of usage and pharmacology of herbal drugs and drug fractions such as essential oils.

Today many people purchase medicinal plants and herbal products to prevent or cure diseases. Therefore specialists (physicians and pharmacists) should become acquainted with medicinal plants and drugs that are used in pharmacotherapy (especially in phytotherapy) both in Hungary and abroad. Our pharmacy students are required to recognize the most important drugs that are traded and/or imported in Hungary and are official in the Hungarian and European Pharmacopoeias. Pharmacognosy 2 digital learning material contains the most important medicinal plants and their drugs which are characterized according to their active compounds, usage, dosage, interactions with other drugs and side-effects. Drugs containing sugars and/or mucilage and fatty oils are introduced in the Pharmacognosy 1 digital learning material. Hopefully, this teaching supplement will be a useful reference text for medical doctors, pharmacists, students and teachers of pharmacognosy, herbalists, botanists, natural product chemists and pharmacologists who require information on medicinal plants.

Notice: Medicines or products containing medicinal plants should only be taken under medical supervision or according to the manufacturer's direction. The authors and the publisher cannot accept any liability for any adverse effects caused by applying the plants, drugs or products metioned in this teaching supplement.

Keywords:
pharmacognosy, medicinal plant, secondary metabolites, herbal drugs, phytotherapy

Photos:
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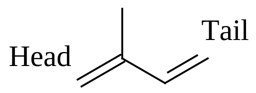
Chapter 1

Drugs containing monoterpenes, essential oils

1.1 Terpenoids

- They are secondary metabolites, approx. 20,000 terpenoids are known.
- They are made up by isoprene units (Figure 1.1), which have C_5H_8 molecular formula.
- The isoprene units may be linked together head to tail or tail to tail.
- The different terpenoid groups can be seen in Table 1.1.



2-methyl-1,3-butadiene
(Isoprene)

Figure 1.1
The chemical structure of isoprene

Table 1.1 Groups of Terpenoids

Name	*Number of isoprene units*	*Structure*
MONOTERPENES	2	$2 \times C_5H_8$
SESQUITERPENES	3	$3 \times C_5H_8$
DITERPENOIDS	4	$4 \times C_5H_8$
TRITERPENES	6	$6 \times C_5H_8$
TETRATERPENES, CAROTENOIDS *	8 8	$8 \times C_5H_8$ * $C_{40}H_{56}$
POLYTERPENOIDS	n	$n \times C_5H_8$

In essential oils terpenes may occur as alcohols (menthol), ethers (cineole), ketones (carvone), etc. The most characteristic compounds of essential oils can be found in Table 1.2.

Table 1.2 Composition of essential oils

Common name	*Botanical name*	*Important constituents*
Monoterpenes or sesquiterpenes		
Juniper	*Juniperus communis*	Terpenes (pinene); sesquiterpene (cadinene)
Alcohols		
Coriander	*Coriandrum sativum*	Linalool (65-80%)
Sandalwood	*Santalum album*	Santalol (sesquiterpene alcohol)
Esters		
Lavender	*Lavandula officinalis*	Linalyl acetate
Peppermint	*Mentha piperita*	Menthyl acetate (4-9%)
Aldehydes		
Cinnamon bark	*Cinnamomum verum*	Cinnamic aldehyde (60-75%)
Lemon	*Citrus limon*	Citral (3.5%)
Ketones		
Caraway	*Carum carvi*	Carvone (60%)
Sage	*Salvia officinalis*	Thujone (50%)
Phenols		
Thyme	*Thymus vulgaris*	Thymol (30%)
Ethers		
Anise and Star-anise	*Pimpinella anisum* and *Illicium verum*	Anethole (80%)
Eucalyptus	*Eucalyptus globulus*	Cineole (70%)
Parsley	*Petroselinum sativum*	Apiole (dimethoxysafrole)
Nutmeg	*Myristica fragrans*	Myristicin (methoxysafrole)
Peroxides		
Chenopodium	*Chenopodium ambrosioides* var. *anthelmintica*	Ascaridole (60-70%)

Monoterpenes can be classified into three groups: **1.** acyclic monoterpenes (e.g. geraniol, nerol, linalool, citronellol), **2.** monocyclic monoterpenes (e.g. menthol, thymol), **3.** bicyclic monoterpenes (e.g. α- and β-pinene, α-thujone).

Monoterpenes are mostly produced in different essential oils. Volatile compounds are secreted by special glandular cells located within the tissues or at the surface of leaves, flowers, fruits, and seeds. Terpenes of resins (when dissolved in essential oils they are called balsams) or oils are located in excretion or resin channels of the bark or wood of stems or roots.

Properties of essential oils

- Essential oils are mixtures of monoterpenes, sesquiterpenes, and/or phenylpropane derivatives. Their components are mostly liquids. The odour and taste of volatile oils is mainly determined by their oxygenated compounds, which are to some extent soluble in water (e.g. rose water, orange-flower water), but more soluble in alcohol. Many oils are terpenoid in origin. Fewer oils such as those of cinnamon or clove contain principally aromatic (benzene) derivatives together with the terpenes.
- The boiling points vary from 140 °C – 180 °C (monoterpenes) to 240 °C (sesquiterpenes).
- They consist of 5-200 components. The most characteristic compounds in the oil are called the main components), while additional components are present in lower amounts.
- They have characteristic smell and colour (colourless, yellow, green, blue).
- They are secreted in oil cells, in secretion ducts or cavities or in glandular hairs. They are often associated with other substances such as gums and resins.
- They can become oxidized (if exposed to light and O_2 – resinification); they cannot be dissolved in water but are soluble in organic solvents (chloroform, toluol, hexane).
- The most important plant families with plants accumulating essential oil: *Lamiaceae, Apiaceae, Myrtaceae, Rutaceae, Asteraceae, Lauraceae*
- Chemotypes: the same plant species can produce essential oils with different chemical components when grown in various conditions. For example, the common herb *Thymus vulgaris* L. produces several oils for medicinal use, depending upon the soil, climate and altitude in which it is cultivated. The environmental factors (climate, type of soil, etc.) and genetic factors can influence the composition of essential oils.
- Storage: Essential oils should be stored in a well-filled, airtight container, protected from light at a temperature not exceeding 25 °C. They are inflammable materials.
- Nomenclature: in the Ph. Eur. – e.g. *Anisi aetheroleum, Anise oil*

1.2 Drugs

Menthae piperitae folium and Menthae piperitae aetheroleum

Plant

Mentha x piperita (L.) Huds. - Peppermint (Lamiaceae)

Mentha x *piperita* is, as implied by its botanical name, a hybrid species from two parents, *M. spicata* (2n = 36 or 48) and *M. aquatica* (2n = 96). The European and American oil are derived to a large extent from the two varieties *M. piperita* var. *vulgaris* Sole ('black mint') and *M. piperita* var. *officinalis* Sole ('white mint'), respectively. The plant is cultivated all over the world.

Figure 1.2
Peppermint (*Mentha x piperita* (L.) Huds.)

Drugs

Menthae piperitae folium (Peppermint leaf, Ph. Eur.), Menthae piperitae aetheroleum (Peppermint oil, Ph. Eur.)

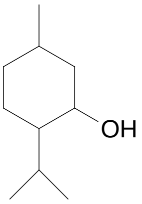
Peppermint leaf consists of the whole or cut dried leaves of *Mentha* x *piperita* L. The whole drug contains not less than 12 ml/kg of essential oil. The cut drug contains not less than 9 ml/kg of essential oil. Peppermint oil is obtained by steam distillation from the fresh overground parts of the flowering plant of *Mentha* x *piperita*.

Figure 1.3
Menthae piperitae folium (Peppermint leaf)

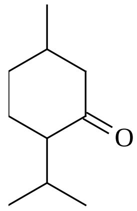
Constituents

The main active component is *essential oil* (1-3 %), of which the principal constituent is usually menthol (35-55%) (Figure 1.4), together with menthon (10-35%) and menthyl acetate. Small amounts of sesquiterpenes occur in the oil, notably viridoflorol. Various *flavonoids* are present including luteolin and its 7-glycoside, rutin, hesperidin and highly oxygenated flavones. Other constituents include *phenolic acids* and small amounts of triterpenes.

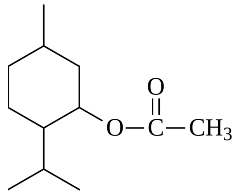
Figure 1.4
Menthol



menthol



menthon



mentyl acetate

Figure 1.5-7
The structure of menthol, menthon and mentyl acetate

Uses

Peppermint leaf is used in the symptomatic treatment of digestive disorders such as dyspepsia, flatulence and gastritis, although no clinical data are available in support of these indications. It has spasmolytic, cholagogue, carminative (in tea) and mild anti-emetic (apply on sugar cube) effects. Peppermint leaf extract and the essential oil are used in external products, e.g. in ointment against itching and in toothpaste. Other uses: in food industry (spice, liqueur, soft drink).

Dosage

Adults: As an infusion 1.5-3 g of the drug in 150-200 ml of water, three times daily. Tincture (1:5, 45% ethanol), 2-3 ml, three times daily. As a cholagogue: 2-4 drop essential oil (EO) on sugar cube. For external use: in ointment - 1-2 % EO content.

Elderly: Dose as for adults.

Children from 4 years of age, daily dose as infusion only: 4-10 years – 3-5 g, 10-16 years – 3-6 g.

Special warnings and precautions for use

Do not use both the drug and EO in infants, babies and little children (until 7 years) because apnoea, collapse of lung and cardiac arrest may occur.

Lavandulae flos and Lavandulae aetheroleum

Plant

Lavandula angustifolia Mill. – Lavender (Lamiaceae)

The plant is native to South-Europe, in Hungary it is cultivated (Tihany, Pannonhalma). France is the principal producer.

Figure 1.8
Lavender (*Lavandula angustifolia* Mill.)

Drugs

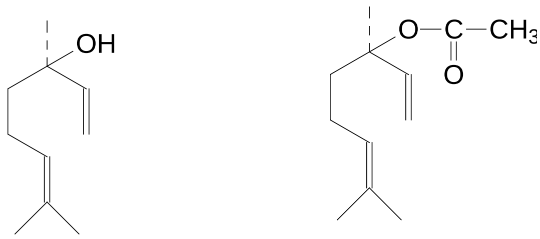
Lavandulae flos (Lavender flower, Ph. Eur.), *Lavandulae aetheroleum* (Lavender oil, Ph. Eur.)

Lavender flower consists of the dried flowers of *Lavandula angustifolia* Mill. (syn. *L. officinalis* Chaix). It contains not less than 13 ml/kg of essential oil, calculated with reference to the dried drug. Lavender oil is obtained by steam distillation from the fresh flowers of *L. angustifolia*.

Figure 1.9
Lavandulae flos (Lavender flower)

Constituents

The characteristic constituents include 1-3% of essential oil, the main components of which are linalool (20-45%), linalyl acetate (25-46%), while other components include terpinene-4-ol, limonene, cineole, camphor, lavandulyl acetate and lavandulol. The flower contains other constituents such as coumarin derivatives, flavonoids, triterpenes and “Labiatae tannin” (rosmarinic acid).



linalool linalyl acetate

Figure 1.10-11
The structure of linalool and linalyl acetate

Uses

Lavender flower can treat the symptoms of mood disturbances such as restlessness, agitation, insomnia and functional abdominal complaints. The flower and oil have mild sedative effect. Topically the oil is used for treating rheumatic pain, in ointments to mask disagreeable odors. Other uses: perfumery, aromatherapy, inhalation, insect repellent (moth).

Dosage

Internal use

Adults and children over 12 years of age: As an infusion 0.8-1.6 g of the drug in 150-200 ml of water, three times daily. Tincture (1:5, 50% ethanol), 60 drops daily. Oil: 1-4 drops (approx. 20-80 mg) on a sugar cube. *Elderly*: Dose as for adults.

Children up to 12 years of age: An infusion of approx. 0.4-1.6 g of the flower.

External use

Adults and children over 12 years of age: As a bath additive – lavender flower, 20-100 g to 20 litres of water; lavender oil, 6 drops per bath. For inhalation – several drops of the oil or 2-20% of the oil in a nebulizer. *Elderly*: Dose as for adults.

Children up to 12 years of age: As a bath additive – lavender flower, 10-100 g to 20 litres of water. As inhalation – 3 drops of a 1:10 dilution of the oil. The flowers are also used traditionally in bags for inhalation by children.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Melissae folium

Plant

Melissa officinalis L. – Lemon balm/Melissa (Lamiaceae)

Plant is native to Europe (South-West part), and it is cultivated in Hungary.

Figure 1.12
Melissa (*Melissa officinalis* L.)

Drug

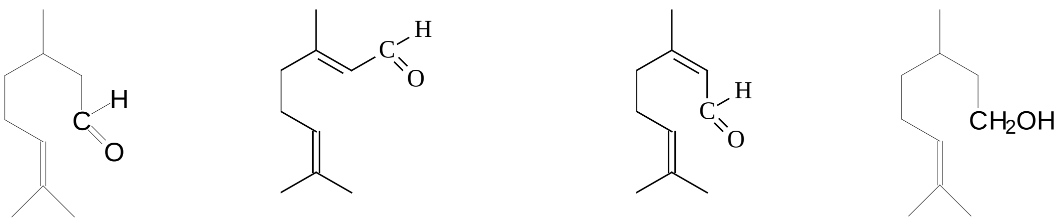
Melissae folium (Melissa leaf, Ph. Eur.)

Melissa leaf consists of the dried leaves of *Melissa officinalis* L. It contains not less than 4.0% of total hydroxycinnamic derivatives expressed as rosmarinic acid, calculated with reference to the dried drug. Fresh material may be used provided that when dried it complies with the monograph of the European Pharmacopoeia.

Figure 1.13
Melissa (*Melissa officinalis* L.)

Constituents

The main constituents are: essential oil (0.05-0.3%) containing monoterpenoid aldehydes, mainly geranial (citral a), neral (citral b), citronellal, citronellol and an alcohol (geraniol); flavonoids including glycosides of luteolin, quercetin, apigenin and kaempferol, “Labiatae tannin” (rosmarinic acid), caffeic acid, chlorogenic acid, triterpenoids (ursolic and oleanolic acids). Because of the low amount of the essential oil content, the oil is adulterated with cheaper lemon-type oils.



citronellal

geranial = citral a
E-isomer of citral

neral = citral b
Z-isomer of citral

citronellol

Figure 1.14-17
The structure of geranial (citral a), neral (citral b), citronellal and citronellol

Uses

Therapeutic indications of Melissa leaf are: restlessness and irritability; symptomatic treatment of digestive disorders such as minor spasms. It has sedative, spasmolytic and antiviral activity. The drug can be used in pediatrics. Externaly Melissa is used for treating *Herpes labialis* (cold sores). The essential oil is insect repellent.

Dosage

Internal use

2-3 g of the drug as an infusion, two to three times daily. Tincture (1:5 in 45% ethanol), 2-6 ml three times daily.

External use

Cream containing 1% of an aqueous extract (70:1) two to four times daily.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Thymi herba

Plants

Thymus vulgaris L. and *T. zygis* L. – Thyme and Spanish thyme (Lamiaceae)

Thyme is native to the Mediterranean countries, and it is cultivated in Hungary.

Figure 1.18
Thyme (*Thymus vulgaris* L.)

Drug

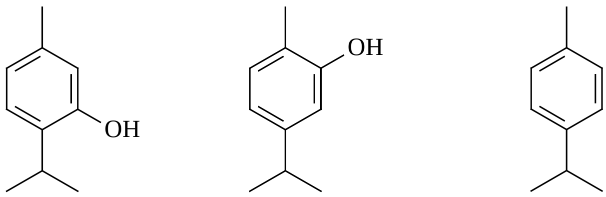
Thymi herba (Thyme, Ph. Eur.), *Thymi aetheroleum* (Thyme oil, Ph. Eur.)

Thyme consists of the whole leaves and flowers separated from the prevoiusly dried stems of *Thymus vulgaris* L. or *T. zygis* L. or a mixture of both species. It contains not less than 12 ml/kg of essential oil, of which not less than 40% is thymol and carvacrol, calculated with reference to the anhydrous drug.

Figure 1.19
Thymi herba (Thyme)

Constituents

Essential oil (1.5%) contains phenols (thymol, carvacrol) and terpenoids (*p*-cymene). Other constituents include flavonoids (e.g. thymonin, cirsilineol and 8-methoxycirsilineol), „Labiatae tannin" (rosmarinic acid), caffeic acid, triterpenoids, long-chain saturated hydrocarbons and aliphatic aldehydes, and an arabinogalactan.



thymol carvacrol *p*-cymene

Figure 1.20-22
The structure of thymol, carvacrol and p-cymene

Uses

Thyme can be used for treating catarrhs of the upper respiratory tract, bronchial catarrh and in the supportive treatment of pertussis. It has expectorant, antitussive, antibacterial, antiseptic and appetizer activity. Other uses: spice, perfumery, liqueur industry.

Dosage

Internal use

Adults and children from 1 year: 1-2 g of dried herb, or the equivalent amount of fresh herb, as an infusion several times a day. Tincture (1:10, 70% ethanol) – 40 drops up to three times daily. Topical use: A 5% infusion as a gargle or mouth-wash. The essential oil is a dermal and mucous membrane irritant, therefore, hypersensitivity reactions may develop.

Children up to 1 year: 0.5-1 g.

Undesirable effects

In very rare cases hypersensitivity reactions have been reported.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Serpylli herba

Plant

Thymus serpyllum L. – Wild thyme (Lamiaceae)

The plant is native to Europe and North Africa. In Hungary it grows wild (on rocky ground).

Figure 1.23
Wild thyme (*Thymus serpyllum* L.)

Drug

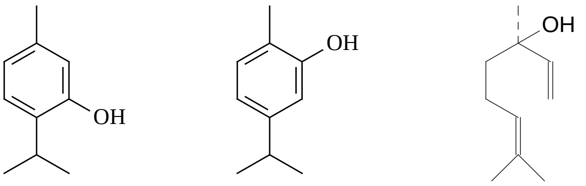
Serpylli herba (Wild thyme, Ph. Eur.)

Wild thyme consists of the whole or cut, dried, flowering aerial parts of *Thymus serpyllum* L. s.l. It contains minimum 3.0 ml/kg of essential oil, calculated with reference to the dried drug.

Figure 1.24
Serpylli herba (Wild thyme)

Constituents

The characteristic constituents of the drug include 0.1-0.6% of essential oil containing thymol, carvacrol and linalool, flavonoids, "Labiatae tannin" (rosmarinic acid) and caffeic acid. The volatile oil of *T. serpyllum* contains more linalool and *p*-cymene than *T. vulgaris*.



thymol carvacrol linalool

Figure 1.25-27
The structure of thymol, carvacrol and p-cymene

Uses and Dosage

See Thyme

Origani herba

Plants

Origanum onites L. (Cyprian), *O. vulgare* subsp. *hirtum* (Link) Ietsw. (Greek) - Oregano (Lamiaceae)

Plants are native to Mediterranean countries, including Cyprus.

Figure 1.28
Oregano (*O. vulgare* L.)

Drug

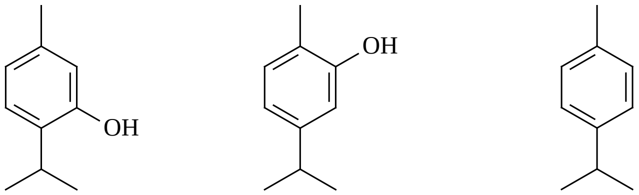
Origani herba (Oregano, Ph. Eur.)

Oregano consists of the dried leaves and flowers separated from the stems of *Origanum onites* L. or *Origanum vulgare* L. subsp. *hirtum* (Link) Ietsw., or a mixture of both species. It contains minimum 25 ml/kg of essential oil and minimum 1.5 per cent of carvacrol and thymol, calculated with reference to the dried drug.

Figure 1.29
Origani herba (Oregano)

Constituents

The characteristic constituents include 1.0 % essential oil, the main components of which are thymol, carvacrol and *p*-cymene. Other constituents are: flavonoids, “Labiatae tannin” (rosmarinic acid), ursolic acid.



thymol carvacrol *p*-cymene

Figure 1.30-32
The structure of thymol, carvacrol and p-cymene

Uses

Oregano can be used internally for treating acute bronchitis and laryngitis. It has expectorant, antitussive, antibacterial, antiseptic and appetizer effects. Externally the drug combined with chamomille can be used for treating wounds. Oregano is a popular spice.

Dosage

Internal use

Adults: As an infusion 3-6 g of the drug in 150-200 ml of water, three times daily.

Contra-indication

Thymol is a skin and mucous membrane irritant, therefore hypersensitivity reactions may develop (its essential oil must not be used in children under 2 years of age).

Saturejae herba and Saturejae aetheroleum

Plant

Satureja hortensis L. – Savory (Lamiaceae)

Plant is native to Mediterranean countries and in Hungary it is cultivated.

Drug

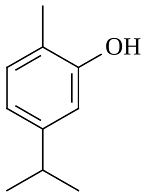
Saturejae herba (= folium) (Savory), Saturejae aetheroleum (Savory oil)

Saturejae herba consists of the dried leaves and flowers of *Satureja hortensis* L. It contains essential oil, which is obtained by steam distillation.

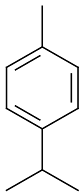
Figure 1.33
Saturejae herba (Savory)

Constituents

Savory contains approx. 0.3-2 % essential oil, the main components of which are carvacrol and *p*-cymene. Other constituents are „Labiatae tannin” (rosmarinic acid) and ursolic acid.



carvacrol



p-cymene

Figure 1.34-35
The structure of thymol, carvacrol and p-cymene

Uses

Savory can be used internally in case of gastrointestinal problems. The drug has appetizer, expectorant, stomachic and carminative effects. Other uses: spice, perfumery.

Dosage

Internal use

Adults: As an infusion 1-2 g of the druf in 150-200 ml of water, three times daily.

Majoranae herba

Plant

Origanum majorana L. - Sweet marjoram (Lamiaceae)

Plant is native to Mediterranean countries and in Hungary it is cultivated.

Drug

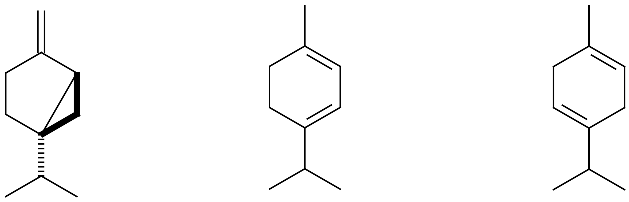
Majoranae herba (Sweet marjoram), *Majoranae aetheroleum* (Sweet marjoram oil)

Sweet marjoram consists of the dried leaves and flowers of *Origanum majorana* L. It contains essential oil, which is obtained by steam distillation from the leaves.

Figure 1.36
Majoranae herba (Sweet marjoram)

Constituents

The characteristic constituents include 0.5-1.3 % essential oil, which contains α- and γ-terpinene and sabinene as the main components. Other constituents are: „Labiatae tannin" (rosmarinic acid), chlorogenic acid, caffeic acid and flavonoids.



sabinene α-terpinene γ-terpinene

Figure 1.37-39
The structure of α- and γ-terpinene and sabinene

Uses

Sweet marjoram can be used both internally and externally. It has appetizer and carminative effects. It can increase the gastric juice secretion. In ointment the drug and its essential oil can be used for treating obstructed nose (in case of cold). Other uses: spice, perfumery

Dosage

Internal use

Adults and children over 12 years of age: As an infusion 1-2 g of the drug in 150-200 ml of water, two times a day.

External use

Adults and children over 12 years of age: In ointment 5% EO content must be applied.

Do not use internally for prolonged time (because of sabinene content), and do not use the ointment externally for infants and babies.

In addition to being commonly used in cooking, marjoram has a long history of medicinal use, by the Greeks as an antidote to poisoning and snake venom, by the Romans for stomach disorders and more recently for digestive and sedative properties. However, the oil is not suitable for use by pregnant women.

Hyssopi herba

Plant

Hyssopus officinalis L. – Hyssop (Lamiaceae)

Plant is native to Mediterranean countries and in Hungary it is cultivated.

Figure 1.40
Hyssop (*Hyssopus officinalis* L.)

Drugs

Hyssopi herba (Hyssop), Hyssopi aetheroleum (Hyssop oil)

Hyssop consists of the dried leaves and flowers of *Hyssopus officinalis* L. It contains essential oil, which is obtained by steam distillation.

Figure 1.41
Hyssopi herba (Hyssop)

Constituents

The characteristic constituents include 0.3-1.0% essential oil, which contains α- and β-pinene as the main components. Other constituents are: „Labiatae tannin" (rosmarinic acid), triterpenoids, flavonoids and diterpene (marrubiin).

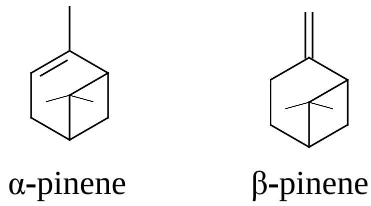


Figure 1.42-43
The structure of α- and β-pinene

Uses

Hyssop can be used both internally and externally. It has appetizer, diuretic and expectorant effects. It can increase the gastric juice secretion. The drug extract has anti-perspirant activity in case of external use. Other uses: spice, perfumery.

Dosage

Internal use

Adults and children over 12 years of age: As an infusion 1-2 g of the drug in 150-200 ml of water, three times a day.

Special warnings and precautions for use

Hyssop essential oil: it readily causes epileptiform convulsions, increases blood pressure, therefore, it should be used with caution.

Salviae officinalis folium

Plant

Salvia officinalis L. – Sage (Lamiaceae)

Sage is native to Mediterranean areas and cultivated world-wide.

Figure 1.44
Sage (*Salvia officinalis* L.)

Drug

Salviae officinalis folium (Sage leaf, Ph. Eur.)

Sage leaf consists of the whole or cut dried leaves of *Salvia officinalis* L. The whole drug contains not less than 15 ml/kg of essential oil and the cut drug not less than 10 ml/kg of essential oil, both calculated with reference to the anhydrous drug.

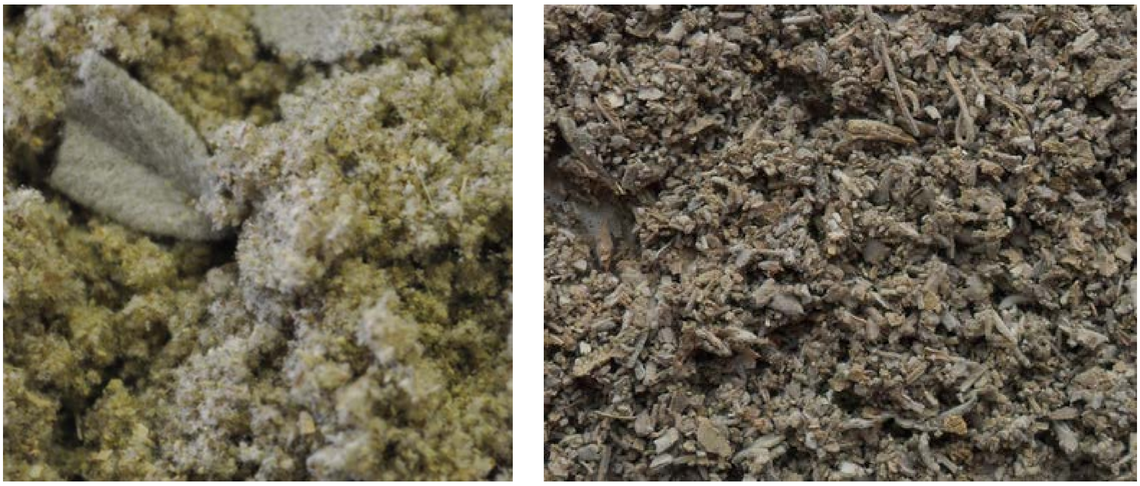
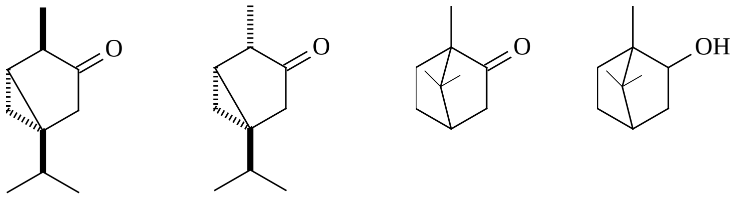


Figure 1.45
Salviae officinalis folium (Sage leaf)

Constituents

The characteristic constituents include 1.5-2.5 % essential oil containing monoterpenes such as α- and β-thujone (up to 63%), camphor, borneol and 1,8-cineole. Other constituents are: „Labiatae tannin" (rosmarinic acid), diterpenes (carnosol), flavonoids (e.g. 5-methoxysalvigenin) and triterpenoids (ursolic and oleanolic acids and their derivatives).



α-thujone β-thujone camphor borneol

Figure 1.46-49
The structure of α- and β-thujone, camphor and borneol

Uses

Sage can be used for treating inflammations and infections of the mouth and throat such as stomatitis, gingivitis and pharyngitis; as well as hyperhidrosis.

Dosage

Topical use

An infusion of 3 g of the drug in 150 ml of water as a mouthwash or gargle.

Oral use (in hyperhidrosis)

Tincture: (1:10) in 55% ethanol, 75 drops daily

Infusion: 1-1.5 g of dried herb in 150 ml of water, once or several times daily

Dry extract: 160 mg of dry aqueous extract corresponding to 880 mg of drug three times daily.

In hyperhidrosis, treatment for 2-4 weeks is recommended, using an aqueous preparation.

Caution is required with the use of alcoholic preparations because of the presence of thujone.

Sage essential oil readily causes epileptiform convulsions, increases blood pressure, therefore, it must be used with caution.

Pregnancy and lactation

Given the potential toxicity of some constituents of the essential oil, the use of sage leaf is not recommended during pregnancy or lactation.

Rosmarini folium and Rosmarini aetheroleum

Plant

Rosmarinus officinalis L. – Rosemary (Lamiaceae)

Rosemary is native to Mediterranean areas and cultivated world-wide. The oil is produced principally in Spain and North Africa.

Figure 1.50
Rosemary (*Rosmarinus officinalis* L.)

Drug

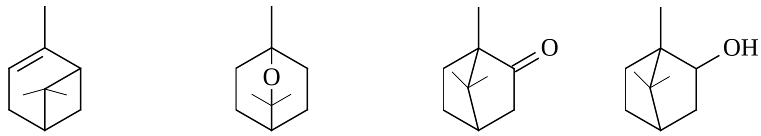
Rosmarini folium (Rosemary leaf, Ph. Eur.), *Rosmarini aetheroleum* (Rosemary oil, Ph. Eur.)

Rosemary leaf consists of the whole, dried leaves of *Rosmarinus officinalis* L. It contains not less than 12 ml/kg of essential oil, and not less than 3% of total hydroxycinnamic derivatives expressed as rosmarinic acid, both calculated with respect to the anhydrous drug.

Figure 1.51
Rosmarini folium (Rosemary leaf)

Constituents

The characteristic constituents include 1.0-2.5% essential oil containing 1,8-cineole, borneol, camphor, α-pinene, bornyl acetate. The composition of the oil may vary according to the chemotype or other factors. Further constituents are phenolic diterpenes such as carnosol (up to 4.6%), carnosolic acid, rosmanol, isorosmanol, „Labiatae tannin" (rosmarinic acid), triterpene alcohols (α- and β-amyrin), and flavonoids (e.g. nepetin, nepitrin).



α-pinene 1,8-cineole (= eucaliptol) camphor borneol

Figure 1.52-55
The structure of 1,8-cineole, borneol, camphor and α-pinene

Uses

Rosemary can be used both internally and externally. The internal therapeutic indication of the herb includes the improvement of hepatic and biliary function. It can be used in case of dyspeptic complaints. The herb has cholagogue, stomachic, carminative and spasmolytic effects. The drugs can be used externally in rheumatic conditions and peripheral circulatory disorders. It can promote wound healing. The plant and its oil have insect repellent activity. Other uses: spice, perfumery, liqueur industry.

Dosage

Internal use

Adults: Infusion - 2-4 g of rosemary leaf daily.

Fluid extract – 1:1, 45% ethanol V/V, 1.5-3 ml daily

Tincture – 1:5, 70% ethanol, 3-8.5 ml daily

External use

Adults: Ethanolic extract (1:20)

Essential oil (2% V/V) in ethanol, as an antiseptic

1 litre of a decoction (1:20, 50 g) added to bath water (twice weekly)

In ointment: 1-2% essential oil content

Special warnings and precautions for use

Rosemary essential oil readily causes epileptiform convulsions, increases blood pressure, therefore it should be used with caution. Hot baths containing rosemary preparations should be avoided by patients with large open wounds, skin lesions, feverish conditions or acute inflammation, severe circulatory disorders or hypertension. Contact dermatitis of the hands, forearms and face was reported in a man working with an extract made from rosemary leaf. The diterpene carnosol was identified as the irritant by patch testing. Rosemary essential oil contains camphor, therefore it is not used in children under 7 years of age. Camphor can pass freely through the placenta.

Pregnancy and lactation

No data available. In accordance with general medical practice, rosemary leaf and essential oil should not be used medicinally during pregnancy and lactation without medical advice.

Rosae flos and Rosae aetheroleum

Plants

Rosa species (Rose), e.g. R. damascena, R. gallica, R. alba, R. centifolia (Rosaceae)

Rose spesies are widely cultivated all over the world, principally in Bulgaria, Turkey and Morocco.

Figure 1.56
Rose (*Rosa* species)

Drugs

Rosae flos (= petalum) (Rose flower), Rosae aetheroleum (Rose oil)

Oil of rose is a volatile oil obtained by distillation from the fresh flowers of different *Rosa* species. The chief producing countries are Bulgaria, Turkey and Morocco, but smaller quantities are prepared elsewhere. Approximately 3000 parts of flowers yield only one part of oil. The oil is very expensive and very liable to adulteration.

Constituents

Rose petals contain approx. 0.2 % *essential oil* containing geraniol, citronellol and nerol. Although the monoterpene alcohols form about 70-75% of the oil, the odour is characteristically modified by the other constituents, such as sulphur containing compounds, thus no artificial mixture of the known constituents can be made to reproduce the odour of the natural oil. Other constituents are: tannins and flavonoids.

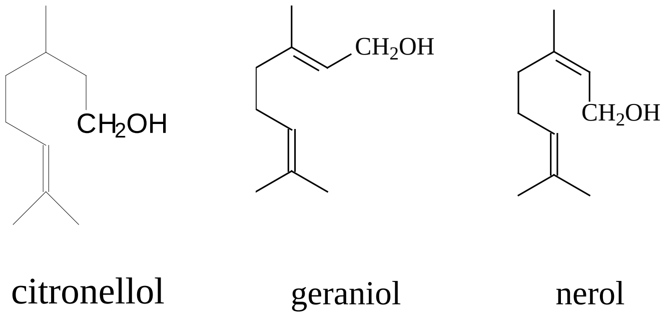


Figure 1.57-59
The structure of geraniol, citronellol and nerol

Uses

The rose extract has adstringent activity, and in floral water it is cleanser and has anti-inflammatory effect. Oil of rose is of great importance in perfumery and cosmetics.

Juniperi pseudo-fructus and Juniperi aetheroleum

Plant

Juniperus communis L. – Juniper (Cupressaceae)

Juniper is a circumpolar species. It can grow on chalky ground and sandy soil. The berries are collected in former Yugoslavia, Italy, Hungary, Poland, Sweden and other countries.

Figure 1.60
Juniper (*Juniperus communis* L.)

Drug

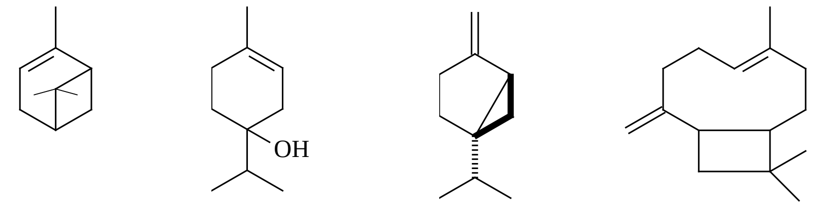
Juniperi pseudo-fructus (Juniper berry, Ph. Eur.), *Juniperi aetheroleum* (Juniper oil, Ph. Eur.)

Juniper berry consists of the dried ripe cone berry of *Juniperus communis* L. It contains not less than 10 ml/kg of essential oil, calculated with reference to the anhydrous drug. The essential oil can be obtained by steam distillation from the ripe cone berries.

Figure 1.61
Juniperi pseudo-fructus (Juniper berry)

Constituents

Essential oil (0.8-2%) of very variable composition depending on the source but consisting mainly of monoterpene hydrocarbons, principally α-pinen (24.1-55.4%). Other compounds of the essential oil are: sabinen, terpinen-4-ol, β-caryophyllene. Other constituents of the drug include condensed tannins, flavonoids, diterpene acids, aldehydes and alcohols, fatty alcohols and about 30% of glucose and fructose.



α-pinen terpinen-4-ol sabinene β-caryophyllene

Figure 1.62-65
The structure of α-pinen, sabinen, terpinen-4-ol and β-caryophyllene

Uses

Juniper has widely documented uses as a remedy to enhance the renal elimination of water and for dyspeptic complaints. It has strong diuretic and antiseptic effects. The ointment made from juniper extract can be used for treating rheumatic pain. In Slovenia an alcoholic drink (gin) is prepared from the berries.

Dosage

Internal use

Adults: 2-3 g of dried berries as an infusion in 150 ml of hot water, 3-4 times daily. Tincture (1:5 in ethanol 45%), 1-2 ml, 3 times daily.

External use

In bath: 30-50 g drug in 1.5 L hot water (filtrate can be used)

Special warnings, interactions

Juniper should not be used for more than 4 weeks without consulting a doctor. Acute or chronic inflammation of the kidney may occur. Juniper may influence glucose levels in patients with diabetes.

Pregnancy and lactation

Juniper should not be used during pregnancy and lactation. Abortifacient activity of juniper has been observed in rats after oral administration of a 50% ethanolic extract at 300 mg/kg bodyweight.

Camphor and Camphorae aetheroleum

Plant

Cinnamomum camphora (L.) Sieb. et Presl. – Camphor (Lauraceae)

The plant is widely grown in Taiwan, Japan and South China.

Drug

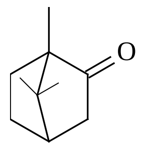
Camphorae aetheroleum (Camphor oil), Camphor (= prepared from the steam distillation of the wood)

The best yield of camphor is obtained from old trees. The wood is cut into chips and treated with steam, when a solid sublimate of camphor and liquid volatile oil pass into the receiver. Camphor can also be prepared from the leaves.

Figure 1.66
Camphor

Constituents

The wood contains essential oil with a high amount of camphor. In China 5 chemotypes can be distinguished: camphor-type, linalool-type, cineol-type, borneol-type and iso-nerolidol-type. Camphor has a characteristic odour and a pungent, aromatic taste, which is followed by a cold sensation.



camphor

Figure 1.67
The structure of camphor

Uses

Camphor is used externally as a rubefacient, and internally as a mild antiseptic and carminative. Oil of camphor tree is of great importance in perfumery and cosmetics.

Special warnings

Camphor should not be used in children under 7 years of age, because it can cause epileptiform convulsions, and passes freely through the placenta.

Eucalypti folium and Eucalypti aetheroleum

Plant

Eucalyptus globulus Labill. – Eucalyptus (Myrtaceae)

Eucalyptus is native to Australia, and is cultivated world-wide. Oil is produced in Portugal, South Africa, Spain, China, Brazil, Australia, India and Paraguay.

Figure 1.68
Eucalyptus (*Eucalyptus globulus* Labill.)

Drug

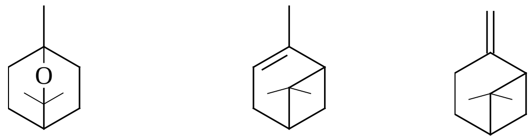
Eucalypti folium (Eucalyptus leaf, Ph. Eur.), *Eucalypti aetheroleum* (Eucalyptus oil, Ph. Eur.)

Eucalyptus leaf consists of the whole or cut dried leaves from older branches of *Eucalyptus globulus* Labill. The whole drug contains not less than 20 ml/kg of essential oil and the cut drug not less than 15 ml/kg of essential oil, both calculated with reference to the anhydrous drug. Eucalyptus oil is obtained by steam distillation and rectification from the fresh leaves or the fresh terminal branchlets of various species of *Eucalyptus* rich in 1,8-cineole. The species mainly used are *Eucalyptus globulus* Labill., *Eucalyptus polybractea* R.T. Baker and *Eucalyptus smithii* R.T. Baker.

Figure 1.69
Eucalypti folium (Eucalyptus leaf)

Constituents

Eucalyptus leaf contains 1-3.5 % essential oil. The rectified oil contains 70-90% of 1,8-cineole. Other components of the oil are α- and β-pinene, γ-terpinene, p-cymene. The leaf contains tannins, flavonoids and triterpenes.



1,8-cineole (= eucalyptol) α-pinene β-pinene

Figure 1.70-72
The structure of 1,8-cineole, α- and β-pinene

Uses

Eucalyptus leaf and oil can be used both internally and externally. In case of internal use the therapeutic indications include adjuvant treatment of chronic obstructive respiratory complaints (bronchitis) and bronchial asthma. It can be used for treating colds and catarrhs of the upper respiratory tract. It has expectorant and antiseptic activity.

It is taken internally in the form of mixtures, lozenges and pastilles, and by inhalation; while externally it is applied in ointments. Externally it can relieve the rheumatic complaints.

Dosage (of the oil)

Internal use

0.05-0.2 ml per dose; in capsules: 100-200 mg, 2-5 times daily

External use

By inhalation: 12 drops per 150 ml of boiling water, or a 1.5% V/V solution prepared from 1 tablespoon (15 ml) per litre of warm water, treatment may be repeated up to three times daily.

As a liniment: containing 25% V/V of oil.

As an ointment: containing 1.3% V/m, for adults and children over 12 years: to be applied as a thick layer, up to three times daily.

As a lozenge: 0.2-15 mg dissolved slowly in the mouth, repeated every 0.5-1 hour.

As a mouthwash: containing 0.9 mg/ml; 20 ml as a gargle twice daily.

Contra-indications, special warnings, interactions

Eucalyptus must not be used internally in cases of inflammation of the gastrointestinal tract or gall bladder, or when liver function is impaired. Eucalyptus oil and its preparations should not be applied to the face, especially the nose, of babies and little children. The oil induced hepatic microsomal enzyme activity in both *in vitro* and *in vivo* tests.

Pregnancy and lactation

Since human data are not available, eucalyptus should not be used during pregnancy and lactation without medical advice.

Carvi fructus

Plant

Carum carvi L. - Caraway (Apiaceae)

It occurs both wild and cultivated in central and northern Europe.

Drug

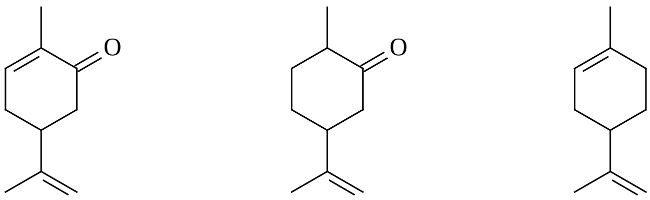
Carvi fructus (Caraway fruit, Ph. Eur.)

Caraway fruit consists of the whole, dry mericarp of *Carum carvi* L. It contains not less than 30 ml/kg of essential oil, calculated with reference to the anhydrous drug.

Figure 1.73
Carvi fructus (Caraway fruit)

Constituents

The characteristic constituent of caraway is essential oil (3-7 %). It consists of the ketone carvone and the monoterpene limonene with small quantities of dihydrocarvone, carveol and dihydrocarveol. It also contains 10-18% of fixed oil, of which the main components are petroselinic (30-43%), linoleic (34-37%), oleic (15-25%) and palmitic (4-5%) acids. Other constituents include about 20% of protein, 15% carbohydrates, phenolic acids, mainly caffeic acid, and traces of flavonoids (quercetin, kaempferol and their glycosides).



carvone   dihydrocarvone   limonene

Figure 1.74-76
The structure of carvone, limonene and dihydrocarvone

Uses

Caraway has carminative and antispasmodic effects, therefore it can be used for treating gastrointestinal problems, such as flatulence, bloating. The carminative and antispasmodic properties have been experimentally verified. It is a culinary herb, spice and liqueur-aroma. Caraway can also treat the flatulent colic of infants.

Dosage

Dried fruits – Internal use

Adults and children over 10 years of age: 1.5-6 g of caraway fruit daily. 1-5 g of caraway fruit, crushed directly before use, covered with 150 ml of boiling water and allowed to stand for 10-15 min. A cup of warm tea is taken 1-3 times daily.

Children from 4 to 10 years: 1-4 g daily

Children from 1 to 4 years: 1-2 g daily

Children up to 1 year: 1 g daily

Caraway oil for children – Internal use

Children above 4 years: 3-6 drops daily

Children from 1 to 4 years: 2-4 drops daily

Children up to 1 year: 1-2 drops daily

Caraway oil for children – External use (in case of flatulent colic)

10% in a carrier oil, for example olive oil

Contra-indication

Sensitivity to Apiaceae (Umbelliferae).

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy without medical advice.

Coriandri fructus and Coriandri aetheroleum

Plant

Coriandrum sativum L. var. vulgare Alef. -Coriander (Apiaceae)

It is indigenous to Italy, but is widely cultivated in the Netherlands, Central and Eastern Europe, the Mediterranean region (Morocco, Malta, Egypt), India, China and Banglades.

Drug

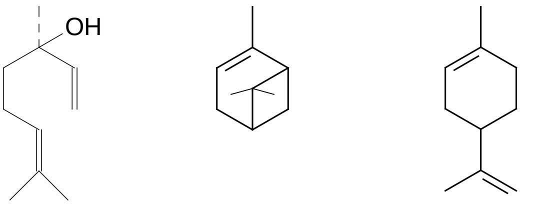
Coriandri fructus (Coriander fruit, Ph. Eur.), *Coriandri aetheroleum* (Coriander oil, Ph. Eur.)

Coriander consists of the dried cremocarp of *Coriandrum sativum* L. It contains not less than 3 ml/kg of essential oil, calculated with reference to the dried drug. Essential oil can be obtained by steam distillation from the fruits of *Coriandrum sativum* L. During ordinary storage of the fruits, the oil composition undergoes considerable alteration.

Figure 1.77
Coriandri fructus (Coriander fruit)

Constituents

The fruits contain 1.5-2.5% of essential oil. The main component of the oil is linalool (65-70%, depending on the source), and other components include α-pinene and limonene. Other constituents isolated from the fruits are coumarins, flavonoids and phenolic acids. The high content of fats (16-28%) and protein (11-17%) in the fruits make distillation residues suitable for animal feed.



linalool α-pinene limonene

Figure 1.78-80
The structure of linalool, α-pinene and limonene

Uses

Pharmaceutically coriander and its oil are used as a flavouring agent (muscat taste), carminative and spasmolytic. It is a culinary herb. The oil is also used in perfumery industry.

Dosage

Dried fruits – Internal use

Adults: 1 g in 200 ml hot water, 3 times daily.

Aurantii amari epicarpium et mesocarpium

Plant

Citrus aurantium L. subsp. *amara* Engl. **–** Bitter orange (Rutaceae)

Bitter orange is native to North India, South China, but is cultivated elsewhere. Sweet orange is more widely cultivated, than bitter orange.

Figure 1.81
Orange (*Citrus aurantium* L.)

Drugs

(in the Ph. Eur.)

1 *Aurantii amari epicarpium et mesocarpium* - Bitter-orange epicarp and mesocarp

Dried epicarp and mesocarp of the ripe fruit of *Citrus aurantium* L. ssp. *aurantium* (*C. aurantium* L. ssp. *amara* Engl.) partly freed from the white spongy tissue of the mesocarp and endocarp. *Content*: minimum 20 ml/kg of essential oil (anhydrous drug).

2 *Aurantii amari epicarpii et mesocarpii tinctura* - Bitter-orange-epicarp and mesocarp tincture

The tincture is produced from 1 part of the freshly powdered drug and 5 parts of *alcohol (70 per cent V/V/)* by an appropriate procedure.

3 *Aurantii amari flos* - Bitter-orange flower

It consists of the whole, dried, unopened flower of *Citrus aurantium* L. ssp. *aurantium* (*C. aurantium* L. ssp. *amara* Engl.). *Content*: minimum 8.0 per cent of total flavonoids, expressed as naringin (dried drug).

4 *Aurantii amari floris aetheroleum* - Bitter-orange-flower oil (Neroli oil)

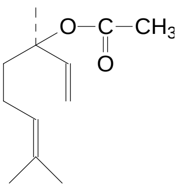
Bitter-orange-flower oil is obtained by steam distillation from the fresh flowers of *Citrus aurantium* L. subsp. *aurantium* (*C. aurantium* L. subsp. *amara* Engl.).

Petitgrain aetheroleum (Paraguay) – from the fruits (is not official)

Figure 1.82
Aurantii amari epicarpium et mesocarpium (Bitter-orange epicarp and mesocarp)

Constituents

Dried bitter orange peel contains not less than 2.5% of essential oil (linalyl acetate is the main component), vitamin C and flavonoid glycosides (hesperidin, neohesperidin).



linalyl acetate

Figure 1.83
Aurantii amari epicarpium et mesocarpium (Bitter-orange epicarp and mesocarp)

Uses

Bitter orange peel is used as a flavouring agent and as a bitter tonic. Its essential oil is used in the perfume industry (perfume, soaps).

Hesperidin in the soluble form functions as “vitamin P” (P = permeability). This molecule can reduce the permeability of capillary vessels.

Dr. Albert Szent-Györgyi had an important role in the discovery of Vitamin P.

Dosage

Single dose: 2 g

Contra-indications, special warnings

Patients with stomach and duodenal ulcer must not use the drug and its oil!

Coumarins have photosensitising effect in case of external use!

Aurantii dulcis aetheroleum

Plant

Citrus aurantium L. subsp. sinensis Engl. – Sweet orange (Rutaceae), (syn.: C. sinensis (L.) Osbeck., C. aurantium L. var. dulcis L.)

Sweet orange is native to India, China, the Mediterranean, and it is cultivated.

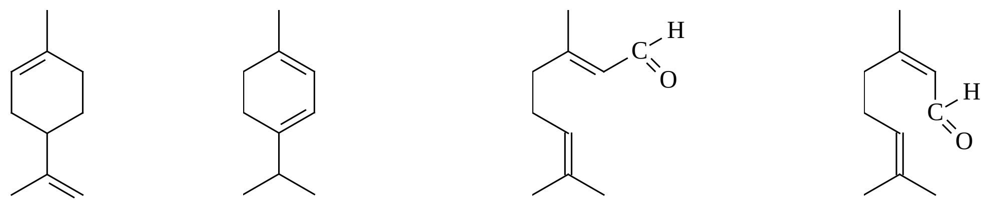
Drug

Aurantii dulcis aetheroleum (Sweet orange oil, Ph. Eur.)

Essential oil obtained without heating, by suitable mechanical squeezing from the fresh peel of the fruit of *Citrus sinensis* (L.) Osbeck (*Citrus aurantium* L. var. *dulcis* L.). A suitable antioxidant may be added. The peel of sweet orange is thinner than that of the bitter variety, its yellow colour is more pronounced and the taste is aromatic. As studied in Valencia orange peel, the colour originates from a complex mixture of carotenoids, the principal components being violeoxanthin (9-*cis*-violaxanthin), di-*cis*-violaxanthin and all-*trans*-violaxanthin together with a number of other carotenoids.

Constituents

Sweet orange peel contains 0.4-0.9 % essential oil. The main components of the oil are limonene, citral, neral, α-terpinene and sinensal. Other constituents include flavonoids (mainly naringenin) and carotenoids (e.g. 9-*cis*-violaxanthin).



limonene α-terpinene geranial = citral a *E*-isomer of citral neral = citral b *Z*-isomer of citral

Figure 1.84-87
The structure of limonene, citral, neral and α-terpinene

Uses

Sweet orange oil is used in the perfumery industry and as a seasoning material in the food industry. Brazil and USA are the largest producers of sweet orange oil.

Cardamom fruit and oil

Plant

Elettaria cardamomum White et Maton - Cardamom (Zingiberaceae)

Principal producers are Sri Lanka, southern India, Guatemala. Although wild plants are found in India and Sri Lanka, cardamoms are mainly obtained from cultivated plants.

Drug

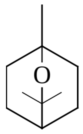
Cardamomi fructus (Cardamom fruit, Hungarian Pharmacopoeia VII.), *Cardamomi aetheroleum* (Cardamom oil)

Cardamom consists of the dried, nearly ripe fruits of *Elettaria cardamomum*. The seeds should be kept in the fruits until required for use. This prevents loss of essential oil and helps one to distinguish the fruits from those of *E. cardamomum* var. *major* (unofficial long wild native cardamom).

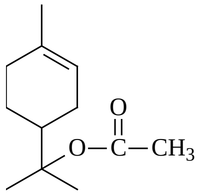
Figure 1.88
Cardamomi fructus (Cardamom fruit)

Constituents

Cardamom contains 1-4% essential oil. 1,8-cineole and terpinyl acetate are the main components of the essential oil. The essential oil composition varies according to the *Elettaria* species and varieties. Other constituents include starch (50%), fixed oil (1-10%) and calcium oxalate.



1,8-cineole
(= eucalyptol)



α-terpinyl acetate

Figure 1.89-90
The structure of 1,8-cineole and terpinyl acetate

Uses

Cardamom is used as a flavouring agent in curries and cakes and as a spice. The oil is applied in perfumery industry and in the manufacture of liqueurs. Pharmaceutically it has carminative effect and is used in tinctures.

Dosage

0.6-2 g seed/daily, 25 drops from the tincture to one glass of water.

Tanaceti herba

Plant

Tanacetum vulgare L. - Tansy (Asteraceae) (syn.: Chrysanthemum vulgare (L.) Bernh.)

Tansy is native to Europe and Asia. Tansy is used as an anthelminhtic in herbal medicine but its poisonous properties are also appreciated.

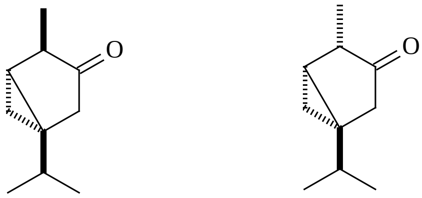
Figure 1.91
Tansy (*Tanacetum vulgare* L.)

Drug

Tanaceti herba (Tansy), Tanaceti aetheroleum (= Chrysanthemi aetheroleum, Tansy oil)

Constituents

It contains 0.5-1 % essential oil. Thujones are the main components of the oil. Several sesquiterpene lactones have been isolated from the flowers and shoot together with flavones. Numerous chemical races (originating from different geographical areas) are known.



α-thujone β-thujone

Figure 1.92-93
The structure of α- and β-thujone

Uses

Anthelminthic (consultation with doctor!)

Dosage

Pregnancy and lactation

Tansy and its essential oil must not be used during pregnancy or lactation.

Myrrha

Plant

Commiphora molmol (Nees) Engl. - Myrrh (Burseraceae)

The plant is native to north-east Africa and Arabia.

Drug

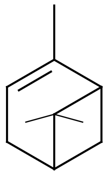
Myrrha (Myrrh, Ph. Eur.), *Myrrhae tinctura* (Myrrh tincture, Ph. Eur.)

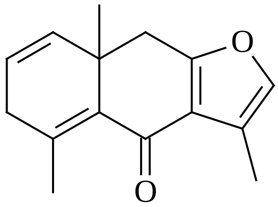
Myrrh consists of a gum-resin, which hardens in air, obtained by incision or produced by spontaneous exudation from the stem and branches of *Commiphora molmol* Engler and/or other species of *Commiphora*. Species other than *C. molmol* which may be acceptable sources of medicinal myrrh include *C. abyssinica* (Berg) Engl., and *C. schimperi* (Berg) Engl. The tincture is produced from 1 part of the drug and 5 parts of ethanol (90 per cent *V/V*) by a suitable procedure.

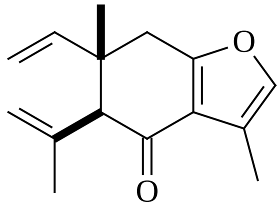
Constituents

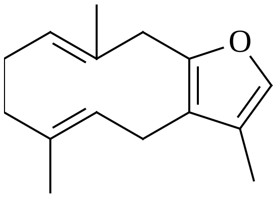
Myrrh can be separated into three components: essential oil (6-7%), resin (25-40%) and gum (30-60%). The main constituents of the essential oil are furanosesquiterpenes of various structural types including furanoeudesma-1,3-diene, furanoeudesma-1,4-diene-

6-one, curzerenone, furanodiene, together with sesquiterpenes such as α-copaene and elemene and monoterpene (α-pinene). Characteristic constituents of the resin are α-, β- and γ-commiphoric acids. The gum consists mainly of a proteoglycan, in which chains of alternating galactose and 4-O-methyl-glucuronic acid, and separate chains of arabinose, are attached to the protein through hydroxyproline links.


α-pinene


furanoeudesma-1,4-diene-6-one


curzerenone


furanodiene

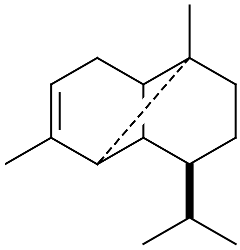

α-copaene

Figure 1.94-98
The structure of furanoeudesma-1,4-diene-6-one, curzerenone, furanodiene, α-copaene and α-pinene

Uses

Therapeutic indications of myrrh include topical treatment of gingivitis, stomatitis (aphthous ulcers), minor skin inflammations, minor wounds, supportive treatment for pharyngitis, tonsillitis.

Dosage

Adults and elderly: As a gargle or mouthwash, 1-5 ml of tincture (1:5, ethanol 90% V/V) in a glass of water several times daily. For use on skin, dab 2-3 times daily with diluted or undiluted tincture.

Children: as for adults except using only diluted tincture on skin.

Special warnings, undesirable effects

Because of alcohol content, a transient burning sensation on the skin may be experienced depending on the level of dilution of the tincture. Very rare cases of allergic contact dermatitis have been reported.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy without medical advice.

Orthosiphonis folium

Plant

Orthosiphon aristatus (Blume) Miq. – Java tea (Lamiaceae) (syn.: O. stamineus Benth., O. spicatus (Thunb.) Bak.)

The plant is native to China, east-Asia, Malaysia and Australia. In Java the native people use this plant against hypertension and as an antirheumatic drug.

Drug

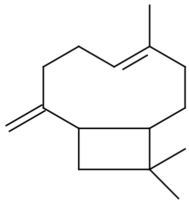
Orthosiphonis folium (Java Tea, Ph. Eur.)

Java tea consists of the fragmented, dried leaves and tops of stems of *Orthosiphon stamineus* Benth. (*O. aristatus* Miq.; *O. spicatus* Bak.). Content: minimum 0.05 per cent of sinensetin (dried drug).

Figure 1.99
Orthosiphonis folium (Java tea)

Constituents

Java tea contains 0.02-0.7% essential oil (the main component is β-caryophyllene). Other characteristic constituents include diterpenes, flavonoids (sinensetin), rosmarinic acid, up to 12% of minerals with a high proportion of potassium.



β-caryophyllene

Figure 1.100
The structure of β-caryophyllene

Uses

Therapeutic indications of the drug include the irrigation of the urinary tract, especially in cases of inflammation and renal gravel, and as an adjuvant in the treatment of bacterial infections of the urinary tract.

Dosage

Adults: An infusion of 2-3 g of dried material in 150 ml of water 2-3 times daily.

Special warnings

Java tea should not be used in patients with oedema due to impaired heart and kidney function.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy without medical advice.

Chapter 2
Essential oils

2.1 Description of essential oils

Definition of essential oils

Essential oils are extracted from plants through steam distillation or expression. They have complex composition. They evaporate completely at room temperature.

Uses of essential oils

1. Pharmaceutical industry: scenting of ointments, creams, seasoning materials
2. Holistic medicine/natural healing, phytotheraphy, aromatheraphy: in herbal medicines, dietary supplements, massage oils, bath oils
3. Cosmetic and perfumery industry
4. Food industry: flavours and essences (confectionery, liqueurs)
5. Plant protection: natural pesticides (against infections), preserving materials
6. Veterinary medicine: massage oils, products against respiratory diseases (in horses)

Fields of their safe applications/uses

- Treatment of infections caused by bacteria and fungi
- Odour control of hospital-wards, prevention of the spread of infections
- Treatment of inflammations in the mouth
- Treatment of respiratory diseases (e.g. pharyngitis, asthma, bronchitis, COPD)
- Treatment of gastrointestinal problems (cramps in the stomach and intestines)
- Treatment of locomotor disorders (e.g. rheuma)
- Treatment of diseases of the skin (e.g. acne, wounds)
- Treatment of respiratory symptoms of smokers
- Treatment of mild depression, anxiety, insomnia, irritability
- To increase the ability to concentrate, to pay attention to something
- To decrease the symptoms of migraine
- To decrease the complaints before or after giving birth/delivery (pain, anxiety, treatment/cleaning of perineal wounds)
- Palliative treatment of patients suffering from a tumor, and long-stay patients (against abscess, decubital ulcer)

For therapeutic purposes essential oils are administered by inhalation (e.g. eucalyptus oil), orally (e.g. peppermint oil), as gargles and mouthwashes (e.g. thyme oil) and transdermally (e.g. lavender oil, rosemary oil).

Definition of aromatherapy

Aromatherapy is a form of alternative medicine that uses volatile plant materials, known as essential oils, and other aromatic compounds for the purpose of altering a person's mind, mood, cognitive function or health.

Essential oils containing **a high amount** (25 -30%) **of ketones**, e.g. peppermint oil, and **phenols,** e.g. thymol, in the thyme oil, **must be used in low dose and for a short period only!**

Extraction techniques of essential oils

The most important extraction techniques of essential oils include distillation (steam or water), expression, solvent extraction, enfleurage and maceration.

Distillation

Distillation is the most commonly used method for the extraction of essential oils. There are two techniques of distillation: *water* and *steam*.

Water distillation

The distillation apparatus, commonly called a ‘still’, consists of a vessel for plant material and water, a condenser to cool and condense the vapour produced and a vessel for collection, or ‘receiver’.

Material from the appropriate part of the plant for extraction is immersed in water in the distillation vessel. This is then heated to boiling point and the steam (water vapour) carries the volatile oils. The water safeguards some components by preventing overheating as the temperature will not exceed 100 °C (the boiling point of water at normal pressure). However, distillation can be a long process and water may damage some other compounds.

Essential oils with a high percentage of esters can become *hydrolyzed* (hydrolysis is a chemical reaction of a substance with water) by contact with the hot water, which breaks them down to their constituent alcohols and carboxylic acids. E.g. in lavender, linalyl acetate can break down into linalool and acetic acid, so a short distillation time is favourable.

Steam distillation

In steam distillation, steam – which is water vapour – is passed through the plant material at high pressure. Constituents that are insoluble in the water but volatile enough to be driven off by the steam come over and are cooled, condensed and collected in the receiving vessel.

The resultant liquid is a mixture of immiscible oil and water, which separate.

Steam distillation is economical in processing large amounts of material, requiring little labour or complex extraction apparatus.

The aqueous (water) portions left over from initial distillation are called hydrosols or floral waters, e.g. lavender, rose. They have many uses alongside essential oils and are utilized in the skin care and perfumery industries.

Essential oils extracted by water or steam distillation need further purification, especially drying to remove water. Essential oils produced by distillation are limited to compounds with a maximum molecular weight of 225–250.

Expression

Expression is the use of a crushing, mechanically applied pressure to squeeze oils from plant material. It was originally done by hand but is now mechanized, with use of centrifugal separators. Expression is used almost exclusively for citrus fruits with oil glands in the outer rind of the fruit. E.g. bergamot and lemon esssential oils, which are very volatile owing to being rich in monoterpenes. Many of these would be lost in distillation because of the high temperatures. It is also a cheap method, using by-products from the juice industry.

Solvent extration

Aromatic plant material is placed into organic solvents such as acetone or hexane, which dissolve the oils. Other solvents used are methanol, ethanol, toluene and petroleum ether.

The materials that become dissolved include not only the essential oil but also natural waxes, resinous materials, chlorophyll and other pigments. Solvent is then recovered in a still at reduced pressure, which lowers the solvent’s boiling point and permits the use of gentle heat. The concentrated extract is not distilled but is retained in the vessel in a liquid state. When it is removed and cooled, the concentrated extract solidifies to a waxy consistency called a *concrete*, which is made up of approximately 50% odourless wax. The unwanted wax is removed by washing with alcohol, which extracts the essential oil. The alcohol mixture is then filtered and alcohol is removed by vacuum distillation. The final residue is called the *absolute*.

Enfleurage

Enfleurage is a method that has long tradition, producing a rather impure product. Thin layers of cold, odourless fat such as lard (from pig) are coated onto glass plates and the plant material is spread in layers onto the top of the fat.

When the fat is saturated, it is washed with hexane to dissolve the essential oil.

After removal of hexane, the residue is washed with alcohol and the resultant solution is evaporated to give purer essential oil, or more strictly an absolute.

The *true pomades* are products of enfleurage as they are the fragrance-saturated fat.

Enfleurage was used to extract oils from delicate petals. It is very labour intensive and can last up to three months.

Pharmacological effects and ways of administration of essential oils (with some examples)

1. **Expectorant, antibacterial:** anise, sweet fennel, thyme, peppermint, sweet orange, lemon, sage, pine, chamomile, cinnamon, eucalyptus
2. **Anti-inflammatory, inhalation, treating of mouth:** chamomile, sage, eucalyptus, cinnamon, thyme
3. **Appetizer:** anise, sweet flag (*Acorus*), sweet fennel, bitter orange, peppermint, cinnamon
4. **Cholagogue:** Acorus, fennel, lavender, peppermint
5. **Carminative:** anise, sweet fennel, fennel, coriander, basil
6. **Spasmolytic:** chamomile, fennel, peppermint, cinnamon, yarrow (*Achillea*)
7. **Diuretic:** lovage, parsley, juniper
8. **Increase local circulation:** rosemary, lavender, pine, lemon, juniper
9. **Against headache (in compress):** lemon, orange, pine, lavender
10. **Treatment of pollen allergy (dry inhalation):** peppermint, chamomile
11. **Air freshener:** lavender, cinnamon, eucalyptus, pine

When essential oils are used externally, they should be diluted in vegetable oils e.g. in sweet almond oil, avocado oil, jojoba or olive oil.

Special warnings, contra-indications

The following essential oils may not used for medicinal purposes or are used with some restriction after medical advice. These oils are not safe in case of aromatherapeutic application.

Peppermint oil

It should not be used in infants, babies and little children (until 7 years of age), because apnoea and collapse of lung or cardiac arrest may occur.

Thyme oil

It should not be used in little children (under 5 years of age) and patients with epilepsy or disease of the thyroid gland. Thyme oil is a dermal and mucous membrane irritant (thymol content).

Oregano oil

Because of thymol content this oil is a skin and mucous membrane irritant. It should not be used in children under 2 years of age.

Rosemary oil

This oil contains camphor, which can readily cause epileptiform convulsions. It should be used with caution (in oral dose).

Juniper oil

It should not be used during pregnancy and in patients with kidney disease. It has abortifacient activity and can enhance the inflammation in the kidney.

Camphor

It should not be used in children under 7 years of age, see peppermint. Epileptiform convulsions may occur. It can pass freely through the placenta.

Bitter orange oil

It should not be used orally in patients with gastric and duodenal ulcer. It has moderate phototoxic effect – if this oil is applied to the skin at a concentration over max. use level (1.4%), skin must not be exposed to sunlight or sunbed rays for 12 h.

Melissa oil

Skin sensitisation reaction possible; citral can cause a rise in ocular tension (oral use should be avoided in patients with glaucoma).

Lemon, Sweet orange oil

See bitter orange.

Eucalyptus oil

See camphor.

Cinnamon bark oil

Moderate dermal irritant, strong dermal sensitiser, moderate mucous membrane irritant; externally max. use level 0.1%!

Essential oils increasing blood pressure

- Rosemary
- Hyssop
- Cedar
- Common Sage (Dalmatian)
- Thyme

Essential oils causing epileptiform convulsions

- Sweet fennel
- Hyssop
- Camphor
- Common Sage (Dalmatian)
- Rosemary

Safe essential oils during pregnancy

In the first trimester essential oils must not be used! After the first trimester the following essential oils may be used after medical consultation: chamomile, roman chamomile, clary sage, ginger, lavender, neroli, rose, sandalwood.

Safe essential oils in babies and children

Chamomile, roman chamomile, lavender, clary sage. These oils may be used after medical consultation.

Essential oil (in the case of external use)

1-6 month: maximum 1%

6-24 month: 2%

2-10 years: 3%

over 10 years: 5%

Drugs

Melaleucae aetheroleum

Plant

Melaleuca alternifolia (Maiden et Betche) Cheel – Tea tree (Myrtaceae)

The plant is native to Australia. 3-6 m high shrub or tree. Australians use the oil against insect bites.

Drug

Melaleucae aetheroleum (Tea tree oil, Ph. Eur.)

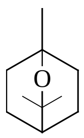
Essential oil obtained by steam distillation from the foliage and terminal branchlets of *Melaleuca alternifolia* (Maiden and Betch) Cheel, *M. linariifolia* Smith, *M. dissitiflora* F. Mueller and/or other species of *Melaleuca*.

Appearance of the essential oil

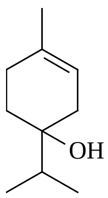
Clear, mobile, colourless to pale yellow liquid with a characteristic odour.

Constituents

2% essential oil. The major components of tea tree oil are the monoterpenes terpinen-4-ol (minimum 30%), γ-terpinene (10-28%) and 1,8-cineole (less than 15%).



1,8-cineole
(= eucalyptol)



terpinen-4-ol

Figure 2.1-2
The structure of terpinen-4-ol and 1,8-cineole

Characteristics

Antiseptic, antibacterial, antifungal, antiviral

Uses

Primary use

Skin care (mycosis of the legs, *Candida* infection, acne, tinea pedis, dandruff)

Other uses

Respiratory infections (cold, influenza, bronchitis), vaginal infections (trichomonal vaginitis, vaginal candidiasis and related cervivitis), cosmetic- and perfumery industry.

Dosage

External application: liquid or semi-solid preparations containing 5-10% m/m of tea tree oil. Higher concentrations have been used for certain conditions, e.g. tinea pedis (25-50% m/m). Female genital tract: depending on the indication, pessaries containing 200 mg of tea tree oil (approx. 10% in an oily vehicle) or tampons/douches containing solutions of 0.4-20% of the oil. Rarely it can cause allergy (contact dermatitis).

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy without medical advice.

Anisi aetheroleum (1) and Anisi stellati aetheroleum (2)

Plants

(1) *Pimpinella anisum* L. – Anise (Apiaceae), (2) *Illicium verum* Hook. – Star Anise (Illiciaceae)

P. anisum is native to the East-Mediterranean, and in Hungary it is cultivated. *I. verum* is native to China and Vietnam.

Drugs

(1) *Anisi aetheroleum* (Anise oil), (2) *Anisi stellati aetheroleum* (Star anise oil, Ph. Eur.)

(1) Essential oil obtained by steam distillation from the dry ripe fruits of *Pimpinella anisum* L. (2) Essential oil obtained by steam distillation from the dry ripe fruits of *Illicium verum* Hook.

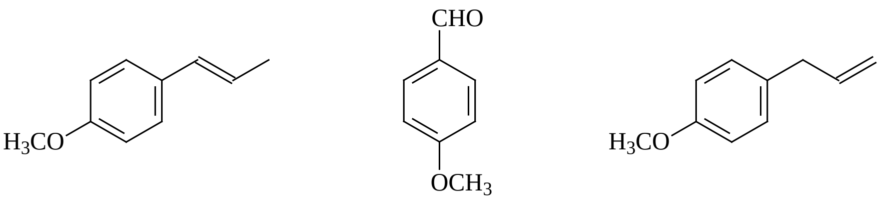
Figure 2.3-4
Anisi fructus (Anise fruit) and *Anisi stellati fructus* (Star anise fruit)

Appearance of the essential oil

Clear, colourless or pale yellow liquid. The oil can be jellified at 14-16 ˚C because of *trans*-anethole content.

Constituents

2-6 % essential oil of anise. The major components of anise oil are *trans*-anethole (80-95%) and anisaldehyde. 5-8% essential oil of star anise. The major components of star anise oil are *trans*-anethole and methyl-cavicol.



trans-anethole | anisaldehyde | methyl chavicol (= estragole)

Figure 2.5-7
The structure of *trans*-anethole, anisaldehyde and methyl-cavicol

Characteristics

Antiseptic, antibacterial, antifungal, spasmolytic, carminative.

Uses

Primary use

Gastrointestinal problems (flatulence, cramps), respiratory complaints (bronchitis, cough).

Other uses

Food industry (in lozenge, liqueur), soap- and toothpaste-scenting.

Contra-indications

Persons with known sensitivity to anethole should avoid aniseed and its oil.

Dosage

0.3 g (12 drops): daily dose (drop on sugar cube). Do not use under 2 years of age.

Pregnancy and lactation

Preparations containing the essential oil or alcoholic extracts should not be used during pregnancy and lactation. Mild oestrogenic activity and antifertility effects of anethole have been demonstrated in rats.

Aurantii dulcis aetheroleum

Plant

Citrus aurantium L. subsp. *sinensis* Engl. – Sweet orange (Rutaceae)

Sweet orange is native to India, China and Mediterranean countries. Elsewhere it is cultivated.

Drug

Aurantii dulcis aetheroleum (Sweet orange oil, Ph. Eur.)

Essential oil obtained without heating, by suitable mechanical treatment from the fresh peel of the fruit of *Citrus sinensis* (L.) Osbeck (*Citrus aurantium* L. var. *dulcis* L.). A suitable antioxidant may be added.

Appearance of the essential oil

Clear, pale yellow to orange, mobile liquid, which may become cloudy when chilled. It has a characteristic odour of fresh orange peel.

Constituents

0.4-0.9 % essential oil. The major components of sweet orange oil are limonene and nerol. Coumarine is found in the peel of sweet orange.

Characteristics

Antiseptic, regenerating of the skin, increase digestion, sedative.

Uses

Primary use

In cosmetics (acne, cellulitis), for oily and combined skin.

Other uses

Aroma bath, oral hygiene. The tincture of the oil is a seasoning material in the food industry.

Special warning

Externally the oil may be phototoxic because of the coumarin content.

Aurantii amari floris aetheroleum

Plant

Citrus aurantium L. subsp. *amara* Engl. – Bitter orange (Rutaceae)

Bitter orange is native to North-east India, South-China and it is also cultivated. The flowers are usually collected from older trees. 1 kg essential oil can be extracted from approx. 1000 kg flowers.

Drug

Aurantii amari floris aetheroleum (Bitter orange flower oil, Ph. Eur.) = *Neroli aetheroleum*

Bitter-orange-flower oil is obtained by steam distillation from the fresh flowers of *Citrus aurantium* L. subsp. *aurantium* (*C. aurantium* L. subsp. *amara* Engl.).

Appearance of the essential oil

A clear, pale-yellow or dark-yellow liquid, with a characteristic odour reminiscent of bitter-orange flowers, miscible with alcohol, with light petroleum, with fatty oils and with liquid paraffin.

Constituents

1-2 % essential oil. The main components of the oil are limonene and citronellol.

Characteristics

Improves digestion, sedative, regenerates the skin.

Uses

Primary use

Appetizer, skin care.

Other uses

In aromatheraphy (bath, sedative).

Special warning

Externally the oil may be phototoxic because of the coumarin content.

Carvi aetheroleum

Plant

Carum carvi L. – Caraway (Apiaceae)

The plant is native to Europe and Asia, and can also be cultivated.

Drug

Carvi aetheroleum (Caraway oil, Ph. Hg. VII.)

Caraway oil is obtained by steam distillation from the dried, ripe fruits of *Carum carvi* L.

Appearance of the essential oil

A clear colourless or yellow liquid with characteristic „caraway smell".

Constituents

3-7% essential oil. The oil consists of the ketone carvone and the terpene limonene with small quantities of dihydrocarvone, carveol and dihydrocarveol.

Characteristics

Improves digestion, spasmolytic, carminative, antifungal.

Uses

Primary use

Gastrointestinal problems. Tea (infusion) made from the fruits can be used in pediatrics.

Dosage

3-6 drops daily

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy without medical advice.

Caryophylli floris aetheroleum

Plant

Syzygium aromaticum (L.) Merill et L.M. Perry – Clove (Myrtaceae)

The plant is indigenous to Madagascar, Mauritius and Molucca Islands. It is cultivated in Zanzibar and in the neighbouring island of Pemba.

Drug

Caryophylli floris aetheroleum (Clove oil, Ph. Eur.)

Clove oil is obtained by steam distillation from the dried flower buds of *Syzygium aromaticum* (L.) Merill et L. M. Perry (*Eugenia caryophyllus* C. Spreng. Bull. et Harr.).

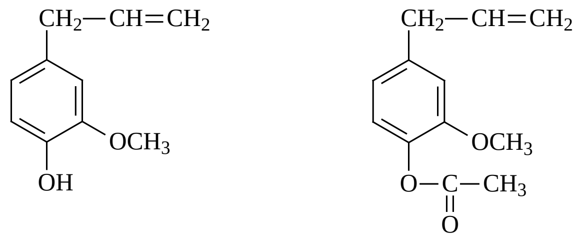
Figure 2.8
Caryophylli flos (Clove bud)

Appearance of the essential oil

A clear, yellow liquid which becomes brown when exposed to air, miscible with methylene chloride, toluene and fatty oils. Its density is higher than that of water. Clove oil, like other essential oils, should be stored in well-filled, airtight containers, protected from light and heat.

Constituents

15-25% essential oil. Clove oil contains 84-95% of phenols (eugenol), sesquiterpenes (α-, β-caryophyllenes) and small quantities of esters, ketones and alcohols.



eugenol eugenyl acetate

Figure 2.9-10
The structure of eugenol and eugenyl acetat

Characteristics

Local anaesthetic, anti-inflammatory, antibacterial, antifungal.

Uses

Primary use

Dentistry, in mouth-wash (1-5% solution).

Other uses

Stimulant, aromatic, flavouring agent. Clove stem oil is produced in Tanzania and in Madagascar. It is used mainly in the flavouring and perfumery industries. Clove leaf oil is distilled in Madagascar, Tanzania and in Indonesia, and is used for the isolation of eugenol.

Special warning

Externally clove oil can cause allergy (oil must be diluted). Do not use in children.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy without medical advice.

Cinnamomi zeylanici corticis aetheroleum

Plant

Cinnamomum zeylanicum Blume – Cinnamon (Lauraceae)

The plant is native to China, Ceylon, and it is cultivated elsewhere.

Drug

Cinnamomi zeylanici corticis aetheroleum (Cinnamon bark oil, Ceylon, Ph. Eur.)

Ceylon cinnamon bark oil is obtained by steam distillation of the bark of the shoots of *Cinnamomum zeylanicum* Nees (*C. verum* J.S. Presl.).

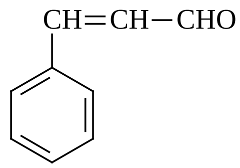
Figure 2.11
Cinnamomi zeylanici cortex (Cinnamon bark, Ceylon)

Appearance of the essential oil

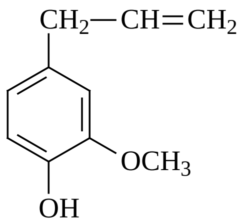
A clear, mobile, light yellow liquid becoming reddish over time, with a characteristic odour reminiscent of cinnamic aldehyde.

Constituents

0.5-4% essential oil. The main components of cinnamon bark oil are cinnamic aldehyde and eugenol. The oil is liable to adulteration with cinnamon leaf oil and with oil of cassia. (Cinnamon leaf oil contains 70-95% of eugenol. Oil of cassia contains approx. 80% of aldehydes.).



cinnamic aldehyde
(= cinnamaldehyde)



eugenol

Figure 2.12-13
The structure of cinnamic aldehyde and eugenol

Characteristics

Antibacterial, antifungal, appetizer, sedative, carminative.

Uses

Primary use

Antiseptic, gastrointestinal problems.

Other use

Aromatherapy.

Dosage

0.05-0.2 g daily dose

Special warning

Cinnamon bark oil can cause allergy (because of cinnamic aldehyde) when used externally. Do not use the oil in children.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy without medical advice.

Citronellae aetheroleum

Plant

Cymbopogon winterianus Jowitt – Citronella (Poaceae)

The plant is native to Java, and it can be cultivated.

Drug

Citronellae aetheroleum (Citronella oil, Ph. Eur.)

Oil obtained by steam distillation from the fresh or partially dried aerial parts of *Cymbopogon winterianus* Jowitt.

Appearance of the essential oil

Pale yellow to brown-yellow liquid, with a very strong odour of citronellal.

Constituents

0.5% essential oil. The main components of the citronella oil are geranial and citronellal.

citronellal

geranial = citral a
E-isomer of citral

Figure 2.14-15
The structure of geranial and citronellal

Characteristics

Bactericide.

Uses

Primary use

Aromatheraphy (in aroma lamp – to sterilize air).

Other uses

Cosmetic and perfumery industry, repellent (cats do not like it).

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy without medical advice.

Coriandri aetheroleum

Plant

Coriandrum sativum L. var. *vulgare* Alef. – Coriander (Apiaceae)

It is indigenous to Italy, but is widely cultivated in the Netherlands, Central and Eastern Europe, East-Mediterranean.

Drug

Coriandri aetheroleum (Coriander oil, Ph. Eur.)

Essential oil obtained by steam distillation from the fruits of *Coriandrum sativum* L.

Appearance of the essential oil

Clear, colourless or pale yellow liquid. It has a characteristic spicy odour.

Constituents

1.5-2.5% essential oil. The oil contains 65-70% of linalool depending on the plant source, and smaller amounts of α-pinene, γ-terpinene and limonene.

Characteristics

Sedative, carminative, flavouring agent, painkiller.

Uses

Primary use

Gastrointestinal problems, muscle relaxation (in liniments).

Other uses

Appetizer.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy without medical advice.

Eucalypti aetheroleum

Plant

Eucalyptus globulus Labill. – Eucalyptus (Myrtaceae)

Eucalyptus species are native to Australia, but they are also cultivated. “Citron-scented” eucalyptus oil, which is obtained from *E. citriodora*, is used in perfumery and contains a high proportion of the aldehyde citronellal.

Drug

Eucalypti aetheroleum (Eucalyptus oil, Ph. Eur.)

Eucalyptus oil is obtained by steam distillation and rectification from the fresh leaves or the fresh terminal branchlets of various species of *Eucalyptus* rich in 1,8-cineole. The most frequently used species are *Eucalyptus globulus* Labill., *Eucalyptus polybractea* R.T. Baker and *Eucalyptus smithii* R.T. Baker.

Appearance of the essential oil

A colourless or pale yellow liquid with an aromatic and camphoraceous odour and a pungent and camphoraceous taste.

Constituents

0.5-3.5% essential oil. The main component of eucalyptus oil is 1,8-cineole (not less than 70%), while minor components include α-pinene (2-8%) and camphor (less than 0.1%). To achieve these parameters and to minimise less desirable substances such as aldehydes, the oil obtained from initial steam distillation is rectified by alkaline treatment and fractional distillation.

Characteristics

Antiseptic, anticatarrhal.

Uses

Primary use

Cough, cold, bronchitis, other respiratory disorders.

Other use

Muscle pain, sauna.

Dosage

Internal use

0.05-0.2 ml per dose; in capsules: 100-200 mg, 2-5 times daily

External use

By inhalation: 12 drops per 150 ml of boiling water, or a 1.5% V/V solution prepared from 1 tablespoon (15 ml) per litre of warm water, treatment may be repeated up to three times daily.

As a liniment: containing 25% V/V of oil.

As an ointment: containing 1.3% V/m, for adults and children over 12 years: to be applied as a thick layer, up to three times daily.

As a lozenge: 0.2-15 mg dissolved slowly in the mouth, repeated every 0.5-1 hour.

As a mouthwash: containing 0.9 mg/ml; 20 ml as a gargle twice daily.

Contra-indications, special warnings, interactions

Eucalyptus oil and its preparations should not be applied to the face, especially the nose, of babies and little children. The oil induced hepatic microsomal enzyme activity in both *in vitro* and *in vivo* tests.

Pregnancy and lactation

Since human data are not available, eucalyptus should not be used during pregnancy and lactation without medical advice.

Foeniculi amari fructus aetheroleum

Plant

Foeniculum vulgare Mill. subsp. *vulgare* var. *vulgare* – Bitter fennel (Apiaceae)

The plant is native to Mediterranean, and it can also be cultivated in West-Europe, Asia and America.

Drug

Foeniculi amari fructus aetheroleum (Bitter fennel fruit oil, Ph. Eur.)

Essential oil obtained by steam distillation from the ripe fruits of *Foeniculum vulgare* Miller, ssp. *vulgare* var. *vulgare*.

Figure 2.16
Foeniculi amari fructus (Bitter fennel fruit)

Appearance of the essential oil

Clear, colourless or pale yellow liquid. It has a characteristic odour.

Constituents

2-6% essential oil. The oil contains predominantly *trans*-anethole (not less than 60%) and fenchone (not less than 15%) with not more than 5% estragole. (*Trans*-anethole can change into anisealdehyde during storage).

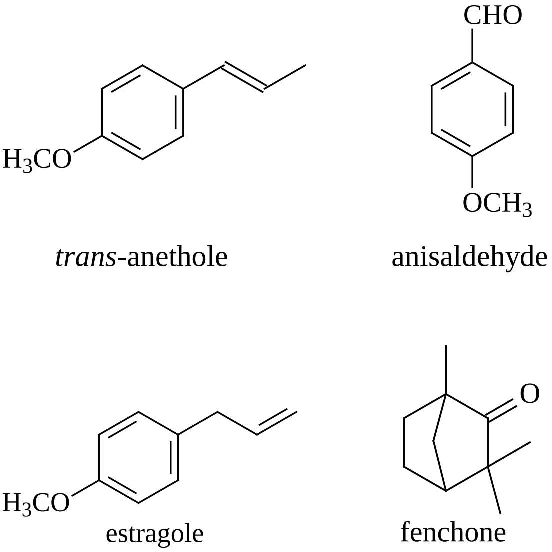


Figure 2.17-20
The structure of *trans*-anethole, fenchone, estragole and anisaldehyde

Characteristics

Spasmolytic, carminative.

Uses

Primary use

Gastrointestinal problems (flatulence, cramps).

Dosage

0.1-0.6 ml daily dose

Contra-indications

Persons with known sensitivity to anethole should avoid the use of fennel. The oil can cause epileptic convulsions, therefore patients with epilepsy should not use fennel oil.

Pregnancy and lactation

Preparations containing the essential oil or alcoholic extracts should not be used during pregnancy and lactation. Mild oestrogenic activity and antifertility effects of anethole have been demonstrated in rats.

Juniperi aetheroleum

Plant

Juniperus communis L. – Juniper (Cupressaceae)

Juniper is found from the Scandinavian Peninsula to the Mediterranean Sea.

Drug

Juniperi aetheroleum (Juniper oil, Ph. Eur.)

Essential oil obtained by steam distillation from the ripe, non-fermented berry cones of *Juniperus communis* L. A suitable antioxidant may be added.

Appearance of the essential oil

Mobile, colourless to yellowish liquid, with a characteristic odour (pine smell).

Constituents

2-3% essential oil. Essential oil (0.8-2 %) of very variable composition depending on the source, consisting mainly of monoterpene hydrocarbons, principally α-pinen (24.1-55.4%). Other compounds of the essential oil are: sabinen, terpinen-4-ol, β-caryophyllen.

Characteristics

Spasmolytic, diuretic, improves blood circulation.

Uses

Primary use

Muscle pain, muscle cramps.

Other uses

Treatment of common cold, antiseptic. In French hospitals juniper oil is used as an antiseptic to sterilize air.

Dosage

20-100 mg daily dose (in capsules)

Contra-indication, Special warnings

Patients with inflammation of renal pelvis or sensitive skin should not use juniper oil.

Pregnancy and lactation

Juniper should not be used during pregnancy and lactation. Abortifacient activity of juniper has been observed in rats after oral administration of a 50% ethanolic extract at 300 mg/kg bodyweight.

Lavandulae aetheroleum

Plant

Lavandula angustifolia Mill. – Lavender (Lamiaceae)

It is native to the Mediterranean, and can also be cultivated in South France and South Europe.

Drug

Lavandulae aetheroleum (Lavender oil, Ph. Eur.)

Essential oil obtained by steam distillation from the flowering tops of *Lavandula angustifolia* Miller (*Lavandula officinalis* Chaix).

Appearance of the essential oil

Colourless or pale yellow, clear liquid. It has a characteristic odour (flower-scented).

Constituents

1.5% essential oil. The main components of the oil are linalool (20-45%) and linalyl acetate (25-46%). Others include terpinene-4-ol, limonene, cineole, camphor, lavandulol.

Characteristics

Sedative, anti-inflammatory, antiseptic.

Uses

Primary use

Skin care (burning, cuts, acne).

Other use

Aromatherapy (bath, ointment, inhalation), against insect bites.

Dosage

1-4 drops (approx. 20-80 mg), e.g. on a sugar cube. For children (up to 12 years of age): by inhalation – 3 drops of a 1:10 diluton of lavender oil. Children over 12 years of age:

as a bath additive – 6 drops per bath or 3 ml of a 20% solution. By inhalation – several drops of the oil or 2-20% of the oil in a nebulizer.

Contra-indication

Allergic reactions to lavender oil or one of its constituents.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy without medical advice.

Limonis aetheroleum

Plant

Citrus limon (L.) Burm. – Lemon (Rutaceae)

Lemons are widely cultivated and the essential oil is prepared around the Mediterranean, North and South America, in Australia and in parts of Africa. Other producing countries are: China, Israel and Turkey.

Drug

Limonis aetheroleum (Lemon oil, Ph. Eur.)

Essential oil obtained by suitable mechanical means, without the aid of heat, from the fresh peel of *Citrus limon* (L.) Burman fil.

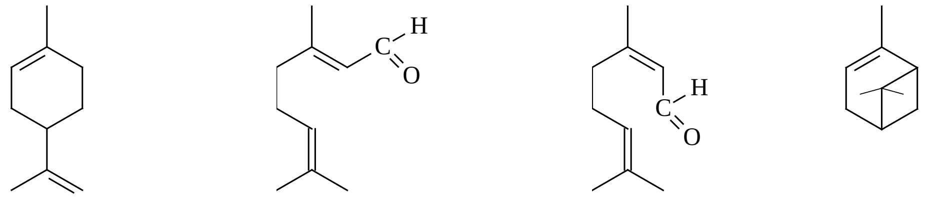
Once the oil has been separated from the peel, it can be distilled without deterioration in quality, and some expressed oil of lemon is fractionally distilled to make terpeneless oil of lemon. Distilled oil of lemon is cheaper than that prepared by expression and large quantities of it are made and used for nonpharmaceutical purposes.

Appearance of the essential oil

Clear, mobile, pale yellow to greenish-yellow liquid with a characteristic odour. It may become cloudy at low temperatures.

Constituents

0.5-1.5% essential oil. Lemon oil contains terpenes (limonene), pinene, aldehydes [(geranial = citral A), (neral = citral B] and esters (geranyl acetate). Lemon oil shows a marked tendency to resinify and should be protected from air and light as much as possible. During storage chemical alteration may occur in the oil.



limonene | geranial = citral A *E*-isomer of citral | neral = citral B *Z*-isomer of citral | α-pinene

Figure 2.21-24
The structure of limonene, geranial (= citral A), neral (= citral B) and α-pinene

Characteristics

Antiseptic, antidepressant.

Uses

Primary use

Treating of respiratory diseases (cold, influenza, sinusitis).

Other uses

Treating of oily skin, air-freshener, perfumery, flavouring agent.

Special warning

Lemon oil may have phototoxic effect in case of external use.

Matricariae aetheroleum

Plant

Matricaria recutita L. – Chamomile (Asteraceae)

The plant is native to and cultivated in southern and eastern Europe, in Asia and in North America.

Drug

Matricariae aetheroleum (Matricaria oil, Ph. Eur.)

Blue essential oil obtained by steam distillation from the fresh or dried flower-heads or flowering tops of *Matricaria recutita* L. (*Chamomilla recutita* L. Rauschert). There are 2 types of matricaria oil which are characterised as rich in bisabolol oxides, or rich in levomenol.

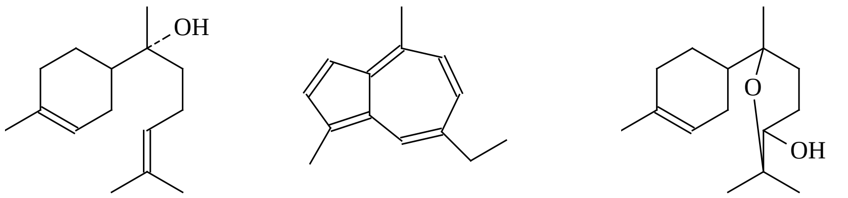
Figure 2.25
Matricariae flos (Chamomile flower)

Appearance of the essential oil

Clear, intensely blue, viscous liquid. It has an intense characteristic odour (bitterish smell).

Constituents

0.5-1.5% essential oil. The oil contains approx. 50% of the sesquiterpenes (chamazulene, and α-bisabolol and its oxides A, B, C), bisabolonoxide A, up to 25% of cis-and trans-en-yn-dicycloethers and β-farnesene. Chamazulene itself does not occur in the plant but is formed from matricin (sesquiterpene lactone) during steam distillation. Chemical alteration may occur during storage.



α-bisabolol chamazulene bisabolol oxide A

Figure 2.26-28
The structure of α-bisabolol, bisabolol oxide A and chamazulene

Characteristics

Antiseptic, anti-inflammatory, pain killer, spasmolytic.

Uses

Primary use

Gastrointestinal problems (ulcer-protective), respiratory complaints (cold, influenza, sinusitis).

Other use

Dermatology.

Contra-indication

Sensitivity to *Matricaria* or other members of the Asteraceae.

Undesirable effects

Rare cases of contact allergy have been reported. *Matricaria* flower of the bisabolol oxide B-type can contain traces of the contact allergen anthecotulide. Most of the described allergic reactions to matricaria were due to contamination with *Anthemis cotula* or related species, which contain high amounts of anthecotulide. However, in cases where matricaria contact allergy has been aquired, cross-reactions to other sesquiterpene lactone-containing plants are common.

Menthae piperitae aetheroleum

Plant

Mentha x *piperita* (L.) Huds – Peppermint (Lamiaceae)

The plant is cultivated worldwide.

Drug

Menthae piperitae aetheroleum (Peppermint oil, Ph Eur.)

Essential oil obtained by steam distillation from the fresh aerial parts of the flowering plant of *Mentha* × *piperita* L.

Appearance of the essential oil

A colourless, pale yellow or pale greenish-yellow liquid. It has a characteristic odour and taste followed by a sensation of cold.

Constituents

1.2-3% essential oil. The oil must contain menthol (30-55%), menthon (14-32%), isomenthone (1.5-10%), menthyl acetate (2.8-10%), menthofuran (1-9%), cineole (3.5-14%), limonene (1-5%), not more than 3% of pulegone and not more than 1% of carvone, with a higher ratio of cineole compared to that of limonene.

Characteristics

Pain killer, spasmolytic, antiseptic.

Uses

Primary use

Symptomatic treatment of digestive disorders (e.g. flatulence, irritable bowel syndrome), symptomatic treatment of coughs and colds.

Other uses

Symptomatic relief of tension-type headache, pruritus, urticaria and pain in irritable skin conditions.

Dosage

Internal use

Adults: For digestive disorders: 0.02-0.08 ml (1-4 drops) up to 3 times daily in dilute aqueous preparation (e.g. peppermint water or emulsion), or as drops on a lump of sugar.

For irritable bowel syndrome: 0.2-0.4 ml 3 times daily in enteric-coated capsules

Children from 4-16 years of age: For digestive disorders: proportion of adult dose according to body weight

External use

Adults: By inhalation: 3-4 drops added to hot water

In dilute liquid or semi-solid preparations, as an anaesthetic or antipruritic (equivalent to 0.1-1.0% m/m menthol) or as a counter-irritant and analgesic (equivalent to 1.25-16% m/m menthol), rubbed on to the affected area.

Tension-type headache: as a 10% solution rubbed on to the skin of forehead and temples.

Children from 4-16 years of age

Semi-solid preparations: 4-10 years: 2-10%, 10-16 years: 5-15%

Hydroethanolic preparations: 4-10 years: 2-4%, 10-16 years: 3-6%

Contra-indication

Contact sensitivity to peppermint oil or menthol.

Special warnings

Direct application of peppermint oil preparations to the nasal area or chest of babies and small children must be avoided because of the risk of laryngeal and bronchial spasms. Inhalation of menthol can cause apnoea and laryngoconstriction in susceptible individuals. Menthol can cause jaundice in newborn babies (glucose-6-phosphate dehydrogenase deficiency).

Interaction

Patients with achlorhydria (caused, e.g. by medication with H_2 receptor blockers) should use peppermint oil only in enteric-coated capsules.

Pregnancy and lactation

No data available. In accordance with general medical practice, peppermint oil should not be used during pregnancy without medical advice.

Myristicae fragrantis aetheroleum

Plant

Myristica fragrans Houtt. – Nutmeg (Myristicaceae)

Nutmeg is native to Malaysia, Maluccu Island (Indonesia), but it can also be cultivated.

Drug

Myristicae fragrantis aetheroleum (Nutmeg oil, Ph. Eur.)

Nutmeg oil is obtained by steam distillation of the dried and crushed kernels of *Myristica fragrans* Houtt.

Figure 2.29
Myristicae semen (Nutmeg)

Appearance of the essential oil

A colourless or pale yellow liquid, with a spicy odour.

Constituents

Nutmeg oil contains myristicin (4%) and elemicin (2%). Myristicin is 4-allyl-6-methoxy-1,2-methylenedioxybenzene. It is toxic to human beings and large doses of nutmeg oil may cause convulsions. Other compounds include pinene, sabinene, camphene (60-80%). Myristicin and elemicin have hallucinogenic effect.

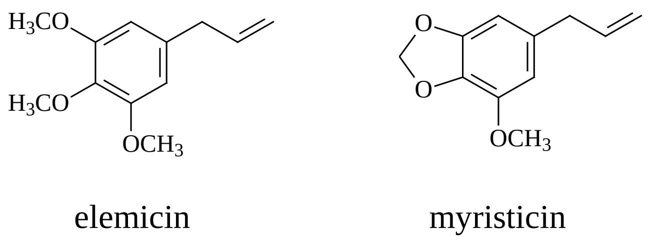


Figure 2.30-31
The structure of myristicin and elemicin

Uses

Primary use

Food industry, liqueurs, perfumery.

In Ajurvedic medicine: the name of the plant is „mada shaunda” = „narcotic fruit”.

Terebinthini aetheroleum ab pinum pinastrum

Plant

Pinus pinaster Aiton – Turpentine tree (Pinaceae)

The plant is native to France, Italy, Portugal and Spain.

Drug

Terebinthini aetheroleum ab pinum pinastrum (Turpentine oil, Pinus pinaster type, Ph. Eur.)

Essential oil obtained by steam distillation, followed by rectification at a temperature below 180 °C, from the oleoresin obtained by tapping *Pinus pinaster* Aiton. A suitable antioxidant may be added. The purification consits of treatment with aqueous alkali to remove traces of phenols, resin acids, etc., and may be followed by redistillation.

Appearance of the essential oil

Clear, colourless or pale yellow liquid. It has a characteristic odour.

Constituents

15-30% essential oil. Turpentine oil consists of the terpenes (+)- and (-)- α-pinene, (-)-β-pinene and camphene. During storage the oil becomes more allergenic.

Characteristics

Pain killer, antibacterial, rubefacient.

Uses

Primary use

Treatment of common cold, rheumatic pain.

Other use

Inhalation.

Contra-indication

Allergy is possible.

Terebene is prepared from the oil of turpentine by the action of cold sulphuric acid, which converts the pinene into the optically inactive (±)-limonene (dipentene). Today, most turpentine is produced to provide its various constituents which find use in the manufacture of fragrances, insecticides, flavours.

Rosmarini aetheroleum

Plant

Rosmarinus officinalis L. – Rosemary (Lamiaceae)

The plant is native to the Mediterranean, in Hungary it can be cultivated.

Drug

Rosmarini aetheroleum (Rosemary oil, Ph. Eur.)

Essential oil obtained by steam distillation from the flowering aerial parts of *Rosmarinus officinalis* L.

Appearance of the essential oil

Clear, mobile, colourless to pale yellow liquid with a characteristic odour.

Constituents

1-2.5% essential oil. Characteristic components of the oil are 1,8-cineole (= eucalyptol, 20-50%), α-pinene (15-26%), camphor (10-25%) and borneol (1-6%).

Characteristics

Spasmolytic, pain killer, antiseptic, improves blood circulation.

Uses

Primary use

Reduce muscle pain, in case of hypotension, backpain. The oil is used in preparations with 6-10% EO contain.

Other use

Treating respiratory complaints (e.g. cough).

Contra-indication

Hypersensitivity to rosemary.

Special warnings

Hot bath containing rosemary preparations should be avoided by patients with large open wounds, large skin lesions, feverish conditions or acute inflammation, severe circulatory disorders or hypertension, epilepsy.

Pregnancy and lactation

No data available. In accordance with general medical practice, rosemary oil should not be used during pregnancy without medical advice.

Salviae sclareae aetheroleum

Plant

Salvia sclarea L. – Clary sage (Lamiaceae)

The plant can be found from the Mediterranean Sea to Iran, it is cultivated in Russia, Turkey, Spain and Hungary.

Figure 2.32
Clary sage (*Salvia sclarea* L.)

Drug

Salviae sclareae aetheroleum (Clary sage oil, Ph. Eur.)

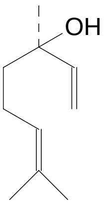
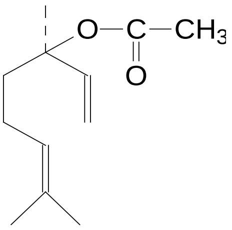
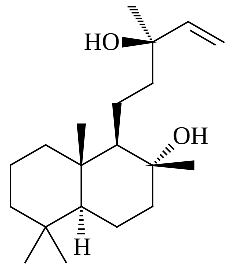
Essential oil obtained by steam distillation from the fresh or dried flowering stems of *Salvia sclarea* L.

Appearance of the essential oil

Colourless to brownish-yellow liquid, usually pale yellow, with a characteristic odour.

Constituents

0.2-1% essential oil. The oil contains linalool, linalyl acetate and sclareol as the main compounds.

linalool linalyl acetate sclareol

Figure 2.33-35
The structure of linalool, linalyl acetate and sclareol

Characteristics

Spasmolytic, sedative.

Uses

Primary use

Decrease the symptoms of menses (headache, cramps), against delivery pain.

Other use

Aromatherapy, skin care, perfumery industry.

Thymi aetheroleum

Plants

Thymus vulgaris L. and *T. zygis* Loefl. ex. L. – Thyme and Spanish thyme (Lamiaceae)

The plants are native to the Mediterranean, in Hungary they can also be cultivated.

Drug

Thymi aetheroleum (Thyme oil, Ph. Eur.)

Essential oil obtained by steam distillation from the fresh flowering aerial parts of *Thymus vulgaris* L., *T. zygis* Loefl. ex L. or a mixture of both species.

Appearance of the essential oil

Clear, yellow or very dark reddish-brown, mobile liquid with a characteristic, aromatic, spicy odour, reminiscent of thymol.

Constituents

1-3% essential oil. The thyme oil contains phenols, mainly thymol and/or carvacrol, and terpenoids.

Characteristics

Antibacterial, antifungal, expectorant, cough-reliever.

Uses

Primary use

Respiratory disorders (bronchial catarrh, supportive treatment of pertussis).

Other use

Dermatology (mycosis of the legs).

Special warnings

Children under 5 years of age and patients with epilepsy or disease of the thyroid gland should not use thyme oil.

Pregnancy and lactation

No data available. In accordance with general medical practice, thyme oil should not be used during pregnancy without medical advice.

Menthae arvensis aetheroleum partim mentholi privum

Plant

Mentha canadensis L. – Lamiaceae (syn: *Mentha arvensis* L. var. *piperascens* Malinv.)

The plant is native to East-Asia, China, Malaysia and Canada.

Drug

Menthae arvensis aetheroleum partim mentholi privum (Mint oil, partly dementholised, Ph. Eur.)

Essential oil obtained by steam distillation from the fresh, flowering aerial parts, recently gathered from *Mentha canadensis* L. (syn. *M. arvensis* L. var. *glabrata* (Benth) Fern., *M. arvensis* var. *piperascens* Malinv. ex Holmes), followed by partial separation of menthol by crystallisation.

Appearance of the essential oil

Colourless or pale yellow to greenish-yellow liquid with a characteristic odour.

Constituents

1-3 % essential oil. The main components of the oil are menthol and menthon.

Use

It has carminative effect. The plant can be used for essential oil production („Japanese peppermint oil”).

Chapter 3
Iridoid-containing drugs

3.1 Iridoids – Biosynthesis

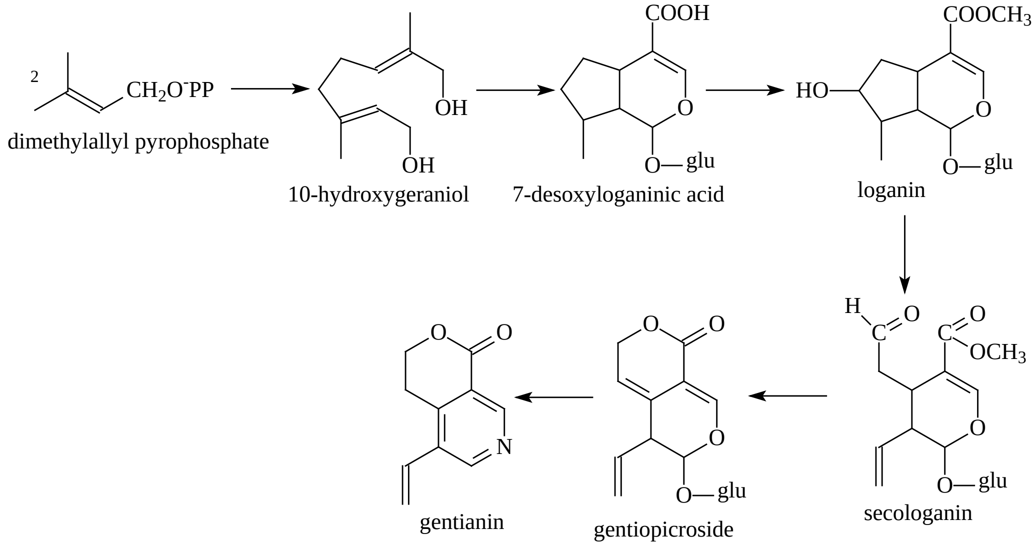


Figure 3.1
The biosynthesis of iridoids (loganin) and secoiridoids (gentiopicroside)

Properties of iridoids

Iridoids are cyclopentan-[c]-pyran monoterpenoids. Most occur as glycosides; some occur free and as bis compounds. The number of these compounds is constantly increasing (several hundred iridoids are known). There are many seco-iridoids in which the pyran ring is open, and in a few the pyran ring oxygen is replaced by nitrogen. Iridoids are less stable compounds, they are easily decomposed by enzymes and are oxidised too. They can be dissolved in water and alcohol. Their name derives from *Iridomyrmex* (ant genus), which produces these compounds as a defensive secretion. Loganin is one of the most important iridoids, which is a precursor of the nonindole portion of some alkaloids. The most important plant families containing iridoid-producing species are: *Apocynaceae, Cornaceae*, *Ericaceae*, *Gentianaceae*, *Lamiaceae, Menyathaceae*, *Valerianaceae*, *Plantaginaceae*. Their pharmacological effects include: antibacterial, anti-inflammatory, sedative, pain killer, appetizer (secoiridoids). They are used as a bitter tonic. Because iridoids are not stable compounds, fast drying (at low temperature, at 40 °C) of the drugs is necessary during the primary processing and after careful packing, these drugs have to be stored protected from light.

Bitterness value in the European Pharmacopoeia 5.0

- **The bitterness value is the reciprocal of the dilution of a compound, a liquid or an extract that still has a bitter taste.**
- **It is determined by comparison with quinine hydrochloride, the bitterness value of which is set at 200 000.**
- *Determination of the correction factor*: A taste panel comprising at least 6 persons is recommended. The mouth must be rinsed with *water R* before tasting. To correct for individual differences in tasting bitterness amongst the panel members it is necessary to determine a correction factor for each panel member.
- *Stock solution*: Dissolve 0.100 g of *quinine hydrochloride R* in *water R* and dilute to 100.0 ml with the same solvent. Dilute 1.0 ml of this solution to 100.0 ml with *water R*.
- *Reference solutions*. Prepare a series of dilutions by placing in a first tube 3.6 ml of the stock solution and increasing the volume by 0.2 ml in each subsequent tube to a total of 5.8 ml; dilute the contents of each tube to 10.0 ml with *water R*.
- **Determine as follows the dilution with the lowest concentration that still has a bitter taste.**
- Bitterness values: *Centaurii herba*: 2000, *Gentianae radix et rhizoma*: 10000, *Menyanthidis trifoliatae folium*: 3000.

Bitters

- Bitters are extensively used in liquid medicaments to stimulate appetite. Bitter constituents stimulate the gustatory nerves in the mouth and give rise to an increase in the psychic secretion of gastric juice.
- Causes of the lack of appetite: infections (caused by bacteria or viruses), psychosomatic diseases (anorexia nervosa, stress), consumption of medicines (e.g. antibiotics), decrease of sensation of taste (in the elderly) and smoking. Other causes: inappropriate production of gastric juice and bile, lack of enzymes produced by pancreas.
- Bitter compounds show a great chemical variation. Iridoids, seco-iridoids, sesquiterpene lactones and diterpenes have bitter taste. But bitter compounds with strong effect, e.g. cardioactive glycosides from *Digitalis* species, or alkaloids (strychnine) must not be used as a bitter tonic.
- Types of drugs containing bitters:
  1. *amara pura* – only bitters, e.g. Gentian, Centaury
  2. *amara aromatica* – aromatic bitters, e.g. Bitter orange
  3. *amara acria* – hot bitters, e.g. Ginger
  4. *amara adstringentia* – adstringent bitters, e.g. Condurango
  5. *amara mucilaginosa* – mucous bitters, e.g. Iceland moss
- Tinctures or hydroalcoholic extracts are usually produced from plants containing bitter compounds. Liquids and tinctures are in touch with taste buds on a bigger

surface, therefore the products can act very fast. Application: 20-30 min. before meal, the effect lasts for 2-3 hours.

- Drugs containing bitters must not be used for a long time, because adverse effects may develop (loss of appetite).

Drugs

Plantaginis lanceolatae folium

Plant

Plantago lanceolata L. – Ribwort plantain (Plantaginaceae)

The plant is native to Eurasia.

Figure 3.2
Ribwort plantain (*Plantago lanceolata* L.)

Drug

Plantaginis lanceolatae folium (Ribwort plantain leaf, Ph. Eur.)

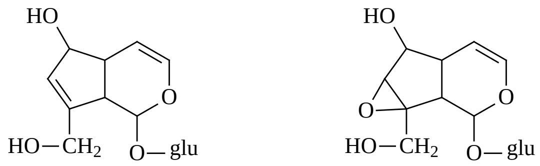
Ribwort plantain leaf consists of the whole or fragmented, dried leaf and scape of *Plantago*

lanceolata L. s. l. It contains not less than 1.5% of total ortho-dihydroxycinnamic acid derivatives, expressed as acteoside and calculated with respect to the dried drug.

Figure 3.3
Plantaginis lanceolatae folium (Ribwort plantain leaf)

Constituents

The characteristic constituents are 2-6.5% mucilage-heteropolysaccharide, iridoid glycosides (aucubin, catalpol), phenylethanoids (acteoside, isoacteoside), flavonoids and silicic acid.



aucubin catalpol

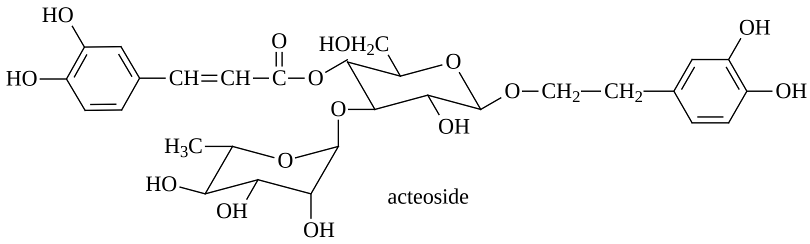


Figure 3.4-6
The structure of aucubin, catalpol and acteoside

Uses

Therapeutic indications include catarrhs of the respiratory tract, bronchitis, temporary, mild inflammations of the oral and pharyngeal mucosa. The drug has anti-inflammatory, antibacterial and cough suppressant activities. In ethnomedicine the leaves are used externally to cure the wounds and haemorrhoids.

Dosage

Internal use

Adults, elderly: average daily dose, 3-6 g of the drug or equivalent preparations.

Children: average daily dose: >1-4 years of age: 1-2 g, 4-10 years: 2-4 g, 10-16 years: 3-6 g.

Black colour of the leaves indicates that the drug must not be used for making preparations.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

Other Plantago species in the European Pharmacopoeia

Psyllium seed; Psyllii semen *(Plantago afra, P. indica)*

Ispaghula seed; Plantaginis ovatae semen *(Plantago ovata)*

Plantago afra and P. indica are native to the Mediterranean, Asia and USA; *P. ovata*: India, Pakistan, Africa.

Figure 3.7-8
Psyllii semen (Psyllium seed) and *Plantaginis ovatae semen* (Ispaghula seed)

Uses

Mild laxative (due to mucilage content), against constipation, Crohn-disease, increases fibre-intake.

Dosage

(After 12 years of age): 10-30 g

Special warnings

It is worth calling the patients' attention to the proper application of the drugs. Drugs containing mucilage can cause obstruction of the bowels, if the patient does not drink appropriate amount of water (or other liquid). Mucilage may prevent the absorption of other medicines, vitamins, glucose in the bowels.

Euphrasiae herba

Plant

Euphrasia rostkoviana Hayne. – Eyebright (Scrophulariaceae)

The plant is native to Europe. In Hungary it can be found in Transdanubia.

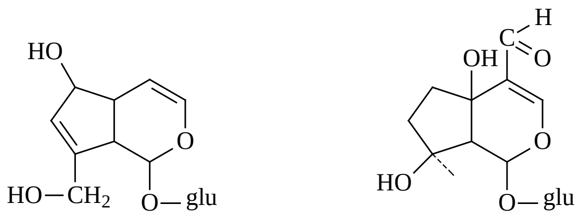
Drug

Euphrasiae herba (Eyebright, DAC)

Eyebright consists of the dried flowering aerial parts of *Euphrasia rostkoviana* Hayne.

Constituents

The characteristic constituents of the drug include iridoids (eufroside and aucubin), tannins and flavonoids.



aucubin eufroside

Figure 3.9
The structure of aucubin and eufroside

Uses

It has antibacterial and anti-inflammatory activity. It can be used for treating conjunctivitis (in the form of sterile infusion).

Dosage

Daily dose 2 g, 2 % infusion – application form: in compress.

Lamii albi flos

Plant

Lamium album L. – White deadnettle (Lamiaceae)

The plant is native to Europe and Asia. It is a ruderal weed.

Figure 3.10
White deadnettle (*Lamium album* L.)

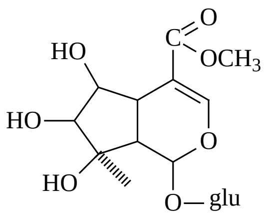
Drug

Lamii albi flos (White deadnettle flower), *Lamii albi herba* (White deadnettle, DAC)

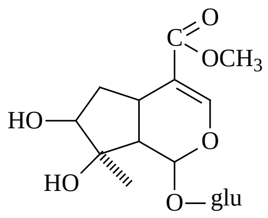
Lamii albi flos consists of the dried flowers of *L. album*. *Lamii albi herba* consists of the dried flowering aerial parts of the plant.

Constituents

Flowers contain iridoids (lamalbid and 6-desoxylamalbid) and flavonoids. The characteristic constituents of the herb are tannins, mucilage and saponins.



lamalbid



6-desoxylamalbid

Figure 3.11-12
The structure of lamalbid and 6-desoxylamalbid

Uses

The drugs of white deadnettle can be used for treating diseases of the upper respiratory system. Because of tannin content, it has adstringent effect. In ethnomedicine, the plant is used to treat benign prostate hypertrophy, leucorrhea and irregular menstruation. External use: treating of ulcus cruris, haemorrhoids.

Dosage

Daily dose 6-9 g, as an infusion.

Harpagophyti radix

Plant

Harpagophytum procumbens (Burch.) DC., *H. zeyheri* – Devil's claw (Pedaliaceae)

These plants are native to Southern and Eastern Africa. It is collected in regions bordering on the Kalahari desert. It derives its trivial name from the characteristic appearance of the fruit.

Drug

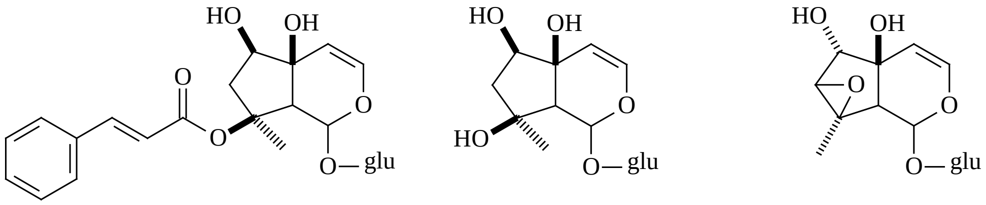
Harpagophyti radix (Devil's claw root, Ph. Eur.)

Devil's claw root consists of the cut and dried tuberous, secondary roots of *Harpagophytum procumbens* D.C. and/or *H. zeyheri* L. Decne. It contains not less than 1.2% of harpagoside, calculated with reference to the dried drug. Devil's claw root is greyish-brown to dark brown and it has a bitter taste.

Figure 3.13
Harpagophyti radix (Devil's claw root)

Constituents

The characteristic constituents are iridoid glycosides (harpagoside, harpagide, procumbide) (1-3% in *H. procumbens,* 0.7-1.7% in *H. zeyheri*). The phenolic glycosides acteoside (verbascoside) and sugars, mainly the tetrasaccharide stachyose (up to 46%) can also be found in the drug. The acylated phenolic glycoside 6-acetylacteoside has been found in *H. procumbens* but not in *H. zeyheri*.



harpagoside (harpagide's cinnamoyl ester) | harpagide | procumbide (epoxyiridoid glycoside)

Figure 3.14-16
The structure of harpagoside, harpagide and procumbide

Uses

The drug has anti-inflammatory and analgesic effect, therefore it can be used in the treatment of painful osteoarthritis and low back pain. On the basis of its bitter tonic properties, the drug is also widely documented as a remedy for loss of appetite and dyspepsia.

Dosage

Symptomatic treatment of painful osteoarthritis

Adults, elderly: 2-5 g (daily dose) of the drug or equivalent dry extract prepared with water or ethanol (max. 60% V/V)/water

Treatment for at least 2-3 months is recommended in cases of painful osteoarthritis.

Relief of low back pain

Adults, elderly: 4.5-9 g (daily dose) of the drug as dry extract prepared with water or ethanol (max. 60% V/V)/water

Loss of appetite or dyspeptic complaints

Adults, elderly: 0.5 g of the drug in decoction, 3 times daily, tincture (1:10, 25% ethanol) 3 ml

Not recommended for children.

Contra-indications

As with other drugs containing bitter substances, patients with gastric ulcers should consult their doctor before use.

Undesirable effects

Mild gastro-intestinal disturbances (e.g. diarrhoea, stomach upset, nausea) may occur in sensitive individuals especially at higher dosage level.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

Agni casti fructus

Plant

Vitex agnus castus L. – Agnus castus (Verbenaceae)

The plant is native to Europe, North-Africa and Asia.

Drug

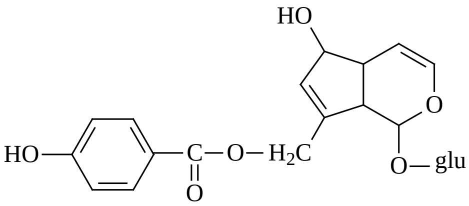
Agni casti fructus (Agnus castus fruit, Ph. Eur. 6.0)

Agnus castus consists of the whole, ripe, dried fruits of *Vitex agnus castus* L. It contains not less than 0.08% of casticin, calculated with reference to the dried drug.

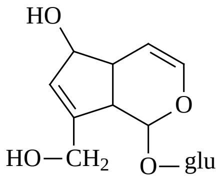
Figure 3.17
Agni casti fructus (Agnus castus fruit)

Constituents

The characteristic constituents of the drug are iridoid glycosides such as agnuside (0.02-0.4%) and aucubin; bicyclic diterpenes of the labdane and clerodane types (e.g. rotundifuran); lipophilic flavonoids such as casticin (3',5-dihydroxy-3,6,7,4'-tetramethoxyflavone, 0.02-0.2%), hydrophilic flavones of O- or C-glycosidic types (e.g. orientin, isovitexin, luteolin-7-glucoside), essential oil (containing monoterpenes) and fatty oil.



agnuside



aucubin

Figure 3.18-19
The structure of agnuside and aucubin

Uses

Agnus castus can treat the PMS (premenstrual syndrome) including symptoms such as mastodynia or mastalgia. It is also used for treating menstrual cycle disorders such as polymenorrhoea, oligomenorrhoea or amenorrhoea.

Dosage

Preparations equivalent to 30-40 mg of the drug daily or up to 240 mg of the drug daily in patients suffering from PMS.

Treatment for a minimum of 3 months may be appropriate, and seeking medical advice is recommended. Patients with tumors in breast or thyroid gland must not use the drug or its preparations.

Interaction

Mutual attenuation of effects might occur in patients under concomitant treatment with dopamine receptor antagonists.

Undesirable effects

Cases of allergic skin reactions have been reported.

Pregnancy and lactation

No data available. Agnus castus should not be taken during pregnancy. Lactation was inhibited in rats after subcutaneous administration of an agnus castus extract twice daily at about 100 times the human daily dose level. A human study showed an increase in lactation. Agnus castus should not be taken during lactation.

Verbenae herba

Plant

Verbena officinalis L. – Vervain (Verbenaceae)

The plant is native to Europe and Asia.

Figure 3.20
Vervain (*Verbena officinalis* L.)

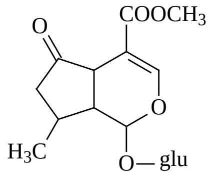
Drug

Verbenae herba (Vervain, DAC)

Vervain consists of the dried, aerial flowering parts of *Verbena officinalis* L.

Constituents

The characteristic constituents of the drug are iridoid glycosides such as verbenalin; flavonoids and triterpenes.



verbenalin

Figure 3.21
The structure of verbenalin

Uses

It has expectorant, cough-suppressant activity, therefore it can be used for treating respiratory disorders and the inflammation of the throat. In ethnomedicine vervain can heal the wounds.

Dosage

2-4 g/daily dose.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

Valerianae radix

Plant

Valeriana officinalis L. – Valerian (Valerianaceae)

Valerian is native to Europe and Asia. It is obtained from wild and cultivated plants in Britain, the Netherlands, Belgium, France, Germany, Hungary and Japan. It is also cultivated in the USA. Polyploidy occurs in *V. officinalis* and there are diploid, tetraploid and octoploid types. Central European valerian is usually tetraploid. Other *Valeriana* species, for example, Indian valerian (*V. wallichii*) may not substitute the drug of *V. officinalis*, because of the risk of the cytotoxicity (higher valepotriate content).

Figure 3.22
Valerian (*Valeriana officinalis* L.)

Drug

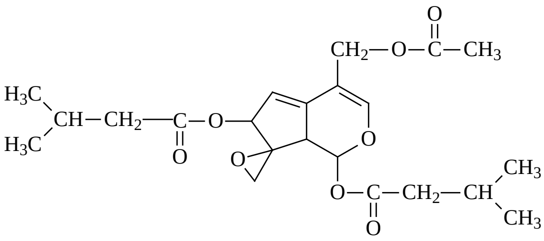
Valerianae radix (Valerian root, Ph. Eur.)

Valerian root consists of the dried, whole or fragmented underground parts of *Valeriana officinalis* L. s.l., including the rhizome surrounded by the roots and stolons. It contains not less than 5 ml/kg of essential oil for the whole drug and not less than 3 ml/kg of essential oil for the cut drug, both calculated with reference to the dried drug and not less than 0.17 per cent of sesquiterpenic acids expressed as valerenic acid, calculated with reference to the dried drug. Valerian root has a characteristic odour.

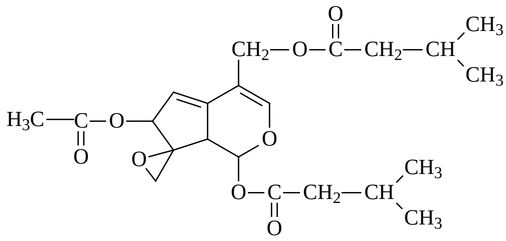
Figure 3.23
Valerianae radix (Valerian root)

Constituents

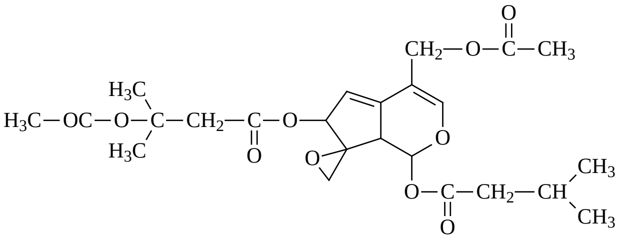
The drug contains 0.5-2% epoxy-iridoids: valepotriates (valtrate, isovaltrate, didrovaltrate, acevaltrate). They are unstable constituents and unlikely to be present in finished products. Similarly, baldrinals, the decomposition products of valepotriates, are not detected in valerian root preparations. Other characteristic constituents include essential oil containing monoterpenes such as bornyl esters, pinenes; sesquiterpenes (valerenal, valeranone); and less volatile sesquiterpenic acids (valerenic acid). Valerenic acid is responsible for the characteristic odour of the drug. Other constituents are monoterpene-alkaloids, GABA (gamma-aminobutyric acid) and flavonoids (6-methylapigenin).



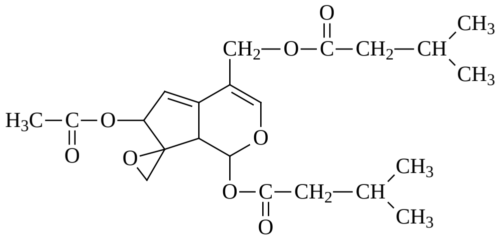
valtrate



isovaltrate



acevaltrate



didrovaltrate

Figure 3.24-27
The structure of valtrate, isovaltrate, didrovaltrate and acevaltrate

Uses

Valerian has a sedative and antispasmodic effect. Therapeutic indication includes the relief of temporary mild nervous tension and/or difficulty in falling asleep (insomnia). Valerian can reduce intestinal cramps.

Dosage

Adult and elderly single dose: 1-3 g of the drug (e.g. as a tea infusion) or equivalent extracts prepared with water or ethanol (max. 70%). For tenseness, restlessness and irritability, up to 3 times daily. As an aid to sleep, a single dose half to one hour before bedtime, with an earlier dose during the evening if necessary.

Children from 3 to 12 years under medical supervision: proportion of adult dose according to body weight, as non-alcoholic preparations. The use of valerian products should not be recommended under 3 years of age.

Neither dependence nor withdrawal symptoms have been reported.

Effect on ability to drive and use machines

Taking valerian root preparations immediately (up to 2 hours) before driving a car or operating hazardous machinery is not recommended. The effect of valerian preparations may be strengthened by consumption of alcohol.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

Gentianae radix and Gentianae tinctura

Plant

Gentiana lutea L. – Gentian (Gentianaceae)

Gentian is native to mountainous districts of central and southern Europe and Turkey. As it is now a protected plant in some areas (e.g. in Hungary), attempts are being made to cultivate it in some EU countries (Germany, France, Italy).

Drug

Gentianae radix (Gentian root, Ph. Eur.), *Gentianae tinctura* (Gentian tincture, Ph. Eur.)

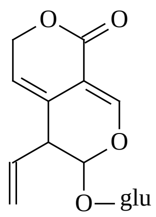
Gentian root consists of the dried, fragmented underground organs of *Gentiana lutea* L. Gentian root occurs as single or branched subcylindrical pieces of various lengths and usually 10 mm to 40 mm thick but occasionally up to 80 mm thick at the crown. Tincture produced from *Gentian root*, from 1 part of the comminuted drug and 5 parts of ethanol (70 per cent *V/V*) by a suitable procedure. It is a yellowish-brown or reddish-brown liquid. It has a strong bitter taste.

Figure 3.28
Gentianae radix (Gentian root)

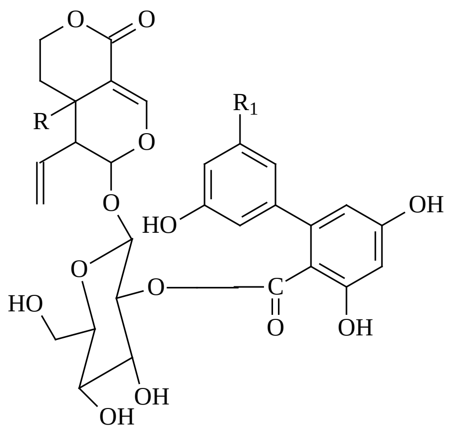
Constituents

The characteristic constituents of gentian root are secoiridoids (gentiopicroside, 1-4%, gentiamarin, amarogentin, amarosverin, amaropanin), oligosaccharides (bitter tasting gentianose and gentiobiose), xanthones (e.g. gentisin, a yellow colouring matter), alkaloids and traces of essential oil.

Bitter value of gentiopicroside is: 12 000; amaropanin: 20 000 000; amarogentin: 58 000 000.



gentiopicroside



R = R_1 = H amaropanin
R = H R_1 = OH amarogentin
R = OH R_1 = OH amarosverin

Figure 3.29-32
The structure of gentiopicroside, amarogentin, amarosverin and amaropanin

Uses

Gentian is a bitter tonic, appetizer (in case of anorexia too). It has cholagogue effect. It is also used in liqueur industry. The drug can reduce dyspeptic complaints.

Dosage

Adult and elderly single dose: 0.1-2 g of the drug in 150 ml of water in infusion, decoction or maceration, up to 3 times daily. Tincture (1:5, ethanol 45-70% V/V): average single dose of 1 ml, up to 3 times daily. Hydroethanolic extracts of equivalent bitterness value.

Children, average daily dose: 4-10 years of age: 1-2 g of the drug, 10-16 years of age: 2-4 g; in ethanol-free dosage forms.

For oral use in liquid preparations: in anorexia a single dose administered half to one hour before a meal, in dyspeptic complaints a single dose after the meal.

Overdose may lead to nausea or even vomiting.

Contra-indication

Patients with gastric or duodenal ulcer or hyperacidity should not consume gentian products.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation. Gentisin, a xanthone component, was proven to be a mutagen *in vitro*.

Centaurii herba

Plant

Centaurium erythraea Rafn. – Centaury (Gentianaceae)

The plant is native to Europe and Asia.

Figure 3.33
Centaury (*Centaurium erythraea* Rafn.)

Drug

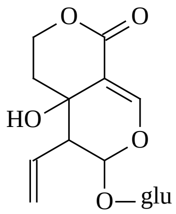
Centaurii herba (Centaury, Ph. Eur.)

Centaury consists of the whole or cut dried flowering aerial parts of *Centaurium erythraea* Rafn (*C. minus* Moench, *C. umbellatum* Gilib., *Erythraea centaurium* (L.) Pers.). Centaury has a very bitter taste.

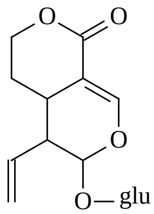
Figure 3.34
Centaurii herba (Centaury)

Constituents

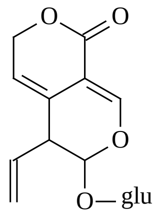
Bitter-tasting constituents are secoiridoids**,** principally swertiamarin, gentiopicrin and sweroside, with bitterness values of about 12.000. Another secoiridoid, centapicrin, has a bitterness value of 4.000.000. Other iridoids include centauroside (a dimeric secoiridoid), secologanin, 6’-*m*-hydroxy-benzoyl-loganin, dihydrocornin (a cyclopentane iridoid) and the secoiridoid alkaloid gentianine. Various methoxylated xanthones are also present. Other constituents are flavonoids, triterpenes, phenolic acids (*p*-coumaric, ferulic).



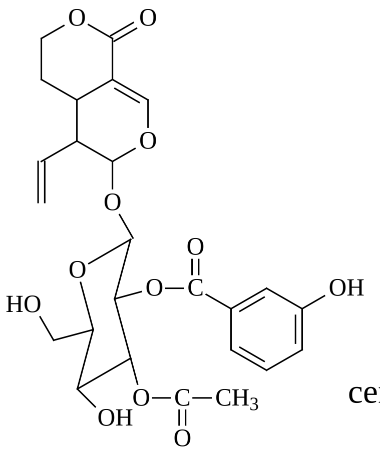
swertiamarin



sweroside



gentiopicrin



centapicrin

Figure 3.35-38
The structure of swertiamarin, sweroside, gentiopicrin and centapicrin

Uses

Therapeutic indications of the drug include dyspeptic complaints and lack of appetite. It can be used as a bitter tonic, cholagogue and appetizer.

Dosage

Adults: 1-4 g of the drug as a maceration, infusion or decoction in 150 ml of water, up to 3 times daily. 2-4 ml of liquid extract (1:1, ethanol 25% V/V), up to 3 times daily. Tincture (1:5, ethanol 70% V/V): 2-5 g daily.

Children: proportion of adult dose according to age or body weight, in ethanol-free dosage form.

For oral use in liquid preparations: for lack of appetite a single dose administered half to one hour before a meal, in dyspeptic complaints a single dose after the meal.

Overdose may lead to nausea or even vomiting.

Contra-indication

Patients with gastric or duodenal ulcer or hyperacidity should not consume centaury products.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

Menyanthidis trifoliatae folium

Plant

Menyanthes trifoliata L. – Bogbean (Menyanthaceae)

The plant is native to Middle- and North-America, Europe, Asia. In Hungary it is protected.

Figure 3.39
Bogbean (*Menyanthes trifoliata* L.)

Drug

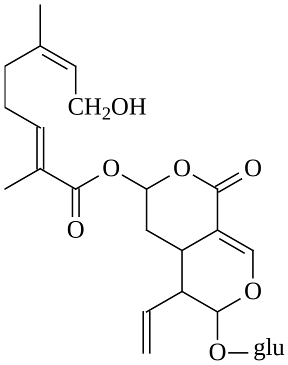
Menyanthidis trifoliatae folium (Bogbean leaf, Ph. Eur.)

Bogbean consists of the dried, entire or fragmented leaf of *Menyanthes trifoliata* L. It has very bitter and persistent taste.

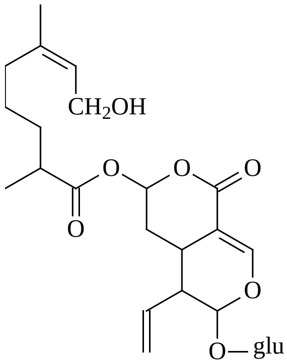
Figure 3.40
Menyanthidis trifoliatae folium (Bogbean leaf)

Constituents

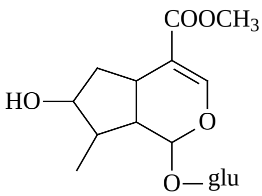
The bitter-tasting constituents are secoiridoids such as foliamenthin and dihidrofoliamenthin, and the iridoid loganin. Other constituents include a monoterpene-alkaloid, flavonoids, triterpenes and coumarins.



foliamenthin



dihidrofoliamenthin



loganin

Figure 3.41-43
The structure of foliamenthin, dihidrofoliamenthin and loganin

Uses

It is a stomachic and bitter tonic. It has antibacterial activity.

Dosage

Single dose: 0.5-1 g as an infusion.

Overdose of the drug may lead to diarrhoea and vomiting.

Contra-indication

Patients with gastric or duodenal ulcer, hyperacidity or appendicitis should not consume bogbean products.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

Oleae folium

Plant

Olea europea L. – Olive tree (Oleaceae)

The plant is native to the Mediterranean countries.

Figure 3.44
Menyanthidis trifoliatae folium (Bogbean leaf)

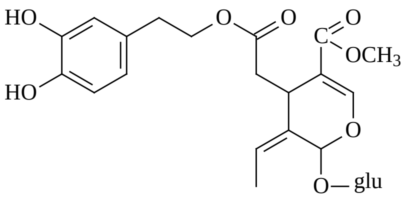
Drug

Oleae folium (Olive tree leaf)

The drug consists of the dried, entire or fragmented leaf of *Olea europea* L.

Constituents

The main constituents are secoiridoids such as oleuropein, flavonoids and triterpenes.



oleuropein

Figure 3.45
The structure of oleuropein

Uses

The leaf extract has spasmolytic effect, it can reduce blood pressure. It is used agains atherosclerosis. The fatty oil (olive oil) extracted from the seeds is principally used.

Dosage

Single dose: 7-8 g as an infusion, 3 times daily.

Chapter 4

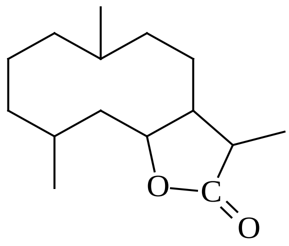
Drugs containing sesquiterpenes, diterpenes and terpenophenols

4.1 Sesquiterpenes

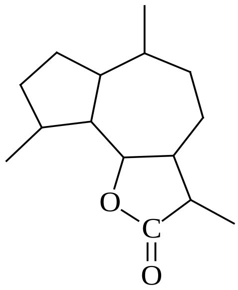
Sesquiterpenes are compounds containing 15 C-atoms. They are biogenetically derived from farnesyl pyrophosphate and may be linear, monocyclic or bicyclic in structure. They constitute a very large group of secondary metabolites, some having been shown to be „stress compounds" formed as a result of disease or injury. More than 100 different types of sesquiterpene skeletons and thousands of sesquiterpenes are known: some of them are components of volatile oils (sesquiterpene hydrocarbons and alcohols). Sesquiterpenes containing strongly oxidized functional groups (hydroxy, epoxy, aldehyde, carbonyl, carboxyl, ester, lactone) are solid, crystalline compounds and sesquiterpene-glycosides are crystalline compounds, too. They are characteristic compounds, first of all, in the plant family *Asteraceae* (= Compositae). Their proven pharmacological effects include: stomachic, anti-inflammatory, sedative, analgesic and antispasmodic to smooth muscle. However, a number of sesquiterpenes can cause allergy: e.g. pollen of *Ambrosia artemisiifolia* (ragweed, incorrectly wild hemp).

Sesquiterpene Lactones

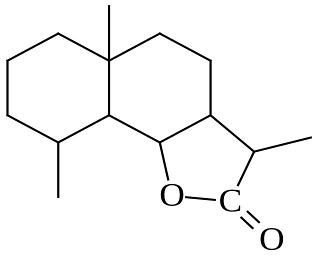
They are particularly characteristic of the *Asteraceae*, but also occur in other plant families. Not only have they received attention from chemical and chemotaxonomic viewpoints, but may also possess antitumor, cytotoxic and antimicrobial activities, as well. They can be responsible for skin allergies in humans and they also act as insect deterrents. Chemically the compounds can be classified according to their carbocyclic skeletons, thus from the germacranolides can be derived the guaianolides, eudesmanolides, xanthanolides (**Figure 4.1**), etc. A structural feature of all these compounds, which appears to be associated with much of the biological activity, is the α,β-unsaturated-γ-lactone. Species of *Asteraceae* containing sesquiterpene lactones include *Taraxacum officinale* (dandelion), *Artemisia absinthium*, *Cichorium* spp., *Eupatorium* spp. Sesquiterpene lactones of Umbelliferae are interesting in that the usual skeletal types (germacranolides, guaianolides, etc.) are found but all differ in their stereochemisty from the analogous compounds of the Compositae.



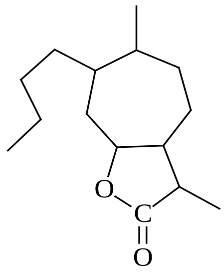
germacranolides



guaianolides



eudesmanolides



xanthanolides

Figure 4.1
The most important carbocyclic skeletons of sesquiterpene lactones

Drugs

Matricariae flos

Plant

Matricaria recutita L. – Chamomile (Asteraceae)

The plant is native to and cultivated in southern and eastern Europe. The flowers bloom in early to midsummer, and have a strong, aromatic smell. The flowers are collected in dry weather and are carefully dried.

Figure 4.2
Chamomile (*Matricaria recutita* L.)

Drug

Matricariae flos (Matricaria flower, Ph. Eur.). **Other drugs:** *Matricariae aetheroleum* (Matricaria oil, Ph.Eur.), *Matricariae extractum fluidum* (Matricaria liquid extract, Ph. Eur.)

Matricaria flower consists of the dried flower-heads of *Matricaria recutita* L. (syn.: *Chamomilla recutita* (L.) Rausch). It contains not less than 4 ml/kg of blue essential oil. Matricaria liquid extract is produced from *Matricaria flower*. It contains not less than 0.30% of blue residual oil. It is a brownish, clear liquid with an intense characteristic odour and characteristic bitter taste; miscible with water and with alcohol with development of turbidity, soluble in alcohol (50% *V/V*).

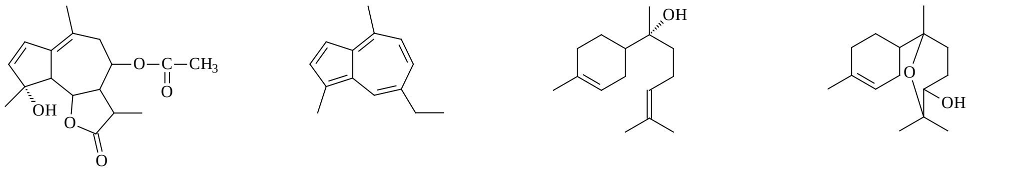
Figure 4.3
Matricariae flos (Matricaria flower)

Matricaria oil is a blue essential oil obtained by steam distillation from the fresh or dried flower-heads or flowering tops of *Matricaria recutita* L. (*Chamomilla recutita* L. Rauschert). There are 2 types of matricaria oil which are characterised as rich in bisabolol oxides, or rich in levomenol. Matricaria oil is a clear, intensely blue, viscous liquid. It has an intense characteristic odour.

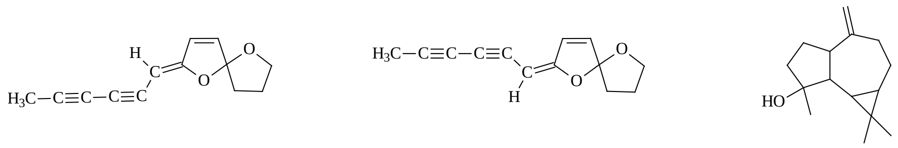
Matricaria liquid extract is produced from *Matricaria flower*. It contains not less than 0.30% of blue residual oil. The extract is produced from the drug and a mixture of 2.5 parts of a 10% *m/m* solution of ammonia (NH_3), 47.5 parts of water and 50 parts of alcohol with an appropriate procedure for liquid extracts. Matricaria liquid extract is a brownish, clear liquid with an intense characteristic odour and characteristic bitter taste; miscible with water and with alcohol with development of turbidity, soluble in alcohol (50% *V/V*).

Constituents

The main active constituent of matricaria flower is essential oil (0.5-1.5%). The essential oil contains approximately 50% of the sesquiterpenes (-)-α-bisabolol and its oxides A, B and C, bisabolonoxide A, up to 25% of cis-and trans-en-yn-dicycloethers (or spiroethers) and chamazulene (up to 15%). A number of chemotypes depending on the proportions of bisabolol, bisabolol oxides and farnesene in the oil have been described. Other constituents of matricaria flower include coumarins, flavone derivatives (apigenin-7-glucoside, 0.5%), phenolic acids and polysaccharides (10%).



matricin chamazulene α-bisabolol bisabolol oxide A



cis-spiroether *trans*-spiroether spatulenol

Figure 4.4-10
The structure of matricin, chamazulene, α-bisabolol, bisabolol oxide A,
cis-spiroether, *trans*-spiroether and spatulenol

Uses

Matricaria flower is used in the symptomatic treatment of gastrointestinal complaints such as minor spasms, flatulence and belching. It has spasmolytic, anti-inflammatory, antibacterial and immunstimulant effects. The ulcer protective properties of German chamomile have been ascribed to bisabolol-type constituents. The drug can also be used for treating minor inflammations of skin and mucosa, including the oral cavity, the gums, the respiratory tract and the anal and genital area.

Dosage

Internal use

Adults: As a tea infusion 3 g of the drug in 150-200 ml of water, three to four times daily.

Fluid extract (1:2, 50% ethanol): 3-6 ml daily. Dry extract: 50-300 mg three times daily.

Elderly: Dose as for adults.

Children: proportion of adult dose according to age or body weight.

External use

For compresses, rinses, gargles: 3-10% m/V infusion or 1% V/V fluid extract or 5% V/V tincture.

For bath: 5 g of the drug, or 0.8 g of alcoholic extract, per litre of water.

For vapour inhalation: 10-20 ml of alcoholic extract per litre of hot water.

Undesirable effects

Rare cases of contact allergy have been reported. *Matricaria* flower of the bisabolol oxide B-type can contain traces of the contact allergen anthecotulide. Most of the described allergic reactions to matricaria were due to contamination with *Anthemis cotula* or related species, which contain high amounts of anthecotulide. However, in cases where matricaria contact allergy has been acquired, cross-reactions to other sesquiterpene lactone-containing plants are common.

Chamomillae romanae flos

Plant

Chamaemelum nobile (L.) All. – Roman chamomile (Asteraceae)

The plant is cultivated in the south part of England, and in Belgium, France, Germany, Hungary, Poland, former Yugoslavia, Bulgaria, Egypt and Argentina. As a result of long cultivation most of the tubular florets present in the wild plant have become ligulate, and it is these 'double' flower-heads which form the commercial drug.

Drug

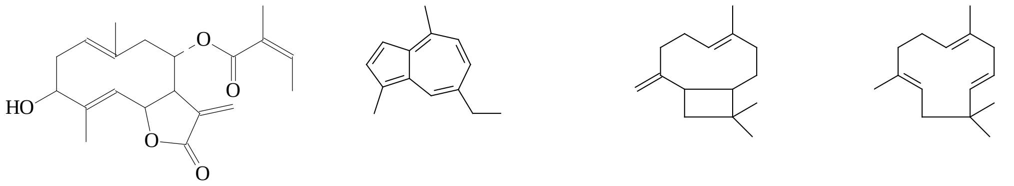
Chamomillae romanae flos (Chamomile flower, Roman, Ph. Eur.)

Roman chamomile flower consists of the dried flower-heads of the cultivated double variety of *Chamaemelum nobile* (L.) All. (*Anthemis nobilis* L.). It contains not less than 7 ml/kg of essential oil.

Figure 4.11
Chamomillae romanae flos (Chamomile flower, Roman)

Constituents

Roman chamomile flowers contain essential oil (0.4-2.4%) which is blue when freshly distilled owing to the presence of azulene. The amount of chamazulene depends on the age and place of origin of the plant. Other components of the oil are *n*-butyl angelate and the esters of iso-butyric acid and tiglic acid. The drug also contains sesquiterpene lactones of the germacranolide type (nobilin, 3-epinobilin), coumarins, flavonoids and phenolic acids (caffeic acid).



nobilin chamazulene β-caryophyllene humulene

Figure 4.12-15
The structure of nobilin, chamazulene, β-caryophyllene and humulene

Uses

The medicinal use of roman chamomile flower is similar to that of matricaria flower. It is used in the symptomatic treatment of gastrointestinal complaints such as spasms and flatulence. It has spasmolytic, anti-inflammatory and carminative effects.

Dosage

Internal use

Adults: 3-12 g (daily dose) of the drug for making tea infusion.

Contra-indication

Sensitivity to *Chamaemelum* or other members of the Compositae.

Millefolii herba

Plant

Achillea millefolium s.l. (L.) – Yarrow (Asteraceae)

Yarrow is native to Europe and Western Asia but is widespread in most temperate regions including North America. It is an extremely diverse aggregate species with varying chromosome numbers and differences in oil composition.

Figure 4.16
Yarrow [*Achillea millefolium* s.l. (L.)]

Drug

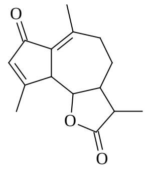
Millefolii herba (Yarrow, Ph. Eur.)

Yarrow consists of the whole or cut, dried flowering tops of *Achillea millefolium* L. It contains not less than 2 ml/kg of essential oil and not less than 0.02% of proazulenes, expressed as chamazulene, both calculated with reference to the dried drug.

Figure 4.17
Yarrow [*Achillea millefolium* s.l. (L.)]

Constituents

The main active constituent of yarrow is essential oil (0.1-0.4%). The tetraploid form of the plant produces higher amounts of chamazulene in the oil than the hexaploid species. Germacranolide- and eudesmanolide-type sequiterpenes are also constituents of the oil together with caryophyllene, sabinene and borneol. Other constituents include sesquiterpene lactones (e.g. achillin), flavonoids (apigenin, luteolin), alkaloids (betonicine), triterpenes and sterols.



achillin

Figure 4.18
The structure of achillin

Uses

Yarrow is used, as is chamomile and matricaria, to treat various skin conditions and gastrointestinal problems (lack of appetite, dyspepsia). Female patients with the inflammation of the lesser pelvis can also use the drug infusion as a bath. The drug can be used for the symptomatic treatment of minor spasm associated with menstrual periods.

Dosage

Internal use

Adults: As a tea infusion 4 g of the drug in 150-200 ml of water, three times daily.

External use

For bath: 100 g of the drug to 20 litre of water.

Undesirable effects

Contact allergy may occur. Thujone present in the essential oil may cause abortion, therefore the drug is not recommended during pregnancy (and lactation).

Absinthii herba

Plant

Artemisia absinthium L. – Wormwood (Asteraceae)

It is native to temperate regions of Eurasia and northern Africa, and it can be cultivated, too.

Figure 4.19
Wormwood (*Artemisia absinthium* L.)

Drug

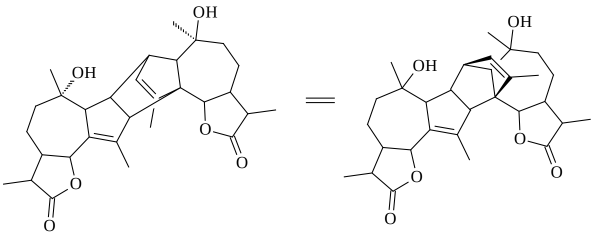
Absinthii herba (Wormwood, Ph. Eur.)

Wormwood consists of the basal leaves or slightly leafy, flowering tops, or of a mixture of these dried, whole or cut organs of *Artemisia absinthium* L. It contains not less than 2 ml/kg of essential oil, calculated with reference to the dried drug.

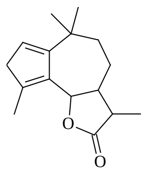
Figure 4.20
Absinthii herba (Wormwood)

Constituents

The main active constituents of wormwood are sesquiterpene lactones (0.15-0.4%) (principally the guaianolides absinthin and artabsin), which are responsible for the bitter taste of the drug. The esssential oil composition is very different according to the source of the plant. The most important components are *cis*-epoxyocimene (40%), *β*-thujone, spatulenol, *trans*-sabinyl acetate. Other constituents include flavonol glycosides, phenolic acids and tannins.



absinthin



artabsin

Figure 4.21-22
The structure of absinthin and artabsin

Uses

Wormwood is used to treat dyspeptic complaints, gastritis and gastrointestinal problems. It is an appetizer.

Dosage

Internal use

Adult single dose: As a tea infusion 1-1.5 g of the drug in 150 ml of water, up to three times daily. *Elderly*: dose as for adults. Children: proportional of adult dose according to body weight. The dosage may be adjusted according to the bitterness sensitivity of the individual.

Wormwood should not be taken continuously for periods of more than 3-4 weeks.

Overdose: excessive doses of wormwood preparations may cause vomiting, severe diarrhoea, retention of urine or dazed feelings. Overdose of alcoholic preparations or the use of the essential oil may cause central nervous system disturbances, which can lead to convulsions and ultimately to unconsciousness and death.

Contra-indications

In the case of gastric and duodenal ulcers.

Pregnancy and lactation

The drug and its preparations should not be used during these periods.

Cardui benedicti herba

Plant

Cnicus benedictus L. - St. Benedict's thistle or Holy thistle (Asteraceae)

It is native to the Mediterranean region, from northern Portugal to southern France and east to Iran. It is known in other parts of the world, including parts of North America, as an introduced species.

Figure 4.23
St. Benedict's thistle or Holy thistle (*Cnicus benedictus* L.)

Drug

Cardui benedicti herba (St. Benedict's thistle flowering shoot)

Holy thistle consists of the whole or cut, dried flowering tops of *Cnicus benedictus* L.

Figure 4.24
Cardui benedicti herba (St. Benedict's thistle flowering shoot)

Constituents

The main active constituents of the drug are sesquiterpene lactones (e.g. cnicin, artemisiifolin). Other constituents include essential oil (*p*-cymene, fenchone, cinnamic aldehyde), lignans (e.g. arctigenin) and flavonoids.

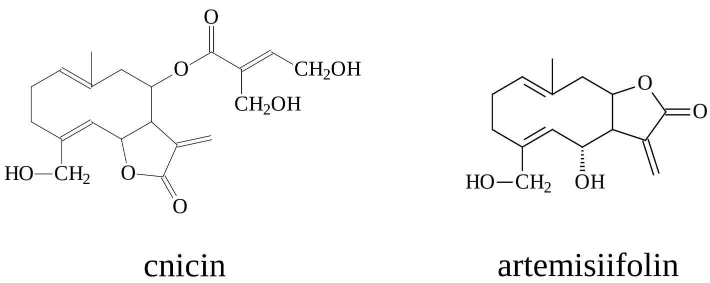


Figure 4.25-26
The structure of cnicin and artemisiifolin.

Uses

Holy thistle is used to treat gastrointestinal problems. It is an appetizer and can induce the production of gastric juice.

Dosage

Internal use

Adult single dose: As a tea infusion 1-1.5 g of the drug in 150 ml of water, up to three times daily. *Elderly*: dose as for adults.

Inulae radix

Plant

Inula helenium L. – Elecampane (Asteraceae)

It is a perennial plant common in many parts of Great Britain, and ranges throughout central and Southern Europe, and in Asia as far eastwards as the Himalayas. It is naturalized in North America. The plant is protected in Hungary.

Figure 4.27
Elecampane (*Inula helenium* L.)

Drug

Inulae radix (Elecampane root)

The root is thick, branching and mucilaginous, and has a warm, bitter taste and a camphoraceous odor.

Figure 4.28
Inulae radix (Elecampane root)

Constituents

The main active constituents of the drug are sesquiterpene lactones (alantolactone, isoalantolactone). Other constituents include inulin (44%), essential oil and triterpenes.

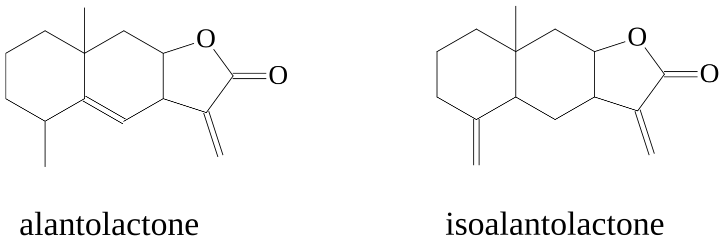


Figure 4.29-30
The structure of alantolactone and isoalantolactone.

Uses

The drug is used to treat respiratory problems because of its expectorant and antibacterial effects. It has diuretic activity.

Dosage

Internal use

Adult single dose: As a tea infusion 1 g of the drug in 150 ml of water, up to three times daily. *Elderly*: dose as for adults.

Arnicae flos

Plant

Arnica montana L. – Arnica (Asteraceae)

Arnica montana is endemic to Europe, from southern Iberia to southern Scandinavia and the Carpathians. It is absent from the British Isles and the Italian and Balkan Peninsulas. *A. montana* grows in nutrient-poor siliceous meadows up to nearly 3,000 metres.

Drug

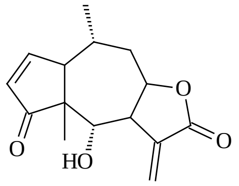
Arnicae flos (Arnica flower, Ph. Eur.)

Arnica flower consists of the whole or partially broken, dried flower-heads of *Arnica montana* L. It contains not less than 0.40% *m/m* of total sesquiterpene lactones expressed as dihydrohelenalin tiglate, calculated with reference to the dried drug.

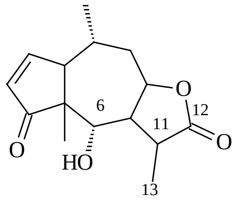
Figure 4.31
Arnicae flos (Arnica flower)

Constituents

The main active constituents of the drug are sesquiterpene lactones (pseudoguaianolide type, 0.2-0.8%), principally helenalin and its esters with acetic, tiglic and other carboxylic acids. Other constituents include diterpenes, flavonoids, pyrrolizidine alkaloids (tussilagine), essential oil containing fatty acids, and carotenoids.



helenalin



11,13-dihydrohelenalin

Figure 4.32-33
The structure of helenalin and 11,13-dihydrohelenalin.

Uses

The drug is used to treat bruises, sprains, inflammation caused by insect bites and rheumatic complaints. The best herbal medicine for treatment of wounds and injuries.

Dosage

Only External use

Ointments, creams, gels or compresses made with 5-25% V/V tinctures or 5-25% V/V fluid extracts, diluted tincture (1:3 to 1:10), diluted fluid extracts or a decoction of 2.0 g of dried arnica flower in 100 ml of water. Not to be used on open wounds.

Contra-indications

Allergy to *Arnica* or other members of the Asteraceae may occur.

Undesirable effects

Skin irritation has been reported. Contact dermatitis may develop in susceptible individuals.

Pregnancy and lactation

There is no restriction for external use, no harmful effects have been reported.

Cichorii radix

Plant

Cichorium intybus L. - Chicory (Asteraceae)

It is indigenous to Europe and is now widespread in northern states of the USA, Canada and parts of Asia. It is widely cultivated.


Figure 4.34
Chicory (*Cichorium intybus* L.)

Drug

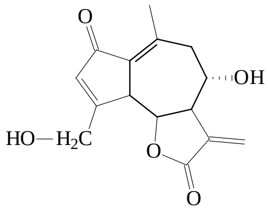
Cichorii radix (Chicory root)

The root consists of the dried roots of *Cichorium intybus* L.

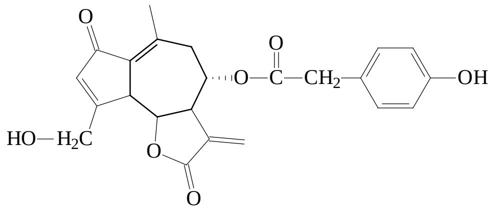
Figure 4.35
Cichorii radix (Chicory root)

Constituents

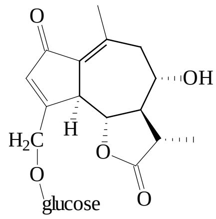
The dried roots contain a high proportion (up to 58%) of inulin together with other sugars. Other important constituents include various sesquiterpene lactones and glycosides, e.g. lactucin, lactucopicrin, cichorioside B (eudesmane type), 8-deoxylactucin (guaiane type) and picriside B (germacrane type).



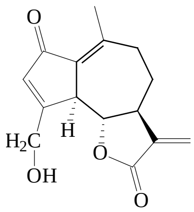
lactucin



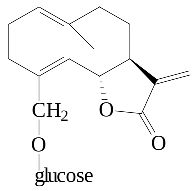
lactucopicrin



cichorioside B
(eudesmane type)



8-deoxylactucin
(guaiane type)



picriside B
(germacrane type)

Figure 4.36-40
The structure of lactucin, lactucopicrin, cichorioside B (eudesmane type), 8-deoxylactucin (guaiane type) and picriside B (germacrane type).

Uses

Decoction of the root is used as a diuretic and to treat liver ailments. The root is also used as a tonic and laxative. The roasted roots are well-known for their use in coffee mixtures and as a coffee substitute.

Dosage

Adults: one dose is 1.5-2 g in 150 ml of water, decoction can be used.

Taraxaci radix

Plant

Taraxacum officinale Weber s.l. - Dandelion (Asteraceae)

It is indigenous to Europe and Asia.

Figure 4.41
Dandelion (*Taraxacum officinale* Weber s.l.)

Drug

Taraxaci radix (Dandelion root)

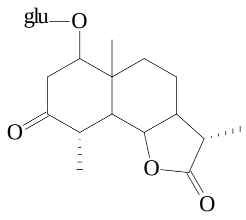
Dandelion root consists of the dried roots and rhizomes of *Taraxacum officinale* Weber s.l.

This drug is official in the Österreichisches Arzneibuch.

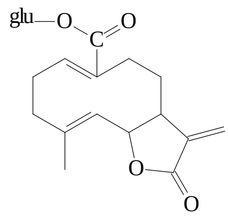
Figure 4.42
Taraxaci radix (Dandelion root)

Constituents

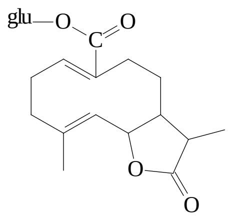
The dried roots contain sesquiterpene lactones including taraxacolide-O-β-D-glucoside, taraxinic acid-β-D-glucoside, and 11,13-dihydro-taraxinic acid- β-D-glucoside. Other constituents are triterpenes, phytosterols (e.g. taraxasterol), γ-butyrolactone glucoside ester (taraxacoside), chlorogenic acid, caffeic acid, potassium and amino acids. In autumn the dried root contains up to 40% of inulin, in spring about 2%.



taraxacolide-O-β-D-glucoside



taraxinic acid-β-D-glucoside



11,13-dihydro-taraxinic acid- β-D-glucoside

Figure 4.43-45
The structure of taraxacolide-O-β-D-glucoside, taraxinic acid-β-D-glucoside, and 11,13-dihydro-taraxinic acid- β-D-glucoside.

Uses

The most relevant therapeutic indications of the drug include the restoration of hepatic and biliary function, treatment of dyspepsia and loss of appetite. The plant extract has a bitter taste. It has choleretic effect.

Dosage

Adults: 3-5 g of the drug or 5-10 ml of tincture (1:5, ethanol 25% V/V), three times daily.

Contra-indications

The drug and its preparation should not be used in case of occlusion of the bile ducts, gall-bladder empyema and obstructive ileus.

Undesirable effects

The drug can produce allergic contact dermatitis due to the presence of the sesquiterpene lactone taraxinic acid β-glucopyranosyl ester.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Tanaceti parthenii herba

Plant

Tanacetum parthenium (L.) Schulz Bip. – Feverfew (Asteraceae)

The plant is indigenous to South-East-Europe, the Caucasus, and Hungary, too.

Figure 4.46
Feverfew (*Tanacetum parthenium* (L.) Schulz Bip.)

Drug

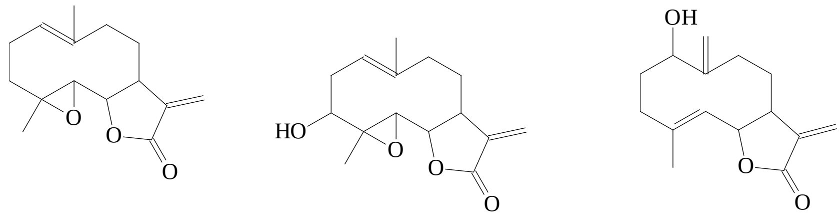
Tanaceti parthenii herba (Feverfew, Ph. Eur.)

Feverfew consists of the dried, whole or fragmented aerial parts of *Tanacetum parthenium* (L.) Schultz Bip. It contains not less than 0.20% of parthenolide, calculated with reference to the dried drug. Fewerfew has a camphoraceous odour.

Figure 4.47
Tanaceti parthenii herba (Feverfew)

Constituents

The characteristic constituents are sesquiterpene lactones with germacranolide structure, e.g. parthenolide, 3-hydroxi-partenolide and artemorine. Quaianolide-type components (canin) occur in significantly smaller amounts. Other constituents include essential oil (its components: camphor, chrysanthemol, *p*-cimene, borneol) and flavonoids.



parthenolide 3-hydroxi-partenolide artemorine

Figure 4.48-50
The structure of parthenolide, 3-hydroxi-partenolide and artemorine.

Uses

The most relevant therapeutic indications of the drug include the prophylaxis of migraine.

Dosage

Adults daily dose: 50-120 mg of powdered drug or equivalent preparations. Treatment for at least a few months is recommended.

Contra-indications

The drug and its preparation should not be used in case of hypersensitivity to feverfew or other members of the *Asteraceae* family.

Undesirable effects

Allergic contact dermatitis, tongue irritation and inflammation may occur. Cases of abdominal pain and indigestion in patients who have taken the drug for long periods have been reported. Rare cases of diarrhoea, flatulence, nausea or vomiting have been noted.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Cynarae folium

Plant

Cynara scolymus L. – Artichoke (Asteraceae)

It is a cultivated plant, but native to Mediterranean countries. It is an important plant of food industry.

Figure 4.51
Artichoke (*Cynara scolymus* L.)

Drug

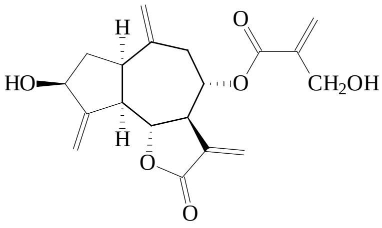
Cynarae folium (Artichoke leaf, Ph. Eur.)

Artichoke leaf consists of the whole or cut, dried leaves of *Cynara scolymus* L. (C. *cardunculus* L. subsp. *flavescens* Wiklund.). It contains not less than 0.8% of chlorogenic acid calculated with reference to the dried drug.

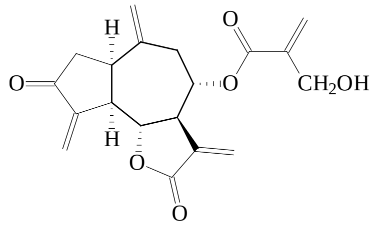
Figure 4.52
Cynarae folium (Artichoke leaf)

Constituents

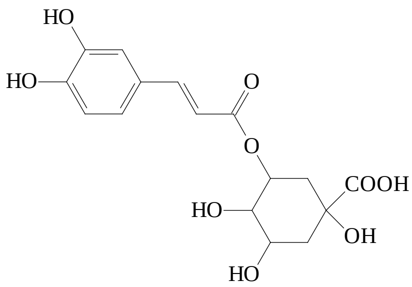
The main characteristic constituents are phenolic derivatives including caffeoylquinic acids, e.g. chlorogenic acid and 1,5-dicaffeoylquinic acids, and flavonoids, e.g. luteolin 7-glucoside (cynaroside), 7-rutinoside (scolymoside). Bitter-tasting sesquiterpene lactones, e.g. cynaropicrin, and various aliphatic acids, especially hydroxy acids, e.g. malic, lactic acids, also present. Cynarin (1,3-dicaffeoylquinic acids) found only in traces in the fresh or dried leaf, is generated from 1,5-dicaffeoylquinic acids during processing with hot water.



cynaropicrin



dehydrocynaropicrin



chlorogenic acid

Figure 4.53-55
The structure of cynaropicrin, dehydrocynaropicrin and chlorogenic acid.

Uses

The most relevant therapeutic indications of the drug include digestive complaints (e.g. stomach ache, nausea, vomiting, feeling of fullness, flatulence) and hepatobiliary disturbances. Adjuvant to a low fat diet in the treatment of mild to moderate hyperlipidaemia.

Dosage

Adults and elderly daily dose: 5-10 g of dried leaf as an aqueous dry extract or infusion or other equivalent preparations.

Children over 4 years: proportion of adult dose according to age or body weight.

Contra-indications

The drug and its preparations should not be used in case of obstruction of the bile duct or known allergy to artichoke or other species of the Asteraceae.

Special warnings

Patients with cholelithiasis should take artichoke leaf only after consulting a physician.

Undesirable effects

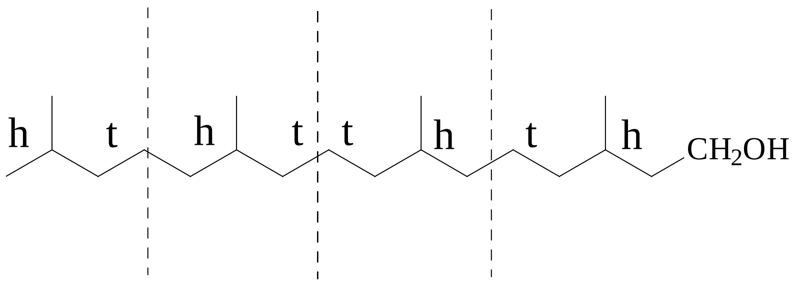
Mild gastro-intestinal disturbances may occur in rare cases, allergic reactions might occur in sensitized patients.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

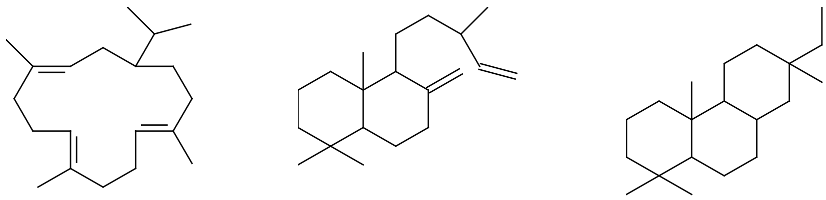
4.2 Diterpenes

Diterpenes are terpenoids with 20 C-atoms. The general formula of diterpene hydrocarbons is: $4 \times (C_5H_8) = C_{20}H_{32}$. They contain 4 isoprene units. The fundamental compound, gerano-geranyl-pyrophosphate is formed from two molecules of geranyl-pyrophosphate or from one molecule of pharnesyl-pyrophosphate and from one molecule of dimethylallyl-pyrophosphate. The number of diterpenes with known structure is more than 600 to date. They may be open chained or cyclic. The most important representative of the open-chained diterpenes is phytol (**Figure 4.56**), which can be found in the structure of chlorophyll-A, chlorophyll-B, and vitamin K1. The most important diterpenes having cyclic structure are cembrane, labdane and pymarane (**Figure 4.57-59**). Diterpenes possess cytotoxic, antibacterial, antifungal, antiviral, anti-inflammatory, spasmolytic and cardioactive effects.



h = head
t = tail

Figure 4.56
The structure of phytol.



cembrane labdane pymarane

Figure 4.57-59
The most important types of diterpenes.

Drugs

Colophonium

Plant

Pinus sp. – Pine (Pinaceae)

Pinus species are native to most of the Northern Hemisphere and they live throughout most temperate and subtropical regions of the world. They are cultivated as ornamental plants in parks and gardens.

Figure 4.60
Scots pine (*Pinus sylvestris* L.)

Drug

Colophonium (Colophony, Ph. Eur.)

The drug is the residue remaining after distillation of the volatile oil from the oleoresin obtained from various species of *Pinus*.

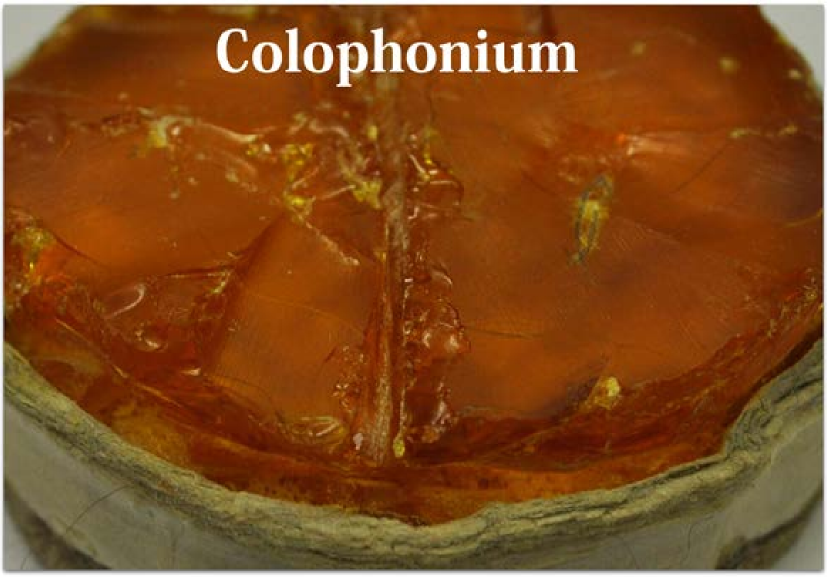


Figure 4.61
Colophonium (Colophony)

Constituents

The resin contains 90 % of diterpene resin acids, especially abietic acid.

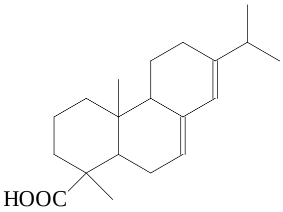


Figure 4.62
The structure of abietic acid.

Uses

Colophony can be used for preparation of rubefacient plasters and ointments. It has also been used to formulate microcapsules and nanoparticles.

Contra-indications

The drug and its preparations should not be used in case of known allergy to the resin.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Marrubii herba

Plant

Marrubium vulgare L. – White horehound (Lamiaceae)

This perennial plant is native to Europe, temperate zone of Asia, North-Africa and India. It may be cultivated.

Figure 4.63
White horehound (*Marrubium vulgare* L.)

Drug

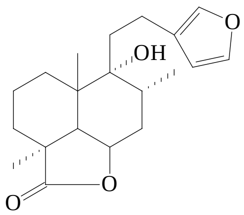
Marrubii herba (White horehound, Ph. Eur.)

The drug consists of the whole or cut, dried flowering part of *Marrubium vulgare* L.

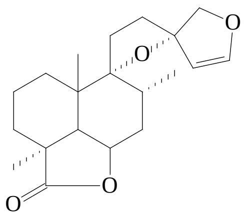
Figure 4.64
Marrubii herba (White horehound)

Constituents

The main characteristic constituents of the drug are diterpenes (e.g. premarrubiin and marrubiin). Other characteristic constituents include essential oil (with *p*-cymene, limonene, α-pinene), triterpenes and flavonoids.



marrubiin



premarrubiin

Figure 4.65-66
The structure of premarrubiin and marrubiin.

Uses

The drug and its products can be used as expectorant in cough associated with cold. It is also used for symptomatic treatment of mild dyspeptic complaints such as bloating and flatulence and in the treatment of temporary loss of appetite.

Dosage

Adults and elderly daily dose: Herbal tea: 1-2 g of the comminuted herbal substance in 250 ml of boiling water as a herbal infusion, 3 times daily. Daily dose: 3-6g.

Liquid extract (1:1; 20-30% V/V ethanol): Single dose: 1.5-4 ml, 3 times daily. Daily dose: 4.5-12 ml.

Contra-indications

The drug and its preparations should not be used in case of hypersensitivity to the active substance and to other plants of the Lamiaceae family and obstruction of the bile duct, cholangitis, liver disease and ileus.

Special warnings

Patients with active peptic ulcer, gallstones and any other biliary disorders should consult a doctor before using *Marrubii herba* preparations. The use in children under 12 years of age has not been established due to lack of adequate data.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Ballotae nigrae herba

Plant

Ballota nigra L. – Black horehound (Lamiaceae)

This perennial plant is native to Europe (Mediterranean region), central Asia and the eastern part of United States.

Figure 4.67
Black horehound (*Ballota nigra* L.)

Drug

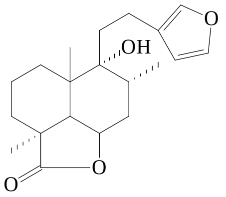
Ballotae nigrae herba (Black horehound, Ph. Eur.)

The drug consists of the dried flowering tops of *Ballota nigra* L. It contains minimum 1.5% of total *ortho*-dihydroxycinnamic acid derivatives, expressed as acteoside and calculated with reference to the dried drug.

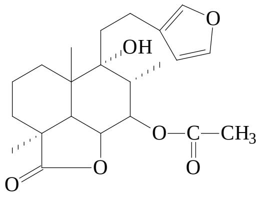
Figure 4.68
Ballotae nigrae herba (Black horehound)

Constituents

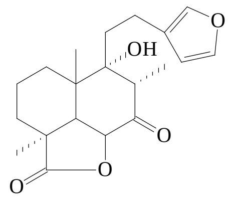
The main characteristic constituents of the drug are phenylpropanoids [e.g. the *ortho*-dihydroxycinnamic acid glucoside acteoside (or verbascoside)] and diterpenes (e.g. marrubiin, 7-acetoxymarrubiin, ballotinone, ballotenol and ballonigrin). Other characteristic constituents include flavonoids (mainly derivatives of apigenin and luteolin), chlorogenic and caffeic acids.



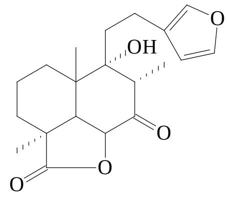
marrubiin



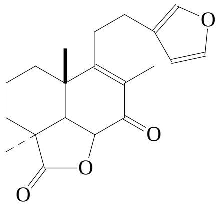
7-acetoxymarrubiin



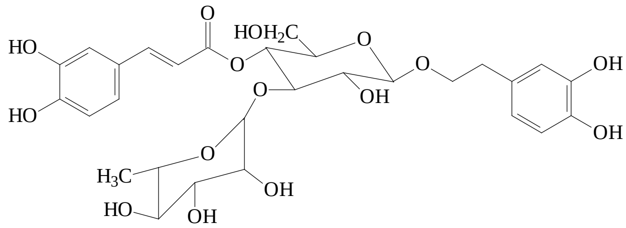
ballotinone



ballotenol



ballonigrin



verbascoside

Figure 4.69-74

The structure of marrubiin, 7-acetoxymarrubiin, ballotinone, ballotenol, ballonigrin and verbascoside.

Uses

The therapeutic indications of the drug include the tenseness, restlessness and irritability with difficulty in falling asleep. It has also been documented for the relief of mild spasmodic gastric complaints.

Dosage

Adults and elderly single dose: Herbal tea: 1.5-5 g of the drug in 250 ml of hot water.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Taxi baccatae folium

Plant

Taxus baccata L. – European yew (Taxaceae)

This plant is a conifer and native to western, central and southern Europe, northwest Africa and southwest Asia. Most parts of the tree are toxic, except the bright red aril surrounding the seeds.


Figure 4.75
European yew (*Taxus baccata* L.)

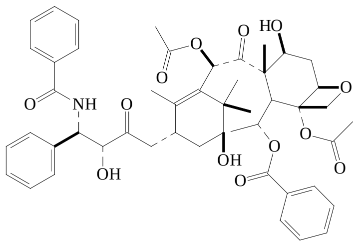
Drug

Taxi baccatae folium (European yew leaf)

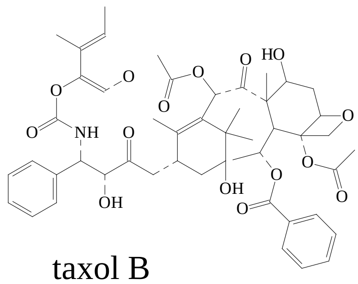
The drug consists of the dried leaves of *Taxus baccata* L.

Constituents

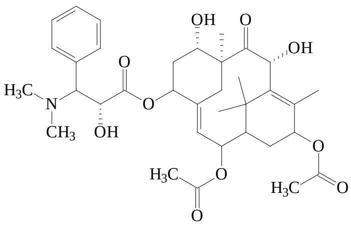
The main characteristic constituents of the drug are diterpenes containing N-atom (e.g. taxol A and B, taxin A and B). Other constituents include biflavonoids and catechin.



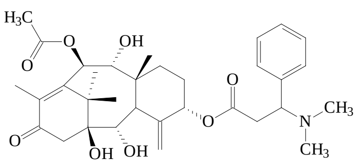
taxol A



taxol B



taxin A



taxin B

Figure 4.76-79
The structure of taxol A and B, taxin A and B.

Uses

The diterpene alkaloids of the drug are highly toxic compounds with antimitotic activity, therefore their semi-synthetic derivatives are used in cancer therapy. Paclitaxel, a mitotic inhibitor used in chemotherapy, was developed from taxol. Taxol can be isolated in higher amounts from the bark of *Taxus brevifolia* L.

4.3 Terpenophenols

Cannabinoids are the most important group of the terpenophenols, and can be isolated from hemp (*Cannabis sativa*). Cannabinoids are snythetised from geranyl pyrophosphate and a phenol compound (olivetol) (**Figure 4.80**). In the course of biosynthesis first cannabigerol is produced, then cannabidiol, cannabinol and finally tetrahydrocannabinol (THC). THC is a psychoactive constituent of the cannabis plant. *Cannabis sativa* contains it only in traces but *Cannabis sativa* subspecies *indica* is a good source of this compound. Marihuana containing 2-6% of THC and hashish containing 5-20% of THC are dangerous drugs. Hop (*Humulus lupulus* L.), also belonging to the family of Cannabaceae, contains the terpenophenol derivatives humulone and lupulone. Humulone (α-lupulic acid), a phloroglucinol derivative with three isoprenoid side-chains, is a bitter-tasting chemical compound found in the resin of mature hops. Two side-chains are prenyl groups and one is an isovaleryl group. Further details about hop can be found in **Chapter 10**.

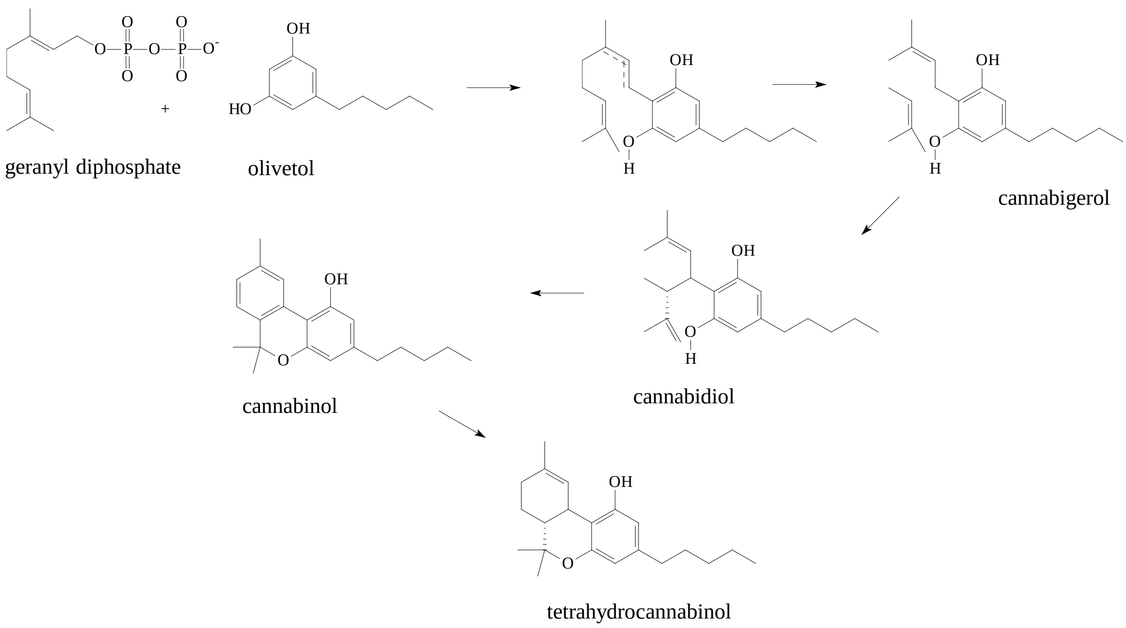


Figure 4.80
Biosynthesis of the terpenophenol tetrahydrocannabinol (THC).

Drug

Cannabis indicae herba

Plant

Cannabis sativa L. ssp. *indica* (Lam.) E. Smallet Cronquist – Indian hemp (Cannabaceae)

This dioecious plant is native to the Indian subcontinent. Despite being illegal, it is widely cultivated. The leaves, the flowering tops or the resin of the female plants are collected. The finely chopped and dried leaf is marijuana, the resin of the plant is hashish. Hash oil is a resinous matrix of cannabinoids produced by a solvent (chloroform) extraction of cannabis and the evaporation of the solvent.

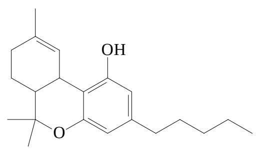
Drug

Cannabis indicae herba (Indian hemp)

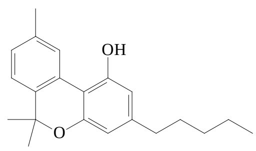
The drug consists of the dried leaves and flowering parts of *Cannabis sativa* L. ssp. *indica* (Lam.) E. Smallet Croquist.

Constituents

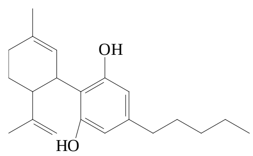
The drug contains terpenophenols such as Δ_9-THC, Δ_9-tetrahydrocannabinol, cannabinol, cannabidiol, cannabinolic acid, tetrahydrocannabinolic acid. A further constituent is about 0.1% of essential oil (with *p*-cymene, humulene).



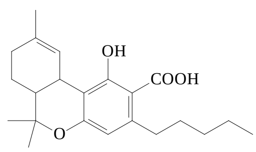
Δ_9-tetrahydrocannabinol



cannabinol



cannabidiol



Δ_9-tetrahydrocannabinolic acid

Figure 4.81-84
The structure of Δ_9-tetrahydrocannabinol, cannabinol, cannabidiol and Δ_9-tetrahydrocannabinolic acid.

Uses

The drug has sedative, antineuralgic and spasmolytic effects. Therefore in the therapy the drug and its products (e.g. Marinol) can be used for decreasing nausea following chemotherapy, relieving muscle cramps and pains of patients with multiple sclerosis and as an appetizer for patients infected with HIV. Other uses of the plant are illegal.

Chapter 5
Drugs containing triterpenes, steroids, saponins and cardenolides

5.1 Triterpenes and saponins

Triterpenes contain 30 C-atoms. They are synthetised from 6 mol isopenthenyl-pyrophosphate (IPP) or 2 mol pharnesyl-pyrophosphate (FPP; C15). They may be open-chained or cyclic (tetra- or pentacyclic) compounds. The fundamental compound of triterpene hydrocarbons is squalene: $C_{30}H_{48}$ (**Figure 5.1**). The interlocking of isoprene units is head-foot (tail); but in the middle of the molecule is foot (tail)-foot (tail). Squalene is the fundamental compound of the biosynthesis of steroids. To the skeleton of cyclic triterpenes different functional groups can be attached (-OCH_3; -CHO; -COOH; -OH; -O-C-R), therefore a large degree of structural variability is possible. If the –OH and –COOH groups are present in glycosidic form, the compounds are called *saponins*. In the case of the presence of more than two sugar-molecules, the chain of the sugar units is mostly branched. Various types and structures of triterpenes can characterize plant taxonomic categories, and they can also cause differences in their pharmacological action and solubility. Saponins have a high molecular weight and a high polarity. As glycosides they can be hydrolysed by acids to yield an aglycone (sapogenin), various sugars and related uronic acids. Based on the structure of the aglycone, two kinds of saponins can be distinguished: 1) the steroidal (commonly tetracyclic) triterpenoids and 2) the pentacyclic triterpenoid types (**Figure 5.2-5**). Both of these have a glycosidic linkage at C-3. Steroidal alkaloids occur in the Solanaceae family. These constituents possess a heterocyclic nitrogen-containing ring, giving the compounds basic properties (e.g. solasodine, **Figure 5.6**). Triterpenes are wide-spread in various plants, they occur first of all in the dicotyledonous plants. Mainly triterpene glycosides (saponins) have important pharmaceutical role. Triterpene saponins are used as expectorant, diuretics, antibacterial, antifungal, antiviral agents and to treat venous insufficiency. Saponins often prevent the absorption of other materials (e.g. drugs). Saponins hemolyse red blood cells (erythrocytes), therefore they are strongly toxic compounds if they enter into the blood vessels. Their aqueous solutions are frothy, similarly to soap-solutions.

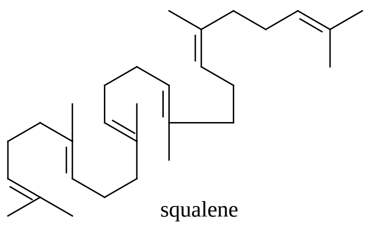


Figure 5.1
The structure of squalene.

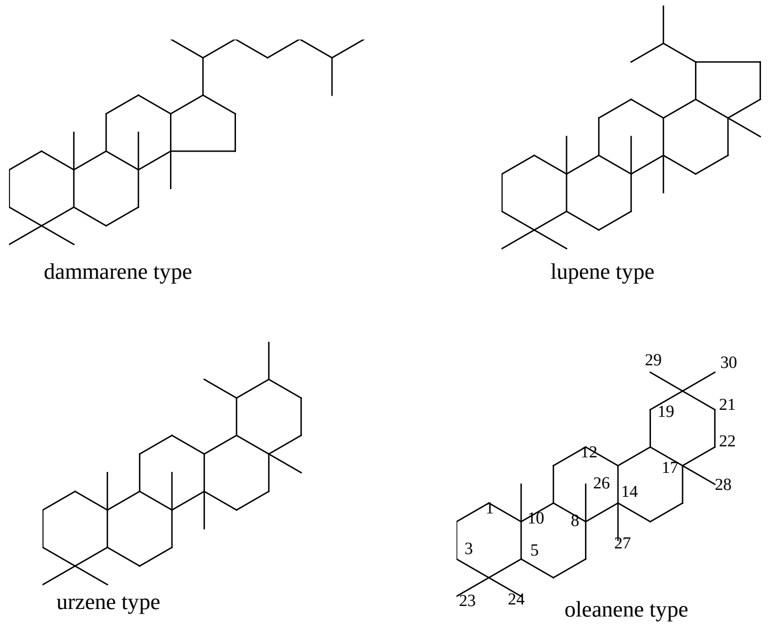


Figure 5.2-5
Two main types of triterpenoids: tetracyclic triterpenoids and pentacyclic triterpenoids.

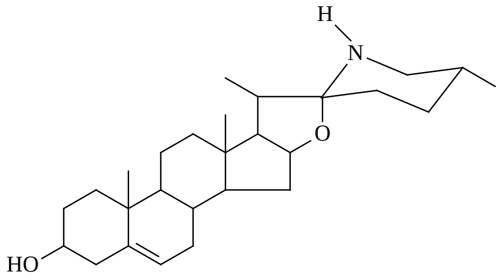


Figure 5.6
The structure of solasodine.

Drugs

Liquiritiae radix

Plant

Glycyrrhiza glabra L. – Liquorice (Fabaceae)

This perennial plant is native to Europe and temperate zone of Asia. It can be cultivated.

Figure 5.7
Liquorice (*Glycyrrhiza glabra* L.)

Drug

Liquiritiae radix (Liquorice root, Ph. Eur.). **Other Drug**

Liquiritiae extractum fluidum ethanolicum normatum (Liquorice ethanolic liquid extract, standardized, Ph. Eur.)

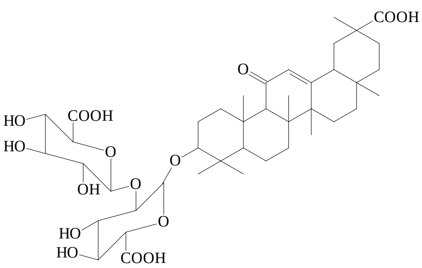
Liquorice root consists of the dried unpeeled or peeled, whole or cut root and stolons of *Glycyrrhiza glabra* L. It contains not less than 4.0% of glycyrrhizic acid, calculated with reference to the dried drug.

Standardised liquorice ethanolic liquid extract is produced from Liquorice root. It contains not less than 3.0% and not more than 5.0% of glycyrrhizic acid. The extract is produced from the drug and alcohol (70% *V/V*), with an appropriate procedure for liquid extracts. It is a dark brown, clear liquid with a faint characteristic odour and a sweet taste.

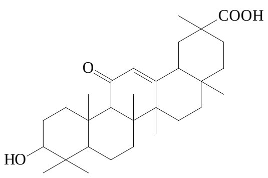
Figure 5.8
Liquiritiae radix (Liquorice root)

Constituents

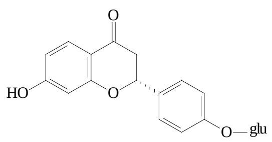
The main characteristic constituents of the drug are triterpene glycosides (saponins, 2-15%), principally glycyrrhizic acid, the 3*β*-diglucuronide of glycyrrhetic acid, which occurs as a mixture of potassium and calcium salts known as glycyrrhizin. Other constituents include flavonoids (e.g. liquiritin, glabrol), isoflavonoids (e.g. glabrene), chalcones (e.g. isoliquiritin), sterols, coumarins (e.g. umbelliferone, herniarin), sugars (glucose, saccharose) and essential oil (approx. 0.05%).



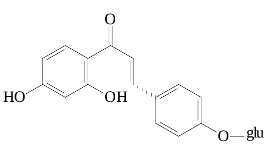
glycyrrhizic acid



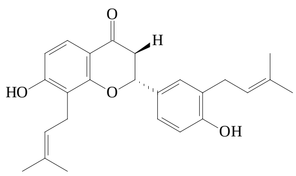
glycyrrhetic acid



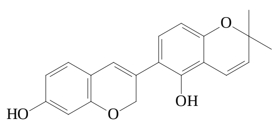
liquiritin



isoliquiritin



glabrol



glabrene

Figure 5.9-14
The structure of glycyrrhizic acid, glycyrrhetic acid, liquiritin, isoliquiritin, glabrol and glabrene.

Uses

The therapeutic indications of the drug include the adjuvant therapy of gastric and duodenal ulcers and gastritis. Moreover the drug and its products can be used as expectorant in the case of coughs and bronchial catarrh. Liquorice root has a sweet taste due to its glycyrrhizin content (this constituent is 50 times sweeter than saccharose).

Dosage

Gastric and duodenal ulcers and gastritis

Adults and elderly daily dose: 5-15 g of liquorice root (equivalent to 200-600 mg of glycyrrhizic acid) taken in divided doses or 5-15 ml of standardized liquorice ethanolic liquid extract.

Coughs and bronchial catarrh

Adults and elderly daily dose: 1.5-5 g of liquorice root (equivalent to 60-200 mg of glycyrrhizic acid) taken in divided doses or 1.5-5 ml of standardized liquorice ethanolic liquid extract.

Children 4 years of age and older: as an expectorant only, in aqueous preparations; portion of adult dose according to age or body weight.

Products of liquorice root should not be taken for more than 4-6 weeks without medical advice.

Contra-indications

The drug and its preparations should not be used in case of cardiovascular-related disorders (e.g. hypertension), renal disorders, cholestatic or inflammatory liver disorders, hypokalaemia and severe obesity.

Special warnings

The maximum daily dose (15 g) of the drug (or a content of 600 mg of glycyrrhizin) should never be exceeded. Consumption of glycyrrhizin as a taste modifier should be limited to 100 mg/day. Overdose of the drug may cause adverse effects in more sensitive patients.

Interaction with other medicaments and other forms of interaction: Hypokalaemia may enhance the action of cardiac glycosides and interact with antiarrhythmic drugs or with drugs which induce reversion to sinus rhythm (e.g. quinidine). Concomitant use with other drugs inducing hypokalaemia may aggravate electrolyte imbalance. Glycyrrhizic acid has been reported to decrease plasma clearance and increase the AUC of prednisolone, and to potentiate hydrocortisone activity in human skin.

Pregnancy and lactation

Liquorice root and its preparations should not be used during pregnancy or lactation.

Quillajae cortex

Plant

Quillaja saponaria Mollina. – Soap bark tree (Rosaceae)

The evergreen, 15-18 m high tree is indigenous in Chile, Peru and Bolivia. In pharmacies it is available in chopped or powdered (pulverized) form. It irritates the throat, the eyes and the nose during the process of pulverizing: it causes watery eyes and sneezing.

Drug

Quillajae cortex (Quillaja bark, ÖAB, Ph. Helv., DAC).

The drug consists of the dried peeled secondary roots of *Quillaja saponaria* Mollina.

Figure 5.15
Quillajae cortex (Quillaja bark)

Constituents

The drug contains a mixture of triterpene-saponin-glycosides (8.5-16.5%), in which the main sapogenine is quillaic acid. It contains tannins (derivatives of gallic acid; 10-15%) and Ca-oxalate.

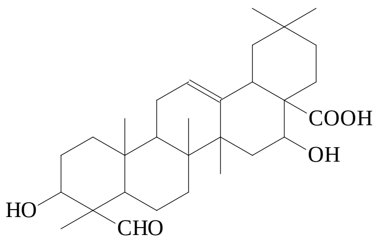


Figure 5.16
The structure of quillaic acid.

Uses

The drug has expectorant, antifungal, antibacterial and immunostimulant actions. It is a cough-reliever and expectorant. It is used in the case of scalp diseases, against dandruff, oily hair and hair loss (alopecia).

Dosage

Coughs

Adults and elderly daily dose: 0.2 g of the drug (2 times a day) in 200 ml of hot water as a tea.

Scalp diseases

Adults and elderly daily dose: 1 g of the drug with 200 ml of hot water as an aqueous extract for rubbing.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Verbasci flos

Plants

Verbascum phlomoides L. (Orange mullein), *V. densiflorum* Bertol. (Dense-flowered mullein) - (Scrophulariaceae)

Verbascum species are native to Europe and Asia, and they possess the highest species diversity in the Mediterranean.

Figure 5.17-18
Orange mullein (*Verbascum phlomoides* L.),
Dense-flowered mullein (*V. densiflorum* Bertol.)

Drug

Verbasci flos (Mullein flower, Ph. Eur.).

Verbasci flos consists of the dried flower, reduced to the corolla and the androecium of *Verbascum thapsus* L., *V. densiflorum* Bertol. (*V. thapsiforme* Schrad), and *V. phlomoides* L.

Figure 5.19
Verbasci flos (Mullein flower)

Constituents

The main characteristic constituents of the drug are triterpene glycosides (saponins), principally verbascosaponin. Other constituents of the drug are iridoids (e.g. aucubin, catalpol), flavonoids (e.g. apigenin, quercetin), cinnamic acid derivatives (e.g. protocatechu acid, caffeic acid, ferulic acid) and mucilage.

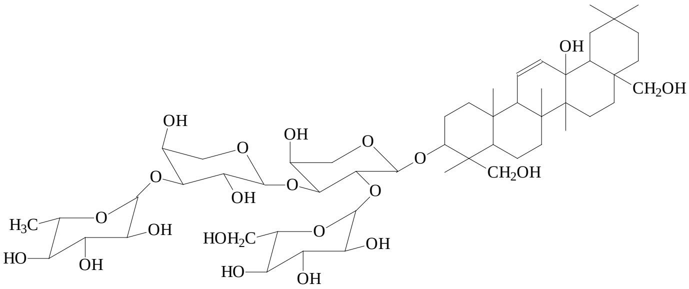


Figure 5.20
The structure of verbascosaponin.

Uses

The therapeutic indications of the drug include the adjuvant therapy of coughs and bronchial catarrh. The infusion of the drug has expectorant, diuretic and antibacterial activities. Verbasci flos is used as a component of tea-mixtures.

Dosage

Adults and elderly daily dose: 1.5 g of the drug in 200 ml of hot water used as an infusion, 2-3 times daily.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Saponariae albae radix

Plant

Gypsophila paniculata L. – Baby's breath (Caryophyllaceae)

This herbaceous perennial plant is native to central and eastern Europe. It can grow on the steppes in dry, sandy and stony places, often on calcareous soils.

Figure 5.21
Baby's breath (*Gypsophila paniculata* L.)

Drug

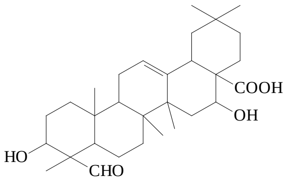
Saponariae albae radix (White soapwort root)

The drug consists of the dried, peeled roots of *Gypsophila paniculata* L

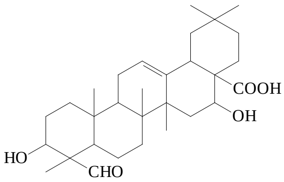
Figure 5.22
Saponariae albae radix (White soapwort root)

Constituents

The main characteristic constituents of the drug are triterpene saponins (6-20%). The main aglycons are gypsogenin and quillaic acid.



gypsogenin



quillaic acid

Figure 5.23-24
The structure of gypsogenin and quillaic acid.

Uses

The therapeutic indications of the drug include the adjuvant therapy of coughs and bronchial catarrh. The decoction of the drug has expectorant effect.

Dosage

Adults and elderly daily dose: 30-150 mg of the pulverized drug in 200 ml of hot water used as a decoction.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Primulae radix

Plants

Primula veris L. (Common cowslip), *P. elatior* (L.) Hill. (True oxlip) – (Primulaceae)

Primula species are perennial, herbaceous plants, native to Europe, North-Africa, West-Asia and the Caucasus; deserving protection.

Figure 5.25
Common cowslip (*Primula veris* L.)

Drug

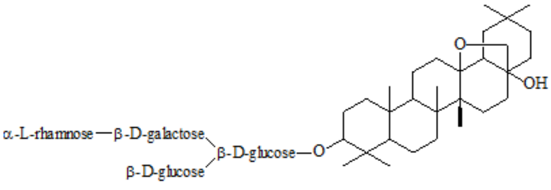
Primulae radix (Primula root, Ph. Eur.)

Primula root consists of the whole or cut, dried rhizome and root of *Primula veris* L. or *P. elatior* (L.) Hill. Primula root has a bitter taste.

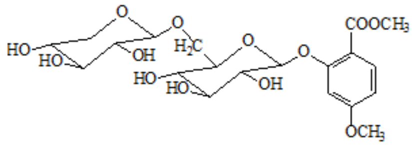
Figure 5.26
Primulae radix (Primula root)

Constituents

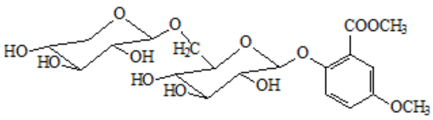
The main characteristic constituents are triterpene saponins (3-10%). The principal saponins have a branched chain of at least four sugars (glucuronic acid, glucose, galactose and rhamnose) at C-3. The main saponin of the drug is protoprimulagenin A. Other important constituents include phenolic glycosides. The main compounds of the essential oil in the root are primverin and primulaverin, which occur in both species, in highly variable amounts up to 2.3%. These compounds are the 2-primeverosides of 4-methoxy- and 5-methoxysalicylic acid methyl esters, respectively. Primula root has a characteristic odour due to its phenolic glycoside content.



protoprimulagenin A



primverin



primulaverin

Figure 5.27-29
The structure of protoprimulagenin A, primverin and primulaverin.

Uses

The therapeutic indications of the drug include productive cough, catarrh of the respiratory system and chronic bronchitis.

Dosage

Adults and elderly dose: 0.5-1.5 g of the drug as a decoction or equivalent preparations. Maximum daily dose of the drug is 5-10 g. Overdose of the drug may lead to stomach upset, vomiting or diarrhoea.

Children: 4-10 years/0.5-1 g daily; 10-16 years/0.5-1.5 g daily.

Contra-indications

Patients with gastritis or gastric ulcer should not use the drug.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Hederae helicis folium

Plant

Hedera helix L. – Ivy (Araliaceae)

This climbing evergreen plant is native to Europe, West-Asia, Caucasus and North-Africa.

Figure 5.30
Ivy (*Hedera helix* L.)

Drug

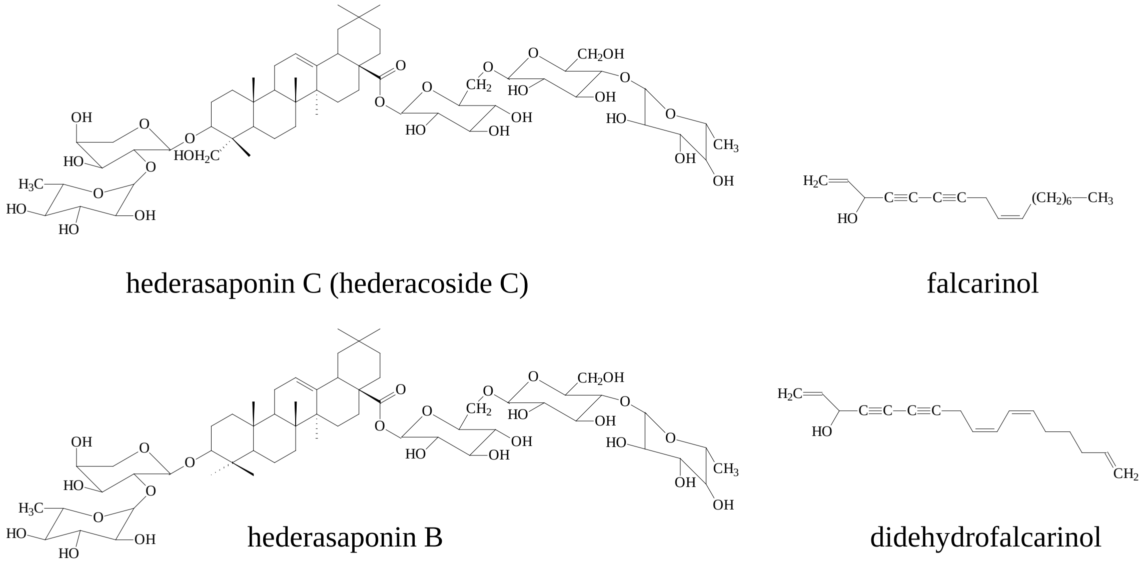
Hederae helicis folium (Ivy leaf, Ph. Eur.)

Ivy leaf consists of the dried leaves of *Hedera helix* L. It contains three main saponins: hederasaponin C (hederacoside C), hederasaponin B and hederasaponin D, with not less than 2.5% of hederasaponin C.

Figure 5.31
Hederae helicis folium (Ivy leaf)

Constituents

The main characteristic constituents are triterpene saponins (2.5-6%), principally hederasaponin C (hederacoside C), hederasaponin B and α-hederin. The aglycone part is hederagenin. Other conctituents include phytosterols (cholesterol, stigmasterol, β-sitosterol), polyines (e.g. falcarinol, didehydrofalcarinol), flavonoids (e.g. rutin), cinnamic acid derivatives (e.g. caffeic acid, chlorogenic acid) and essential oil.



hederasaponin C (hederacoside C) falcarinol

hederasaponin B didehydrofalcarinol

Figure 5.32-35

The structure of hederasaponin C (hederacoside C), hederasaponin B, falcarinol and didehydrofalcarinol.

Uses

The therapeutic indications of the drug include productive cough (when associated with hypersecretion of viscous mucus). The drug and its products can be used as an adjuvant treatment of inflammatory bronchial diseases. The drug can be used in suppositories.

Dosage

Oral use

Adults and elderly daily dose of ethanol-containing preparations: 250-420 mg; *for children of 4-12 years:* 150-210 mg; *for children of 1-4 years:* 50-150 mg; *for children <1 year:* 20-50 mg.

Adults and elderly daily dose of ethanol-free preparations: 300-945 mg; *for children of 4-12 years:* 200-630 mg; *for children of 1-4 years:* 150-300 mg; *for children <1 year:* 50-200 mg.

Overdose: it can provoke nausea and vomiting.

Rectal use

In suppositories: *for children of 4-10 years*: 960 mg.

Undesirable effects

Fresh leaves can cause allergic contact dermatitis. Polyines of the drug have been reported to be allergenic.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Betulae folium

Plants

Betula pendula Roth. (Silver birch), *B. pubescens* Ehrh. (Downy birch) – (Betulaceae)

Betula species are widespread in the Northern Hemisphere, particularly in northern temperate and boreal climates.

Figure 5.36
(Silver birch) (*Betula pendula* Roth.)

Drug

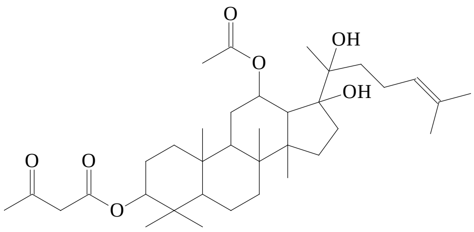
Betulae folium (Birch leaf, Ph. Eur.)

Birch leaf consists of the whole or fragmented dried leaves of *Betula pendula* Roth and/or *Betula pubescens* Ehrh., as well as hybrids of both species. It contains not less than 1.5% of flavonoids, calculated as hyperoside with reference to the dried drug.

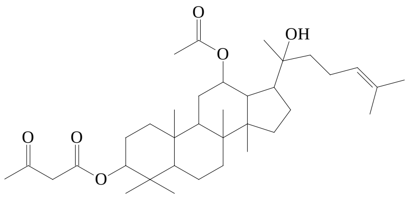
Figure 5.37
Betulae folium (Birch leaf)

Constituents

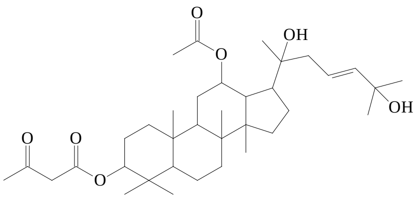
The main characteristic constituents are flavonoids (1-3%), principally hyperoside and other quercetin glycosides, myricetin and kaempferol glycosides. The drug also contains triterpene saponins (e.g. triterpenesaponin 1, 2, 3). Other constituents include chlorogenic acid, monoterpenes, sesquiterpenes, potassium and traces of essential oil.



triterpenesaponin 1



triterpenesaponin 2



triterpenesaponin 3

Figure 5.38-40
The structure of triterpenesaponin 1, 2 and 3.

Uses

The therapeutic indications of the drug include the rinsing of the urinary tract, especially in cases of inflammation and kidney stones, and as an adjuvant in the treatment of bacterial infections of the urinary tract.

Dosage

Adults and elderly dose: 2-3 g of the drug as an infusion, 2-3 times daily. Tincture (1:10): 2 ml, 3 times daily. Fresh juice: 15 ml, 3 times daily.

Special warnings and precautions for use

Patients with impaired heart and kidney fuction should not use the drug and its preparations.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Veronicae herba

Plant

Veronica officinalis L. – Common speedwell (Scrophulariaceae)

This herbaceous plant is native to Europe, West-Asia and Caucasus. In Hungary it is widespread in the mountains and in the oak forests of Transdanubia.

Figure 5.41
(Common speedwell) (*Veronica officinalis* L.)

Drug

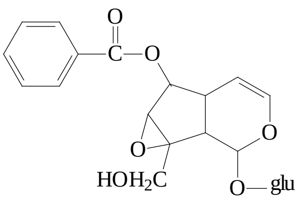
Veronicae herba (Common speadwell flowering shoot, Veronica herb)

The drug consists of the dried flowering shoot of *Veronica officinalis* L

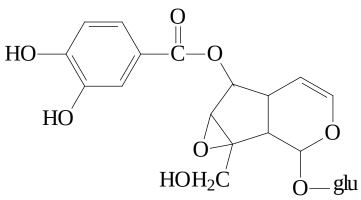
Figure 5.42
Veronicae herba (Common speadwell flowering shoot, Veronica herb)

Constituents

The drug contains triterpenes, iridoid glycosides (0.5-1%, e.g.: catalpol, veronicoside, verproside), flavonoids (e.g. luteolin), caffeic acid, chlorogenic acid, D-mannitol, tannins and β-sitosterol.



veronicoside



verproside

Figure 5.43-44
The structure of veronicoside and verproside.

Uses

The drug has expectorant, antibacterial and anti-inflammatory activities. It can be used for the treatment of asthma bronchiale and rheumatic conditions.

Dosage

Adults and elderly daily dose: 2-3 g of the drug as an infusion, 2-3 times daily.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Ononidis radix

Plant

Ononis spinosa L. – Restharrow (Fabaceae)

The plant is an approx. 0.8 m high perennial semi-shrub. It is native to Europe, North-Africa, West-Asia and India. It often occurs on meadows and pastures.

Drug

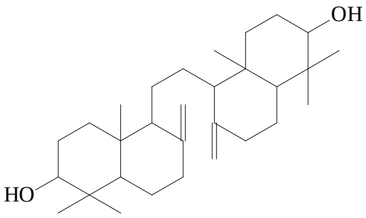
Ononidis radix (Restharrow root, Ph. Eur.)

The drug consists of the whole or cut, dried root of *Ononis spinosa* L.

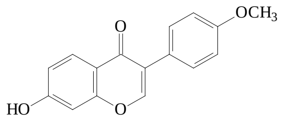
Figure 5.45
Ononidis radix (Restharrow root)

Constituents

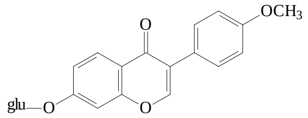
The drug contains triterpenes, principally α-onocerin (onocol), isoflavonoids (e.g. formononetin, ononin, biochanin A 7-O-glucoside-6″-malonate), phytosterols (e.g. β-sitosterol), phenolic acids, tannins, minerals and essential oil (containing mainly *trans*-anethole, carvone, menthol).



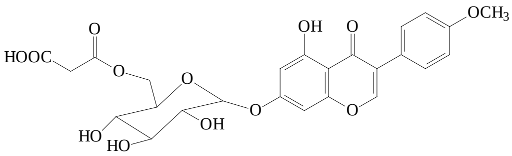
α-onocerin (onocol)



formononetin



ononin



biochanin A 7-O-glucoside-6″-malonate

Figure 5.46-49
The structure of α-onocerin (onocol), formononetin, ononin and biochanin A 7-O-glucoside-6″-malonate.

Uses

The therapeutic indications include the rinsing the urinary tract, especially in cases of inflammation and kidney stones, and as an adjuvant in the treatment of bacterial infections of the urinary tract. The drug and its preparations have diuretic effect.

Dosage

Adults and elderly daily dose: 2-3 g of the drug as a decoction, 2-3 times daily.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Solidaginis virgaureae herba

Plant

Solidago virgaurea L. – European goldenrod (Asteraceae)

This plant is native to Europe, North-Africa, temperate zones of Asia and India.

Figure 5.50
European goldenrod (*Solidago virgaurea* L.)

Drug

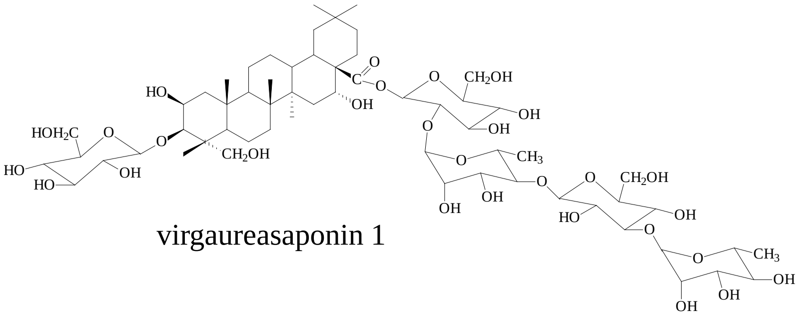
Solidaginis virgaureae herba (European goldenrod, Ph. Eur.)

It consists of the whole or cut, dried, flowering aerial parts of *Solidago virgaurea* L. It contains minimum 1.0% of flavonoids, expressed as hyperoside and calculated with reference to the dried drug.

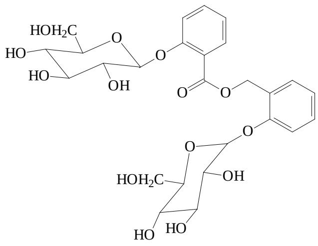
Figure 5.51
Solidaginis virgaureae herba (European goldenrod)

Constituents

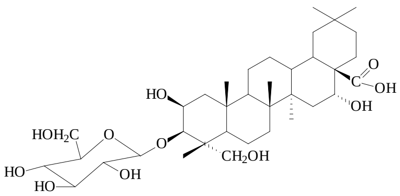
The drug contains triterpene saponins (up to 2%) which are derived from virgaureagenin (e.g. virgaureasaponin 1), polygalacic acid (e.g. polygalacic acid-3-β-D-glucoside) and other sapogenins. Other constituents include flavonoids (minimum 1.0%), phenol glycosides (e.g. virgaureoside A), phenolic acids such as chlorogenic and caffeic acids and a small amount of essential oil.



virgaureasaponin 1



virgaureoside A



polygalacic acid-3-β-D-glucoside

Figure 5.52-54

The structure of virgaureasaponin 1, polygalacic acid-3-β-D-glucoside and virgaureoside A.

Uses

The therapeutic indications include the rinsing of the urinary tract, especially in cases of inflammation and kidney stones, and as an adjuvant in the treatment of bacterial infections of the urinary tract. The drug and its preparations have diuretic effect.

Dosage

Adults and elderly dose: 3-4 g of the drug as an infusion in 150 ml water, 2-3 times daily. *Children*: 1-4 years of age: 1-2 g; 4-10 years of age: 2-5 g; 10-16 years of age: 4-8 g.

Contra-indications

The drug should not be used in patients with oedema due to impaired heart or kidney function.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Hippocastani semen

Plant

Aesculus hippocastanum L. – Horse-chestnut (Hippocastanaceae)

This tree is native to Europe. It is widely cultivated in streets and parks.

Figure 5.55
Horse-chestnut (*Aesculus hippocastanum* L.)

Drug

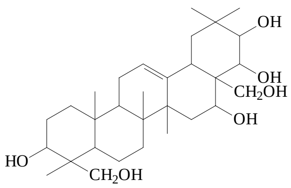
Hippocastani semen (Horse-chestnut seed, DAB)

The drug consists of the dried seeds of *Aesculus hippocastanum* L. containing not less than 3.0% of triterpene glycosides, expressed as anhydrous aescin and calculated with reference to the dried drug.

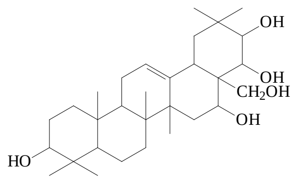
Figure 5.56
Hippocastani semen (Horse-chestnut seed)

Constituents

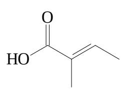
The characteristic constituents, collectively known as aescin (3-10%), are a mixture of acylated triterpene saponins based on two main aglycones, protoaescigenin and barringtogenol C. All the saponins have a trisaccharide group at C-3 (comprising glucuronic acid with substituent sugars such as glucose, galactose or xylose at the 2- and 4-positions. The two major saponins, both arising from protoaescigenin, are esterified at the 21*β*-position, one with angelic acid, the other with tiglic acid, and with acetic acid at the 22*α*-position. Other constituents include flavonoids (mostly di- and triglycosides of quercetin and kaempferol), sterols, essential oil and a high proportion of starch (30-60%).



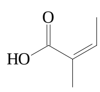
protoaescigenin



barringtogenol C



tiglic acid



angelic acid

Figure 5.57-60
The structure of protoaescigenin, barringtogenol C, tiglic acid and angelic acid.

Uses

The therapeutic indications include the treatment of chronic venous insufficiency and varicosis. The saponin-mixture of the drug regulates the permeability of blood vessels and increases capillary resistency and the tone of veins.

Dosage

Adults and elderly daily dose: drug or hydroalcoholic extract containing 50-150 mg of triterpene glycosides (calculated as aescin), usually in divided doses. The drug is not recommended for children.

Pregnancy and lactation

The seed extracts have been used in clinical studies involving pregnant women, with some studies excluding those in the third trimester. No adverse effects have been reported, but in accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Calendulae flos

Plant

Calendula officinalis L. – Common marigold (Asteraceae)

The plant can be cultivated in warm temperate regions of the world.

Figure 5.61
Common marigold (*Calendula officinalis* L.)

Drug

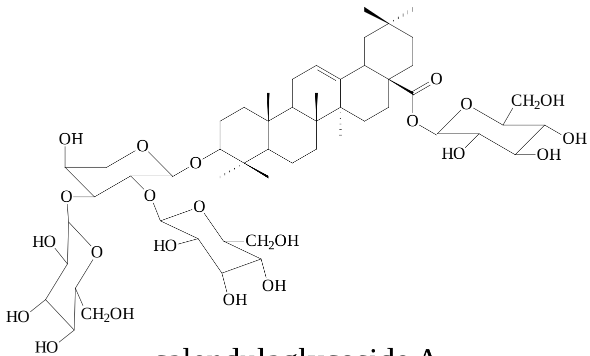
Calendulae flos (Calendula flower, Ph. Eur.)

Calendula flower consists of the whole or cut, dried, and fully opened flowers which have been detached from the receptacle of the cultivated, double-flowered varieties of *Calendula officinalis* L. It contains not less than 0.4% of flavonoids, calculated as hyperoside with reference to the dried drug.

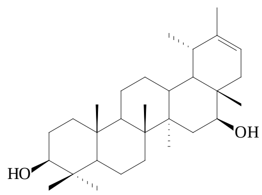
Figure 5.62
Calendulae flos (Calendula flower)

Constituents

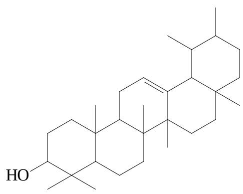
The characteristic constituents are triterpene saponins (mainly oleanolic acid glycosides, e.g. calendulaglycoside A), triterpenes in free state (e.g. faradiol, α-amirin, lupeol). Other constituents include flavonoids, carotenoids (e.g. β-carotene, licopene, zeaxanthin, violaxanthin), polysaccharides, sterols, sesquiterpenoids and essential oil.



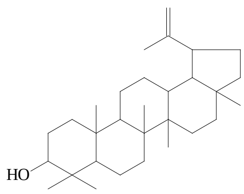
calendulaglycoside A



faradiol



α-amirin



lupeol

Figure 5.63-66
The structure of calendulaglycoside A, faradiol, α-amirin and lupeol.

Uses

The therapeutic indications include the symptomatic treatment of minor inflammations of the skin and mucosa. The drug and its preparations aid the healing of minor wounds, leg ulcer and burns.

Dosage

Infusion for topical application: 1-2 g of dried flower per 150 ml of water. *Fluid extract* 1:1 in 40% ethanol or tincture 1:5 in 90% ethanol. For the treatment of wounds the tincture is applied undiluted; for compresses the tincture is usually diluted at least 1:3 with freshly boiled water. *Semi-solid preparations* containing 2-10% of fluid extract 1:1.

Pregnancy and lactation

No data available. However, there are no objections to external use during pregnancy and lactation.

Polygalae radix

Plant

Polygala senega L. – Seneca snakeroot (Polygalaceae)

This plant is native to the eastern part of Canada and USA.

Drug

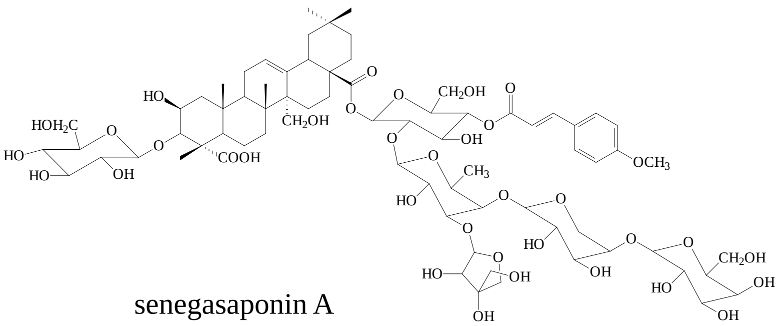
Polygalae radix (Senega root, Ph. Eur.)

Senega root consists of the dried and usually fragmented root and root crown of *Polygala senega* L. or of certain other closely related species or of a mixture of these *Polygala* species. Senega root has a faint, sweet odour, slightly rancid or reminiscent of methyl salicylate. Reduced to a powder, it is irritant and sternutatory (causes sneezing). When shaken with water, the powder produces a copious froth.

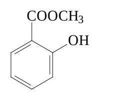
Figure 5.67
Polygalae radix (Senega root)

Constituents

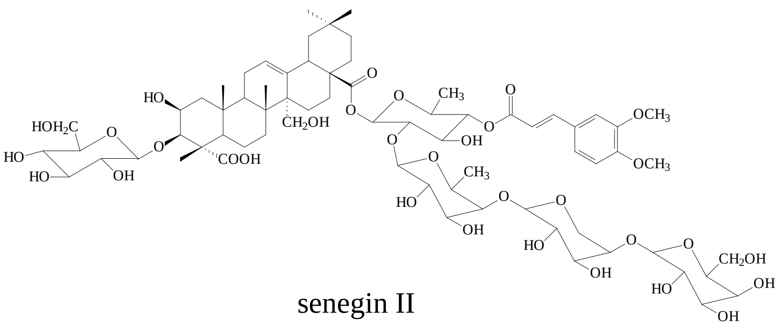
The drug contains triterpene saponins (6-16%), for example senegasaponin A and B, senegin II and III. Other constituents include methyl salicylate, sugars and traces of essential oil.



senegasaponin A



methyl salicylate



senegin II

Figure 5.68-70
The structure of senegasaponin A, senegin II and methyl salicylate.

Uses

Because of the saponin content the drug can be used as an expectorant in the treatment of bronchitis and the inflammation of the upper respiratory tract.

Dosage

Adults and elderly daily dose: 1.5-3 g of the drug (divided into 2 or 3 parts) with 250 ml of water, as a decoction. **Overdose:** nausea, vomiting, diarrhoea may occur!

The use of the drug is not recommended in children under 12 years of age

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Pruni africanae cortex

Plant

Prunus africana Kalkm. – Red stinkwood (Rosaceae)

This evergreen tree is native to the montane regions of Sub-Saharan Africa.

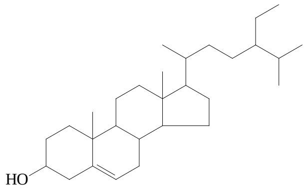
Drug

Pruni africanae cortex (Pygeum africanum bark, Ph. Eur.)

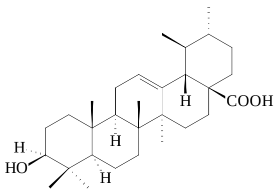
The drug consists of the whole or cut, dried bark of the stems and branches of *Prunus africana* (Hook f.) Kalkm. (syn. *Pygeum africanum* Hook f.).

Constituents

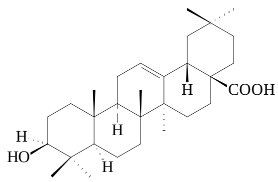
The main constituents are phytosterols, e.g. β-sitosterol, β-sitosterol 3-glycoside, free C_{12}-C_{24} fatty acids, pentacyclic triterpenic acids (e.g. ursolic and oleanolic acid derivatives) and long chain apiphatic alcohols (*n*-docosanol, *n*-tetracosanol and their *trans*-ferulic acid esters).



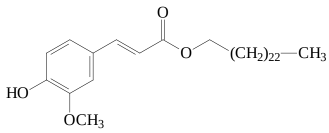
β-sitosterol



ursolic acid



oleanolic acid



ferulic acid *n*- tetracosanol ester

Figure 5.71-74
The structure of β-sitosterol, ursolic acid, oleanolic acid and ferulic acid *n*- tetracosanol ester.

Uses

Therapeutic indications of the drug include the symptomatic treatment of micturition disorders (dysuria, pollakisuria, nocturia, urine retention) in benign prostatic hyperplasia (BPH) at stages I and II as defined by Alken or stages II and III as defined by Vahlensieck.

Stages I and II of benign prostatic hyperplasia as defined by Alken

Stage I: Dysuria, pollakisuria, possibly nocturia, reduction in projection of the urine stream, no residual urine (stage of compensation of the bladder musculature)

Stage II: Same symptoms as at stage I, except with residual urine (incipient decompensation of the bladder musculature)

Stages II and III of benign prostatic hyperplasia as defined by Vahlensieck

Stage II: intermittent micturition problems (frequency, calibre of urine stream), more or less marked BPH, urine stream: between 10 and 15 ml/s maximal flow, no or low (< 50 ml) residual urine, no or incipient bladder trabeculation

Stage III: permanent micturition problems (frequency, calibre of urine stream), more or less marked BPH, urine stream: less than10 ml/s maximal flow, residual urine more than 50 ml, trabeculated bladder

Dosage

Adults and elderly daily dose: 100-200 mg of the lipophilic extract of the drug.

Special warnings and precautions for use

All cases of difficulty urination require clarification by a doctor and regular medical checks in order to rule out the need for other treatment, e.g. surgical intervention. Consultation with a physician is particularly necessary in cases of blood in the urine or acute urine retention.

Pregnancy and lactation

Not applicable.

Cimicifugae rhizoma

Plant

Cimicifuga racemosa (L.) Nutt. – Black cohosh (Ranunculaceae)

This plant is native to North-America.

Drug

Cimicifugae rhizoma (Black cohosh rhizome)

The drug consists of the dried rhizomes and roots of *Cimicifuga racemosa* (L.) Nutt.

Figure 5.75
Cimicifugae rhizoma (Black cohosh rhizome)

Constituents

The main constituents are triterpene glycosides, e.g. cimicifugoside (cimigenol-3-O-β-D-xyloside), actein (formerly known 27-deoxyactein) and cimiracemoside F and G. All these glycosides are 3-O-xylosides or 3-O-arabinosides of aglycones of the cycloartane type. Other constituents include fukiik and piscidic acid and their esters, e.g. fukinolic acid, aromatic acids (caffeic, ferulic and isoferulic acids) and cimiracemates A-D (phenylpropanoid ester dimers).

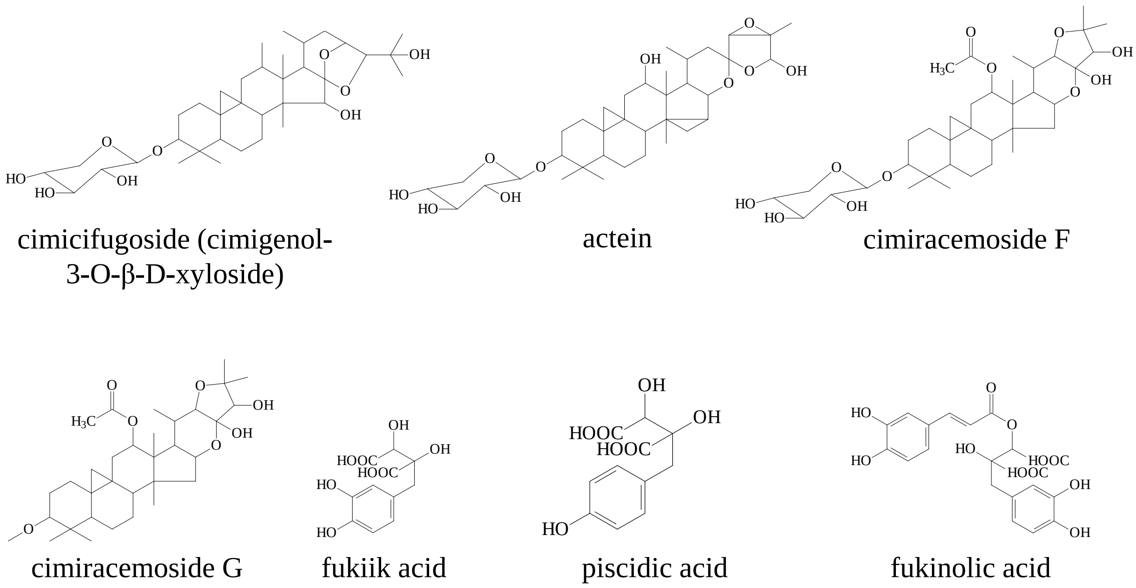


Figure 5.76-86
The structure of cimicifugoside (cimigenol-3-O-β-D-xyloside), actein, cimiracemoside F and G, fukiik acid, piscidic acid, fukinolic acid and cimiracemates A-D.

Uses

Therapeutic indications of the drug include climacteric symptoms such as hot flushes, profuse sweating, sleep disorders and nervous irritability.

Dosage

Adult daily dose: isopropanolic (40% V/V) or ethanolic (40-60% V/V) extracts corresponding to 40-140 mg of the drug or equivalent preparations.

Onset of action can be expected within 2-4 weeks. For further improvement medication should be taken for at least 6-8 weeks, maximum effects are seen within 3 months.

Special warnings and precautions for use

The use of the drug in patients with existing oestrogen-dependent tumors should be approached with caution. Clinical experience suggests a lack of risk, but relevant human toxicological data are unavailable.

Pregnancy and lactation

The drug and its preparations should not be taken during pregnancy and lactation.

Centellae asiaticae herba

Plant

Centella asiatica (L.) Urban. – Centella (Apiaceae)

This plant is native to the tropical and subtropical parts of Asia, Australia, Africa and America.

Drug

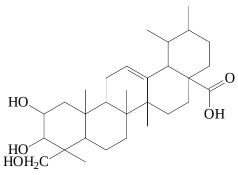
Centellae asiaticae herba (Centella)

Centella consists of the dried, fragmented aerial parts of *Centella asiatica* (L.) Urban. It contains not less than 6.0% of total triterpenoid derivatives, expressed as asiaticoside, calculated with reference to the dried drug.

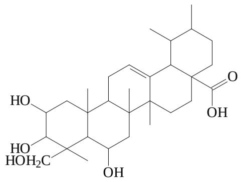
Figure 5.87
Centellae asiaticae herba (Centella)

Constituents

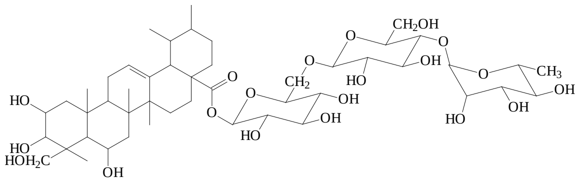
The main characteristic constituents are triterpene acids, e.g. asiatic and madecassic acids, and their sugar esters, principally asiaticoside with small amounts of asiaticoside A and B. Depending on the source of the plant material, the amount of triterpenoids may vary from 1% to 8%. Other constituents include essential oil (with compounds of β-farnezene, β-caryophyllene, α-pinene, β-pinene), flavonoids (mainly quercetin and kaempferol glycosides) and phytosterols.



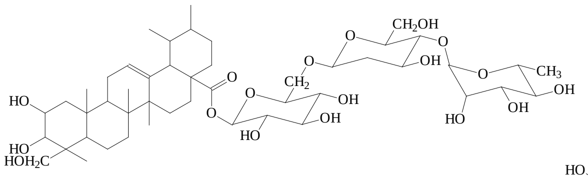
asiatic acid



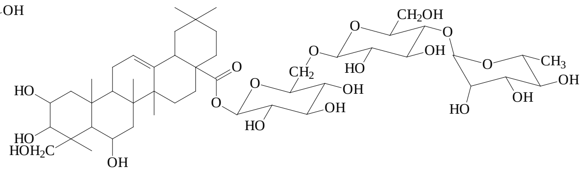
madecassic acid



asiaticoside A



asiaticoside



asiaticoside B

Figure 5.88-92
The structure of asiatic acid, madecassic acid, asiaticoside, asiaticoside A and B.

Uses

Therapeutic indications of the drug include the treatment of chronic venous insufficiency, varicosis and wound healing.

Dosage

Internal use

Adult dose: 0.6 g of the dried drug as an infusion, tincture or extract, up to four times daily.

External use

Semi-solid preparations containing 1% of extract or tincture.

Undesirable effects

A few cases of contact allergy have been reported after topical application.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

5.2 Triterpenes in adaptogens

Adaptogenic drugs:

- are not toxic; intervene as mild disturbing factors into the physiological processes
- they increase the resistance of organisms against different physical, chemical, biological actions and against stress
- they act as regulators in order to normalize the altered functions of organisms; decrease hyperfunctions, increase hypofunctions

- act as a tonic; improve the physical productivity, stimulate the central nervous system, act against premature exhaustion, increase the non-specific resistance of organisms, and the rate of protein- and RNA-synthesis

The drug of *Eleutherococcus senticosus* (Eleutherococci radix) will be introduced in the **Chapter 10** because its lignan compounds.

Drugs

Ginseng radix

Plant

Panax ginseng C.A. Meyer – Ginseng (Araliaceae)

This plant is native to China, Japan, Korea and Russia; and is cultivated in China, Japan and Korea. Korean ginseng is the most valuable. The root of *Panax quinquefolius*, which is native to North-America, can also be used as ginseng radix, but this drug is less valuable than the radix of *Panax ginseng*.

Drug

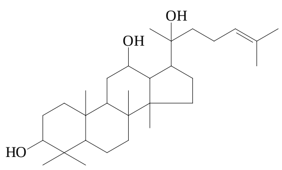
Ginseng radix (Ginseng, Ph. Eur.)

Ginseng consists of the whole or cut dried root of *Panax ginseng* C.A. Meyer. It contains not less than 0.40% of combined ginsenosides Rg1 and Rb1, calculated with reference to the dried drug.

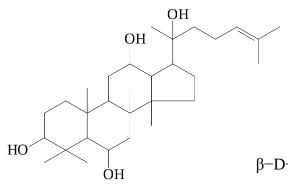
Figure 5.93
Ginseng radix (Ginseng)

Constituents

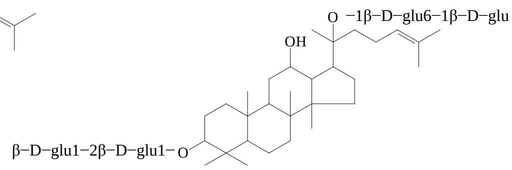
The main characteristic constituents are triterpene saponins of the dammarane type, as derivatives of either protopanaxadiol or protopanaxatriol. Protopanaxadiol saponins are: ginsenosides Ra_1, Ra_2 and Ra_3, ginsenosides Rb_1, Rb_2 and Rb_3, ginsenosides Rc and Rd. Protopanaxatriol saponins are: ginsenosides Re and Rf, ginsenosides Rg_1, Rg_2 and Rh_1. The total ginsenoside content of a 6-year-old main root varies between 0.7-3%. The lateral roots can contain two or three times more saponins than the main root. Other constituents include peptidoglycans called panaxans, acetylenic compounds (e.g. panaxinol), oligo- and polysaccharides, phenolic compounds such as vanillic acid and salicylic acid and traces of essential oil containing mainly sesquiterpenes.



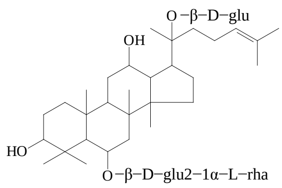
protopanaxadiol



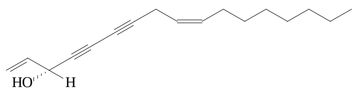
protopanaxatriol



ginsenoside Rb_1



ginsenoisde Re



panaxinol

Figure 5.94-98
The structure of protopanaxadiol, protopanaxatriol, ginsenoside Rb_1, ginsenoside Re and panaxinol.

Uses

Therapeutic indications of the drug include the treatment of decreased mental and physical capacities such as weakness, exhaustion, tiredness and loss of concentration, as well as during convalescence.

Dosage

Adult daily dose: 0.5 g up to a maximum of 2 g of dried root or equivalent preparations.

Interaction with other medicaments

Ginseng may slightly reduce blood glucose level. A case of possible interaction of ginseng with warfarin anticoagulant therapy has been reported, but the mechanism remains unknown.

Undesirable effects

The excessive and uncontrolled intake of ginseng products should be avoided.

Pregnancy and lactation

No human data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

5.3 Steroids

Similarly to terpenes, steroids are compounds with isoprene-skeleton.

Their most important groups in plants:

sterols (with 27-29 C-atoms)

spirostanols, furostanols, steroid-alkaloids (with 27 C-atoms)

ekdisteroids (with 27 C-atoms)

bufadienolids (with 24 C-atoms)

cardenolides (with 23 C-atoms)

pregnane-derivatives (with 21 C-atoms)

oestrone (with 18 C-atoms)

The biosynthesis of steroids starts from squalene. From this compound squalene-2,3-oxide and cycloartenol will be formed (**Figure 5.99**).

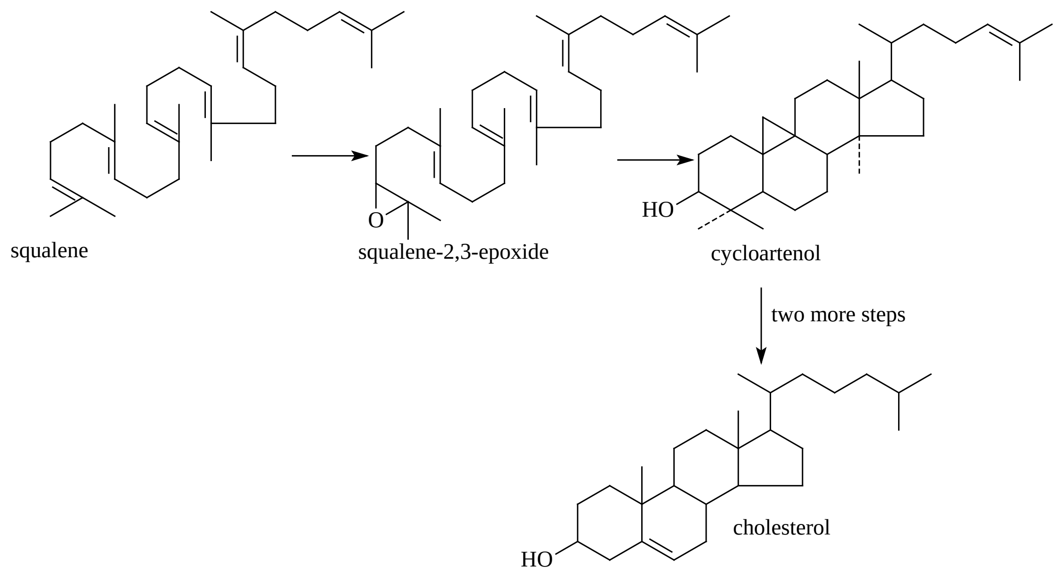


Figure 5.99
The formation of cholesterol in higher plants.

Sterols: These compounds frequently occur in higher plants, but in small amounts and typically in glycosidic form. In the latter case the sugar part is attached to the OH-group at C3-atom. The most well-known sterols are: β-sitosterol, stigmasterol, campesterol and cholesterol, having important role in the stabilization of membranes. They possess various pharmacological effects such as anti-inflammatory, antibacterial, antifungal and they can inhibit the growth of tumors.

Drugs

Urticae radix

Plants

Urtica dioica L., (Great nettle), *U. urens* L. (Small nettle) (Urticaceae)

These plants are native to Europe.

Figure 5.100
Urtica sp. (Nettle)

Drug

Urticae radix (Nettle root, Ph. Eur.). **Other Drug**

Urtica dioica ad praeparationes homoeopathicas (Common stinging nettle for homoeopathic preparations, Ph. Eur.)

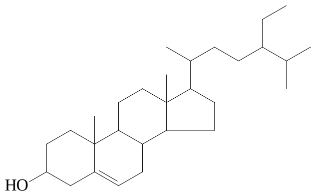
The drug consists of the whole, cut or powdered dried roots and rhizomes of *Urtica dioica* L., *Urtica urens* L., their hybrids or mixture of these plants.

Common stinging nettle for homoeopathic preparations: It is produced from the whole, fresh, flowering plant of *Urtica dioica* L.

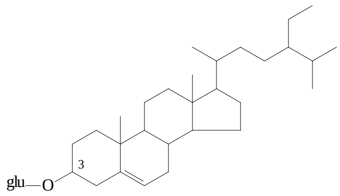
Figure 5.101
Urticae radix (Nettle root)

Constituents

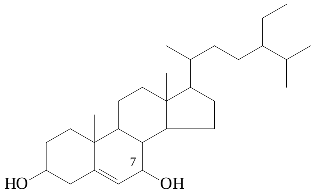
The main characteristic constituents are sterols, e.g. β-sitosterol, β-sitosterol-3-O-glucoside, 7β-hidroxy-β-sitosterol. Other constituents include lignans such as (+)-neo-olivil, (-)-secoisolariciresinol, fatty acids, monoterpene diols, polysaccharides and coumarins (scopoletin).



β-sitosterol



β-sitosterol-3-O-glucoside



7β-hidroxy-β-sitosterol

Figure 5.102-104

The structure of β-sitosterol, β-sitosterol-3-O-glucoside and 7β-hidroxy-β-sitosterol.

Uses

Therapeutic indications of the drug include the symptomatic treatment of micturition disorders (dysuria, pollakisuria, nocturia, urine retention) in benign prostatic hyperplasia (BPH) at stages I and II as defined by Alken or stages II and III as defined by Vahlensieck.

Stages I and II of benign prostatic hyperplasia as defined by Alken

See: Pruni africanae cortex

Stages II and III of benign prostatic hyperplasia as defined by Vahlensieck

See: Pruni africanae cortex

Dosage

Adult daily dose: 4-6 g of the drug as an infusion; 378-756 mg of dried extract (12-16:1, 70% V/V ethanol); 4.5-7.5 ml of fluid extract (1:1, 45% ethanol).

Special warnings and precautions for use

All cases of difficult urination require clarification by a doctor and regular medical checks in order to rule out the need for other treatment, e.g. surgical intervention. Consultation with a physician is particularly necessary in cases of blood in the urine or acute urine retention.

Pregnancy and lactation

Not applicable.

Epilobii herba

Plants

Epilobium parviflorum Schreb. (Small-flowered willowherb), *E. roseum* Schreb. (Pale willowherb), *E. montanum* L. (Broad-leaved willowherb) (Onagraceae)

Epilobium species are native to Europe.

Figure 5.105
Pale willowherb (*Epilobium roseum* Schreb.)

Drug

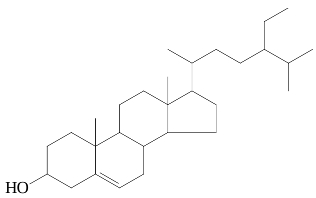
Epilobii herba (Epilobium)

The drug consists of the dried aerial flowering parts of *Epilobium parviflorum* Schreb., *E. roseum* Schreb., *E. montanum* L. or other *Epilobium* species.

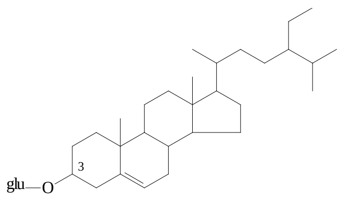
Figure 5.106
Epilobii herba (Epilobium)

Constituents

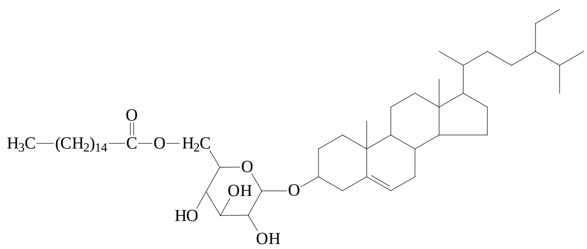
The main characteristic constituents are sterols, e.g. β-sitosterol, β-sitosterol-3-O-glucoside and esters of β-sitosterol (e.g. β-sitosterol-3-O-(6'-O-palmitil)-β-D-glucoside). Other constituents include flavonoids (mainly quercetin and kaempferol glycosides) and tannins (gallic acid and ellagic acid derivatives).



β-sitosterol



β-sitosterol-3-O-glucoside



β-sitosterol-3-O-(6'-O-palmitil)-β-D-glucoside

Figure 5.107-109
The structure of β-sitosterol, β-sitosterol-3-O-glucoside and
β-sitosterol-3-O-(6'-O-palmitil)-β-D-glucoside.

Uses

Therapeutic indications of the drug include the symptomatic treatment of micturition disorders (dysuria, pollakisuria, nocturia, urine retention) in benign prostatic hyperplasia (BPH) at stages I and II as defined by Alken or stages II and III as defined by Vahlensieck.

Stages I and II of benign prostatic hyperplasia as defined by Alken

See: Pruni africanae cortex

Stages II and III of benign prostatic hyperplasia as defined by Vahlensieck

See: Pruni africanae cortex

Dosage

Adult daily dose: 3-4 g of the drug as an infusion with 200 ml of water.

Special warnings and precautions for use

All cases of difficult urination require clarification by a doctor and regular medical checks in order to rule out the need for other treatment, e.g. surgical intervention. Consultation with a physician is particularly necessary in cases of blood in the urine or acute urine retention.

Pregnancy and lactation

Not applicable.

Cucurbitae semen

Plant

Cucurbita pepo L. – Pumpkin (Cucurbitaceae)

Pumpkin is a cultivated plant.

Figure 5.110
Pumpkin (*Cucurbita pepo* L.)

Drug

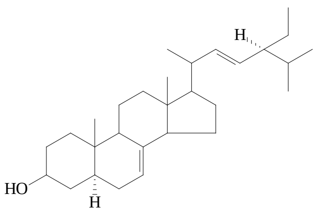
Cucurbitae semen (Pumpkin seed)

The drug consists of the whole, dried, ripe seeds of *Cucurbita pepo* L. and/or certain cultivars.

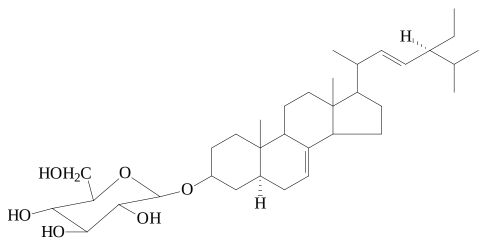
Figure 5.111
Cucurbitae semen (Pumpkin seed)

Constituents

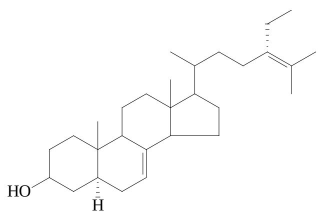
The main characteristic constituents are phytosterols, principally Δ_7-sterols such as stigmasta-7,22-dien-3β-ol (spinasterol), spinasterol-3β-D-glucoside, peposterol. β-sitosterol is present to a lesser extent. Other constituents include triglycerides, free fatty acids, amino acids, selenium, carotenoids and β- and γ-tocopherols.



spinasterol



spinasterol-3β-D-glucoside



peposterol

Figure 5.112-114
The structure of spinasterol, spinasterol-3β-D-glucoside and peposterol.

Uses

Therapeutic indications of the drug include the symptomatic treatment of micturition disorders (dysuria, pollakisuria, nocturia, urine retention) in benign prostatic hyperplasia (BPH) at stages I and II as defined by Alken or stages II and III as defined by Vahlensieck.

Stages I and II of benign prostatic hyperplasia as defined by Alken

See: Pruni africanae cortex

Stages II and III of benign prostatic hyperplasia as defined by Vahlensieck

See: Pruni africanae cortex

Dosage

Adult daily dose: 10-20 g of the seeds or a corresponding amount of an extract.

Special warnings and precautions for use

All cases of difficulty urination require clarification by a doctor and regular medical checks in order to rule out the need for other treatment, e.g. surgical intervention. Consultation with a physician is particularly necessary in cases of blood in the urine or acute urine retention.

Pregnancy and lactation

Not applicable.

Sabalis serrulatae fructus

Plant

Serenoa repens (Bartram) Small. – Saw palmetto (Arecaceae)

This palm is native to USA.

Drug

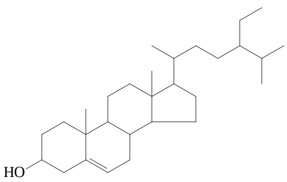
Sabalis serrulatae fructus (Saw palmetto fruit, Ph. Eur.)

The drug consists of the dried ripe fruit of *Serenoa repens* (Bartram) Small. (*Sabal serrulata* (Michaux) Nichols). It contains minimum 11.0% of total fatty acids, calculated with reference to the dried drug. It has characteristic, strong, unpleasant but not rancid odour.

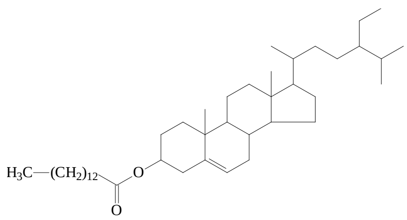
Figure 5.115
Sabalis serrulatae fructus (Saw palmetto fruit)

Constituents

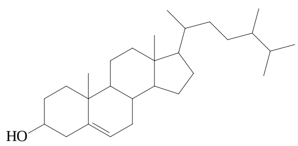
The main characteristic constituents are sterols, e.g. β-sitosterol and its 3-glucoside (and fatty acid derivatives of these, e.g. β-sitosterol-3-O-miristate), campesterol and stigmasterol. Other constituents include free fatty acids such as capric, caproic, caprylic, lauric, myristic, oleic, linoleic, stearic and palmitic acids; triglycerides, flavonoids, polysaccharides and essential oil.



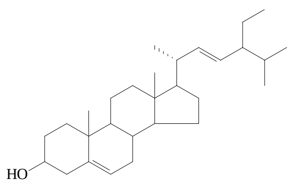
β-sitosterol



β-sitosterol-3-O-miristate



campesterol



stigmasterol

Figure 5.116-119
The structure of β-sitosterol, β-sitosterol-3-O-miristate, campesterol and stigmasterol.

Uses

Therapeutic indications of the drug include the symptomatic treatment of micturition disorders (dysuria, pollakisuria, nocturia, urine retention) in benign prostatic hyperplasia (BPH) at stages I and II as defined by Alken or stages II and III as defined by Vahlensieck.

Stages I and II of benign prostatic hyperplasia as defined by Alken

See: Pruni africanae cortex

Stages II and III of benign prostatic hyperplasia as defined by Vahlensieck

See: Pruni africanae cortex

Dosage

Adult daily dose: 1-2 g of the drug or 320 mg of lipophilic extract or other equivalent preparation.

Special warnings and precautions for use

All cases of difficult urination require clarification by a doctor and regular medical checks in order to rule out the need for other treatment, e.g. surgical intervention. Consultation with a physician is particularly necessary in cases of blood in the urine or acute urine retention.

Pregnancy and lactation

Not applicable.

5.4 Spirostanes, furostanes and steroidal saponins

Spirostanes and furostanes are steroids containing 27 C-atoms; they are formed from sterols (e.g. cholesterol).

Furostanes: a furan- (tetrahydro-furan)-ring (E-ring) is formed from the side-chain attached to the C-17-atom of the steroid-skeleton. **Spirostanes:** they contain a tetrahydro-furan (E-ring) and a tetrahydro-piran ring (F-ring), e.g. diosgenin. Sometimes the 6-membered ring is a piperidin-ring containing N-atom (e.g. solasodine). These constituents are **steroidglycoalkaloids** and occur principally in the family of Solanaceae. In the group of spirostanes there may be differences in the configuration of C-5 and C-25 carbon atoms. The configuration of the C-5-atom depends on the *cis-trans* position of A/B-rings. In the case of *trans*-configuration the H-atom being on the C-5-atom has α-position (5α), but in the case of cis-configuration this H-atom has β-position (5β) (see **Figure 5.120-127**). Between carbon atoms C-5-6 a double bond is also possible (Δ^5-type). According to the configuration of the C-25 carbon atom we distinguish two main groups of spirostanes: 25D (25α) and 25L (25β).

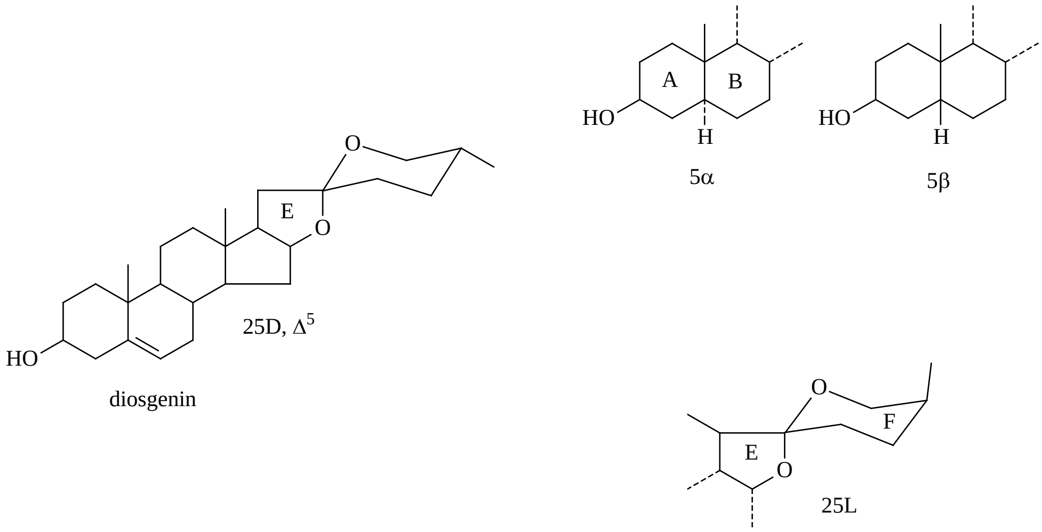


Figure 5.120-122
The most important types of spirostanes.

Furostanes and spirostanes occur both in free and glycosidic form in various plants. If there is a sugar moiety in the molecule, the resulting compounds are called **steroidal saponins**. Similarly to triterpene saponins, their aqueous solutions can produce a soap-like froth and they hemolyze red blood cells.

They occur mainly in monocotyledons (Liliaceae, Agavaceae, Dioscoreaceae, Poaceae) and sporadically in dicotyledons (e.g.: *Digitalis* species). Drugs containing steroid-saponins have expectorant effect, they can be used for the treatment of purulent wounds, furuncles and different dermatological diseases. However, their main pharmaceutical significance lies in the fact that they are excellent raw materials for the pharmaceutical industry. Some are used as starting materials for the synthesis of sex hormones, cortisone or vitamin D.

Drugs

Dioscoreae tuber

Plant

Dioscorea mexicana, D. composita, D. floribunda, other Dioscorea species – Yams (Dioscoreaceae)

These plants are native to tropical and warm temperate regions of the world.

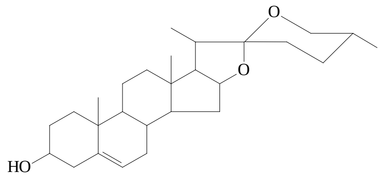
Drug

Dioscoreae tuber (Yam root)

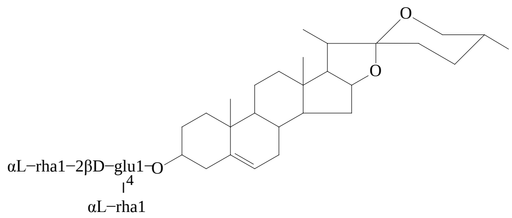
The drug consists of the succulent, tuberous rhizome and branches (secondary roots) of *Dioscorea mexicana, D. composita, D. floribunda* or other *Dioscorea* species.

Constituents

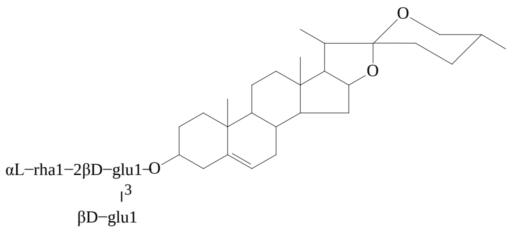
The main characteristic constituents are steroidal saponins (1-8%), e.g. diosgenin aglycon and dioscin, gracillin. The root also contains starch and proteins.



diosgenin



dioscin



gracillin

Figure 5.123-125
The structure of diosgenin, dioscin and gracillin.

Uses

The aqueous extract of *D. villosa* is used as a spasmolytic, antiphlogistic and antirheumatic drug in the USA. In the pharmaceutical industry diosgenin is used as a raw material for producing pregnadienolon-acetate. This compound is a starting material of steroid drugs.

Avenae herba

Plant

Avena sativa L. – Common oat (Poaceae)

It is an annual plant and native to Europe, the Mediterranean region, Middle East and China. It can be cultivated.

Drug

Avenae herba (Oat herb)

Avenae herba consists of the fresh or dried aerial parts of *Avena sativa* L.

Figure 5.126
Avenae herba (Oat herb)

Constituents

The drug contains silicic acid, oligosaccharides, special amino acids, flavonoids (e.g. apigenin, vitexin, isovitexin, luteolin) and steroidal saponins (e.g. avenacoside A and B).

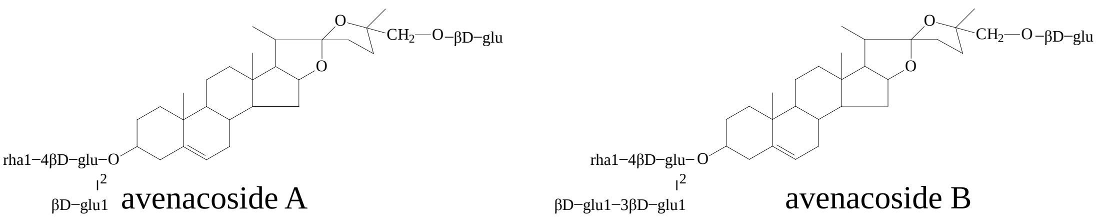


Figure 5.127-128
The structure of avenacoside A and B.

Uses

The therapeutic indications include the symptomatic treatment of minor inflammations of the skin and mucosa and the relief of mild symptoms of mental stress and help falling asleep. The drug and its preparations aid the healing of minor wounds, leg ulcers and burns.

Dosage

Adults and elderly dose:

Comminuted herbal substance (single dose): 3 g for the preparation of an infusion. Liquid extract (1:4-6 ethanol 15-50% v/v): up to 5 ml up to 3 times daily. Liquid extract (1:4-6 water): up to 5 ml up to 3 times daily.

The use of the drug is not recommended in children under 12 years of age.

Special warnings and precautions for use

Caution is advised when used in patients with coeliac disease because data on the protein content are not available.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Trigonellae foenugraeci semen

Plant

Trigonella foenum-graecum L. – Fenugreek (Fabaceae)

It is an annual plant and native to Europe, Mediterranean region, Middle East, China. It can be cultivated.

Figure 5.129
Fenugreek (Trigonella foenum-graecum L.)

Drug

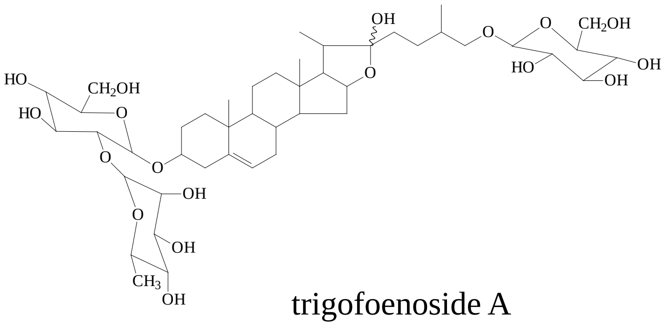
Trigonellae foenugraeci semen (Fenugreek, Ph. Eur.)

Fenugreek consists of the dried, ripe seeds of *Trigonella foenum-graecum* L. It has a strong characteristic aromatic odour.

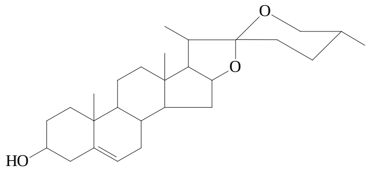
Figure 5.130
Trigonellae foenugraeci semen (Fenugreek)

Constituents

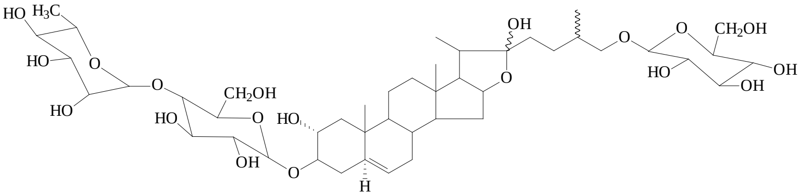
The characteristic constituents are steroidal saponins, occurring mainly as furostanol 3,26-diglycosides such as trigofoenosides A-G. On hydrolysis the saponins yield 0.6-1.7% of spirostanol sapogenins consisting mainly (approx. 95%) of diosgenin and its 25β-epimer yamogenin in a 3:2 ratio, together with tigogenin. Steroidal sapogenin-peptide esters such as fenugreekine are also present. Other constituents include mucilage galactomannane polysaccharides, trigonelline (= coffearine, N-methylbetaine of nicotinic acid), protein, amino acids, enzymes, flavonoids, sterols, lecithin and choline. The characteristic aroma compound of the drug is 3-hydroxy-4,5-dimethyl-2-(5*H*)-furanone (sotolone).



trigofoenoside A



diosgenin



trigofoenoside B

Figure 5.131-136
The structure of trigofoenoside A and B, diosgenin, yamogenin, trigonelline and 3-hydroxy-4,5-dimethyl-2-(5*H*)-furanone (sotolone).

Uses

Internally the drug can be used in the adjuvant therapy of diabetes mellitus, in the case of anorexia, as an adjunct to a low fat diet in the treatment of mild to moderate hypercholesterolaemia. Externally the drug and its products are used to treat furunculosis, ulcers and eczema.

Dosage

Internal use

Adults:

Diabetes mellitus or hypercholesterolaemia: 25 g of powdered seeds or equivalent preparations daily.

Lack of appetite: 1-6 g of powdered seeds up to three times daily with water, before meals.

Overdose: 100 g of the drug taken daily can cause minor gastrointestinal symptoms such as diarrhoea and flatulence.

External use

It can be used as an emollient. 50 g of powdered seeds boiled in 250 ml of water for 5 min, then applied as a warm moist poultice.

Interactions with other medicaments

Because of mucilage content fenugreek may affect the absorption of drugs taken simultaneously.

Pregnancy and lactation

Fenugreek should not be used during pregnancy and lactation.

Rusci rhizoma

Plant

Ruscus aculeatus L. – Butcher's broom (Liliaceae)

This plant is native to Europe.

Figure 5.137
Butcher's broom (*Ruscus aculeatus* L.)

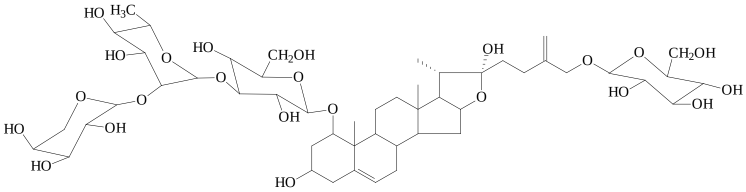
Drug

Rusci rhizoma (Butcher's broom, Ph. Eur.)

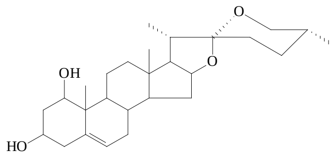
The drug consists of the dried, whole or fragmented underground parts of *Ruscus aculeatus* L. It contains minimum 1.0% of total sapogenins, expressed as ruscogenins (mixture of neoruscogenin and ruscogenin), calculated with reference to the dried drug.

Constituents

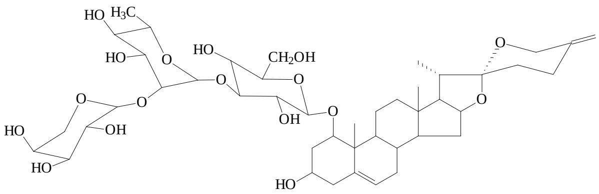
The characteristic constituents of the drug are steroidal saponins based upon (25R)-spirost-5-ene-1β,3β-diol (ruscogenin) and spirosta-5,25(27)-diene,10,3β-diol (neoruscogenin), such as ruscoside, ruscin, deglucoruscoside and deglucoruscin. Other constituents are flavonoids, anthraquinones, essential oil and sterols.



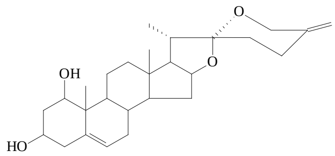
ruscoside



ruscogenin



ruscin



neoruscogenin

Figure 5.138-141
The structure of ruscogenin, neoruscogenin, ruscoside and ruscin.

Uses

The therapeutic indications include the supportive therapy for relieving the symptoms of chronic venous insufficiency, such as painful and heavy legs, tingling and swelling. Supportive therapy for symptoms of haemorrhoids, such as itching and burning.

Dosage

Adult and elderly daily dose: Solid or liquid extracts in amounts corresponding to 7-11 mg of total ruscogenins.

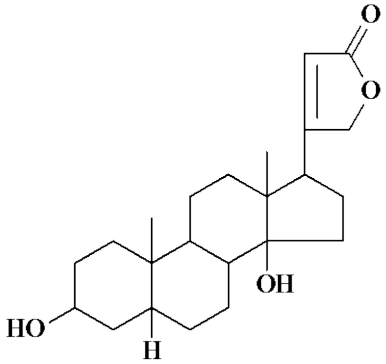
Pregnancy and lactation

In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice. No adverse effects have been reported in mothers or newborn babies when used in late pregnancy.

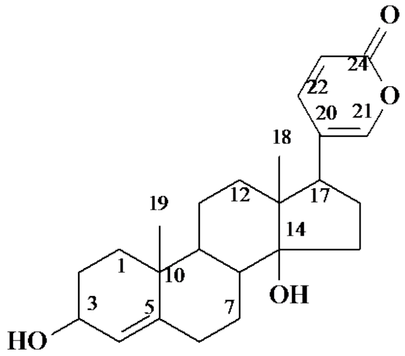
5.5 Cardenolides and bufadienolides

Cardioactive glycosides are a kind of steroid glycosides, which act on the human heart. We can distinguish two main aglycone types of the cardioactive glycosides: cardenolides and bufadienolides. Medicinally the cardenolide group is more important. Cardenolides have a steroid skeleton with 23 C-atoms and contain γ-lacton (butenolide) ring, e.g. digitoxygenin.

Bufadienolides with 24 C-atoms contain, on the C-17 carbon atom, a δ-lacton ring (α, β - γ, δ doubly unsaturated), e.g. scillarenin (**Figure 5.142-148**).



digitoxygenin (cardenolide type)



scillarenin (bufadienolide type)

Figure 5.142-143
The structure of cardenolides and bufadienolides.

In both types of aglycones, a sugar molecule or a side chain containing sugar molecules is connected to the β-OH group of C-3 carbon atom. The sugar components of cardioactive glycosides are mainly deoxy-sugars and glucose. If glucose is present in the chain, it can always be found at the end of the chain. The deoxy-sugars are 6-deoxy-sugars (e.g. L-rhamnose, D-fucose, D-digitalose, L-tevetose) or 2,6-deoxy-sugars (e.g. D-digitoxose, D-cymarose, L-oleandrose) (**Figure 5.144**). Recently, 2-O-methyl and 2-O-acetyl sugars have also been discovered.

The biosynthesis of cardenolides and bufadienolides starts from cholesterol (C_{27}) through pregnane derivatives [(by side-chain shortening (C_{21}); e.g. progesterone)] (**Figure 5.145**). In the formation of these compounds the incorporation of the active acetyl group of acetyl-CoA plays an important role. Cardenolides dissolve in alcohols (eg. methanol, ethanol). Cardioactive glycosides occur rarely in higher plants, their occurrence is not characteristic even at the level of plant families, they are associated rather with some genera or species. Some families with cardiac glycoside-containing taxa are: Apocynaceae, Liliaceae, Ranunculaceae, Fabaceae, Moraceae, Scrophulariaceae, Euphorbiaceae. Cardioactive glycosides exert their pharmacological effect on the heart muscles. In therapeutic dose they improve cardiac output by increasing the force of heart muscle contraction and increasing the volume of blood pumped into the vascular system (positive inotropic action). They can decrease heart rate (negative chronotropic action) and venous pressure, while diuresis shows an upward tendency. The action of cardenolic glycosides is always greater than the action of the corresponding aglycones. Cardenolide glycosides are employed in the case of heart insufficiency, which occurs as a consequence of aherosclerosis, hypertonia, asthma cardiale or problems with a cardiac valve (valvular or cardiac insufficiency).

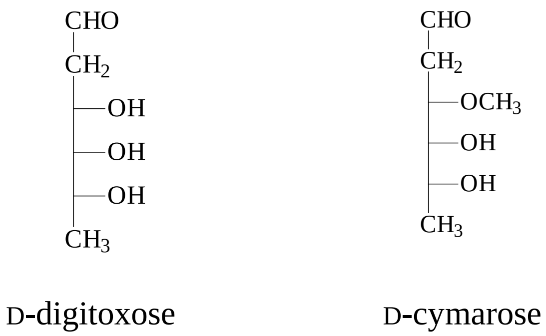


Figure 5.144
The structure of D-digitoxose and D-cymarose.

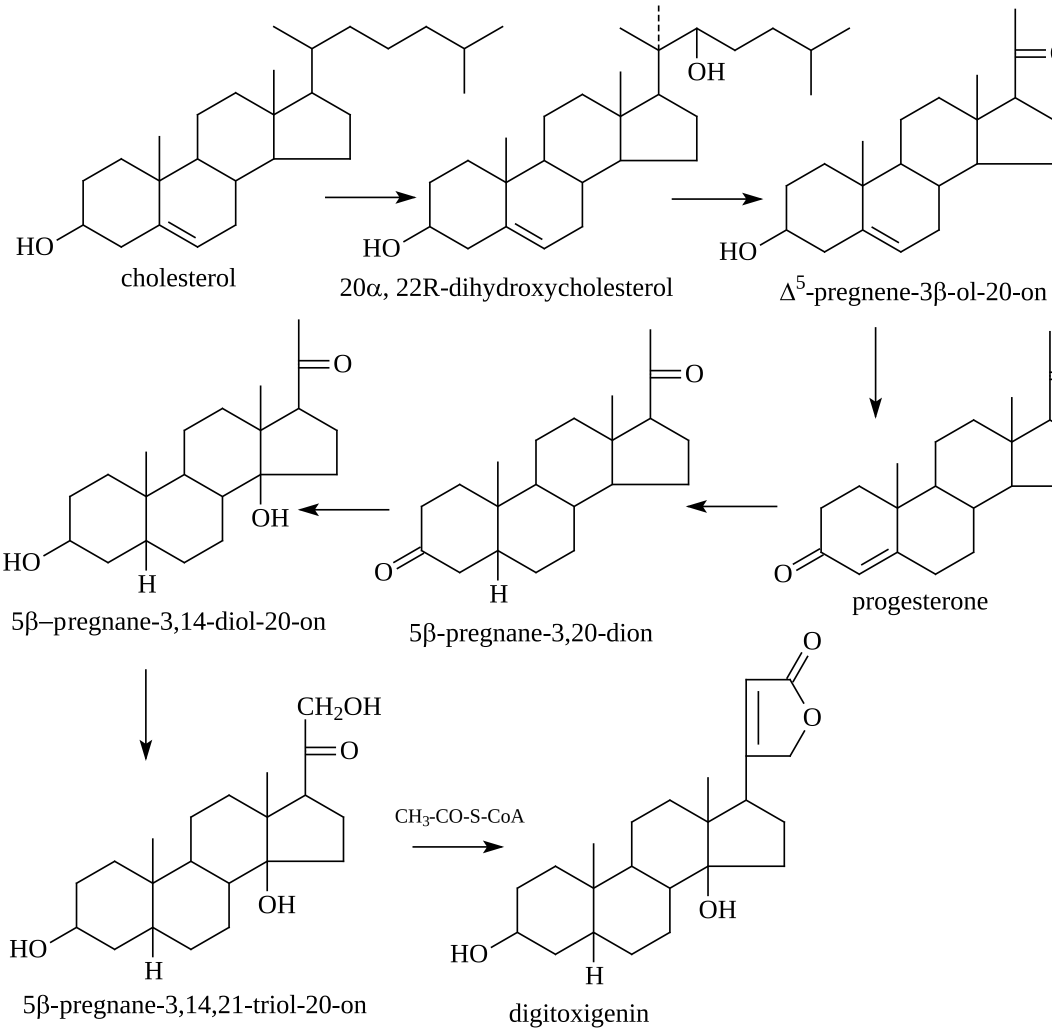


Figure 5.145
The formation of cardenolides from cholesterol.

Drugs

Digitalis purpureae folium

Plant

Digitalis purpurea L. – Purple foxglove (Scrophulariaceae)

This biennial or short-lived perennial plant is native to most of temperate-Europe and North-Africa. It is cultivated as an ornamental and medicinal plant.

Figure 5.146
Purple foxglove (*Digitalis purpurea* L.)

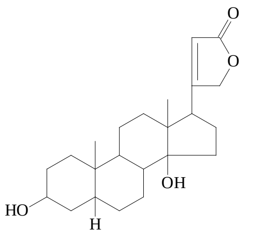
Drug

Digitalis purpureae folium (Purple foxglove leaf)

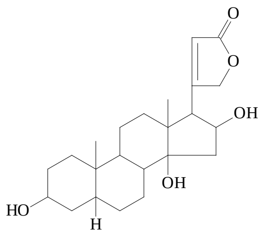
The drug consists of the dried first- or second-year leaves of *Digitalis purpurea* L. It contains not less than 0.3% of total cardenolides calculated as digitoxin.

Constituents

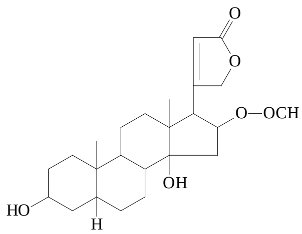
The characteristic constituents of the drug are cardenolide glycosides (0.15-0.4%). Their aglycones are: digitoxigenin, gitoxigenin and gitaloxigenin. The main glycosides include purpurea glycoside A, purpurea glycoside B and purpurea glycoside C, digitoxin, gitoxin and gitalotoxin. Other constituents are steroidal saponins, flavonoids (e.g. apigenin, luteolin), derivatives of cinnamic acid such as caffeic acid and chlorogenic acid and anthraquinone-derivatives.



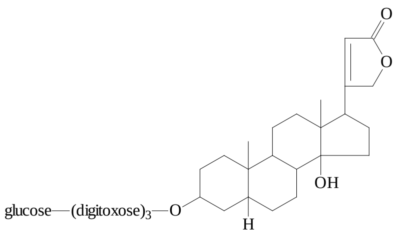
digitoxigenin



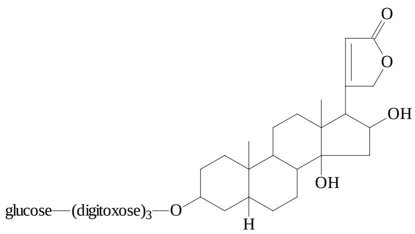
gitoxigenin



gitaloxigenin



purpurea glycoside A



purpurea glycoside B

Figure 5.147-155
The structure of digitoxigenin, gitoxigenin, gitaloxigenin, purpurea glycoside A, purpurea glycoside B, purpurea glycoside C, digitoxin, gitoxin and gitalotoxin.

Uses

The isolated constituents act on the heart. They have positive inotropic effects. The fine powder of the dried leaves is used in pharmaceutical technology for preparing pellets. Digitoxin prepared in a pure crystalline form is used to make tablets.

The drug or extracts or its pure constituents are very toxic, therefore they should not be used without medical advice.

Digitalis lanatae folium

Plant

Digitalis lanata Ehrh. – Woolly foxglove (Scrophulariaceae)

This perennial or biennial plant is native to central and south-eastern Europe. It can be cultivated. This plant is protected in Hungary.

Figure 5.156
Woolly foxglove (*Digitalis lanata* Ehrh.)

Drug

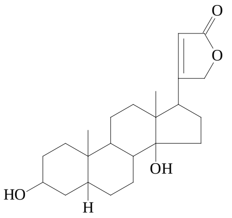
Digitalis lanatae folium (Woolly foxglove leaf)

The drug consists of the dried first-year leaves of *Digitalis lanata* Ehrh.

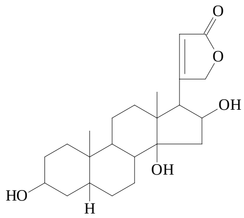
Figure 5.157
Digitalis lanatae folium (Woolly foxglove leaf)

Constituents

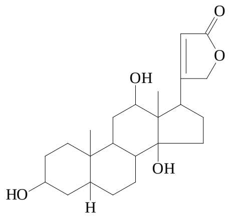
The characteristic constituents of the drug are cardenolide glycosides (1%). Their aglycones are: digitoxigenin, gitoxigenin, digoxigenin, diginatigenin and gitaloxigenin. The main glycosides include lanatoside A, lanatoside B, lanatoside C, lanatoside D, lanatoside E, digitoxin, digoxin, acetyldigoxin and glucoverodoxin. Other constituents are steroidal saponins, flavonoids (e.g. apigenin, luteolin), caffeic acid and *p*-coumaric acid and anthraquinone-derivatives.



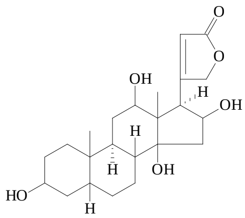
digitoxigenin



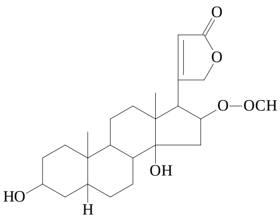
gitoxigenin



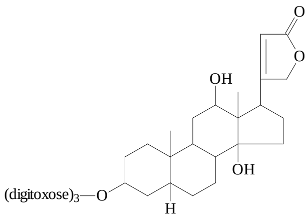
digoxigenin



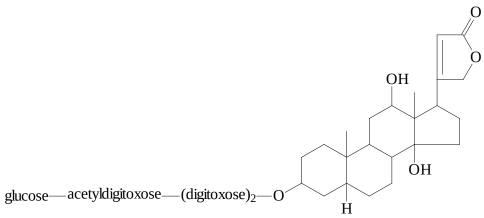
diginatigenin



gitaloxigenin



digoxin



lanatoside C

Figure 5.158-164
The structure of digitoxigenin, gitoxigenin, digoxigenin, diginatigenin, gitaloxigenin, digoxin and lanatoside C.

Uses

The isolated constituents act on the heart. They have positive inotropic effects. The leaves are used principally for the preparation of lanatosides and digoxin. Digoxin has become the most widely used drug in the treatment of congestive heart failure. Digoxin is more rapidly absorbed from the gastrointestinal tract than the purpurea glycosides. Lanatoside C is less well absorbed than digitoxin but it is less cumulative.

Overall the pharmacological effects of the *Digitalis* glycosides start approx. 6 to12 hours after administration, but the constituents break down completely after 10 to 20 days.

The drug or extracts or its pure constituents are very toxic, therefore they should not be used without medical advice.

Strophanthi semen

Plant

Strophanthus kombe Oliver – Strophanthus (Apocynaceae)

This plant is a climbing shrub and native to tropical East-Africa.

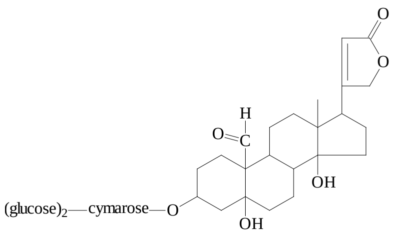
Drug

Strophanthi semen (Strophanthus seed)

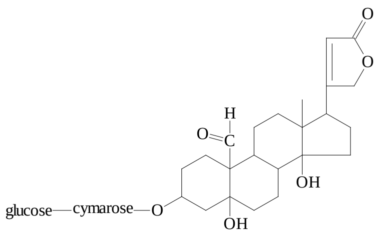
The drug consists of the the seeds without their feathery hairs of *Strophanthus kombe* Oliver.

Constituents

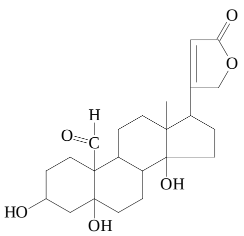
The characteristic constituents of the drug are cardenolide glycosides (8-10%). The main glycosides are K-strophanthoside, K-strophanthin-β and cymarin, all based on the aglycone of strophanthidin. The other constituents of the seeds include 30% of fatty oil, trigonelline, choline and mucilage.



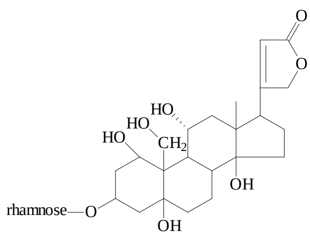
K-strophanthoside



K-strophanthin-β



strophanthidin



G- strophanthin (= ouabain)

Figure 5.165-168
The structure of K-strophanthoside, K-strophanthin-β, strophanthidin and G- strophanthin (= ouabain).

Uses

The cardioactive constituents of the drug in a pure crystalline form are used for the preparation of injections. Cardioactive glycosides of the drug administered in intravenous injections act within a few minutes, and their effect lasts for approx. 36 hours. Their pharmacological activity is similar to that of *Digitalis* glycosides, but *Strophanthus* glycosides do not accumulate, therefore these cardenolides are used in the case of acute cardiac insufficiency as life-saving medicines. *Strophanthus gratus* seeds (*Strophanthi grati semen*) contain 4-8% cardioactive glycosides with G-strophanthin (= ouabain), which can also be used in injections. *Strophanthus gratus* is native to West-Africa.

The drug or extracts or its pure constituents are very toxic, therefore they should not be used without medical advice.

Convallariae herba

Plant

Convallaria majalis L. – Lily of the valley (Liliaceae)

This perennial plant is native to Europe and in the temperate zones of Asia. It occurs in oak-woods and other deciduous forests.

Figure 5.169
Lily of the valley (*Convallaria majalis* L.)

Drug

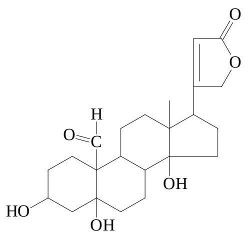
Convallariae herba (Lily of the valley)

The drug consists of the dried aerial parts (collected when the flowers are beginning to open) of *Convallaria majalis* L.

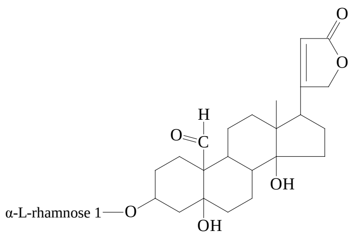
Figure 5.170
Convallariae herba (Lily of the valley)

Constituents

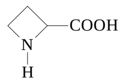
The characteristic constituents of the drug are cardenolide glycosides (0.2-0.5%). The principal glycoside is convallatoxin which on hydrolysis yields strophanthidin and (-)-rhamnose. The plant contains several minor cardenolides (about 40 glycosides associated with nine different aglycones). Other constituents are steroidal saponins, flavonoids (mainly apigenin, luteolin, kaempferol, quercetine and their derivatives) and azetidin-2-carboxylic acid.



strophanthidin



convallatoxin



azetidin-2-carboxylic acid

Figure 5.171-173
The structure of strophanthidin, convallatoxin and azetidin-2-carboxylic acid.

Uses

The therapeutic indications include the treatment of cardiac insufficiency, cor pulmonale and cardiac failures associated with oedema formation. It has diuretic effect. The drug or extracts or its pure constituents are very toxic, therefore they should not be used without medical advice.

Adonidis herba

Plant

Adonis vernalis L. – Spring pheasant's eye (Ranunculaceae)

This perennial plant is native to Europe, Caucasus and Siberia. In Hungary it is protected because of its rare occurrence. It occurs in Mecsek and Bakony mountains.

Figure 5.174
Spring pheasant's eye (*Adonis vernalis* L.)

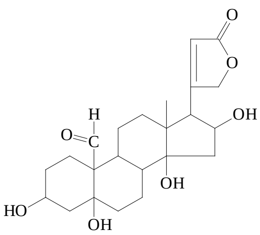
Drug

Adonidis herba (Spring pheasant's eye)

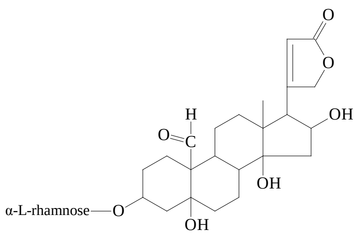
The drug consists of the dried aerial flowering parts of *Adonis vernalis* L.

Constituents

The characteristic constituents of the drug are cardenolide glycosides (0.25-0.5%). The principal glycoside is adonitoxin which is the glycoside of adonitoxigenin. The drug also contains strophanthidin-type cardenolides. Other constituents are flavonoid-glycosides, ascorbic acid (vitamin C) and sugar alcohols.



adonitoxigenin



adonitoxin

Figure 5.175-176
The structure of adonitoxigenin and adonitoxin.

Uses

The cardenolides of the drug are poorly absorbed from the gastrointestinal tract, but they are broken down more quickly than *Digitalis* cardenolides, therefore they cannot accumulate. The therapeutic indications include nervous cardiac troubles, angina pectoris, cardiac failures associated with oedema formation. It has diuretic effect. The drug or its extracts and pure constituents are very toxic, therefore they should not be used without medical advice.

Nerii folium

Plant

Nerium oleander L. – Oleander (Apocynaceae)

This perennial woody shrub (or small tree) is native to South-Europe and West-Asia. It is cultivated as ornamental plant.

Figure 5.177
Oleander (*Nerium oleander* L.)

Drug

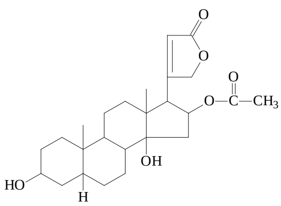
Nerii folium (Oleander leaf)

The drug consists of the dried leaves (collected during flowering period) of *Nerium oleander* L.

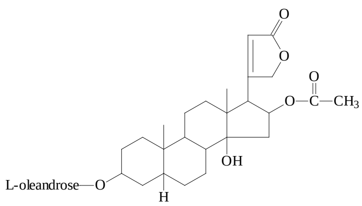
Figure 5.178
Nerii folium (Oleander leaf)

Constituents

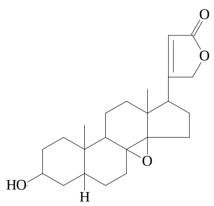
The characteristic constituents of the drug are cardenolide glycosides (1-2%). The principal glycosides are oleandrin, adynerin, odoroside A and oleasides A-F. The main aglycones include oleandrigenin (=16-acetylgitoxigenin), adynerigenin (= 3-hydroxy-8,14-epoxycardenolide), digitoxigenin, oleagenin and uzarigenin (= 5α-digitoxigenin). The drug also contains flavonoids such as rutin and kaempferol-3-O-rhamnoglucoside; as well as ursolic and oleanolic acids.



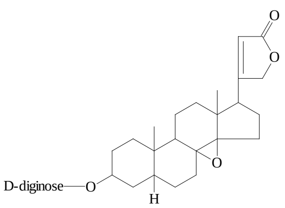
oleandrigenin



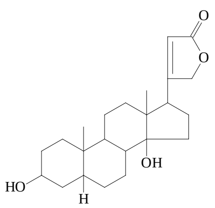
oleandrin



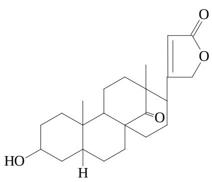
adynerigenin



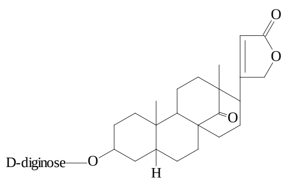
adynerin



digitoxigenin



oleagenin



oleaside A

Figure 5.179-185
The structure of oleandrigenin, oleandrin, adynerigenin, adynerin, digitoxigenin, oleagenin and oleaside A.

Uses

The cardenolides of the drug act similarly to the *Digitalis* cardenolides. The industrial preparations of the drug can be used for the treatment of arrhythmia and circulatory disorders, as well as other cardiac complaints associated with changes in the weather. The drug or its extracts and pure constituents are very toxic, therefore they should not be used without medical advice.

Erysimi herba et semen

Plant

Erysimum diffusum Ehrh. – Gray diffuse wallflower (Brassicaceae)

This perennial, overwintering, herbaceous plant is native to Europe and Asia.

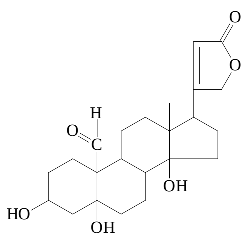
Drug

Erysimi herba et semen (Gray diffuse wallflower flowering shoot and seed)

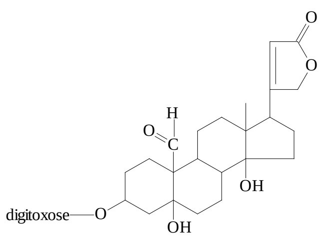
The drug consists of the dried aerial flowering parts and seeds of *Erysimum diffusum* Ehrh.

Constituents

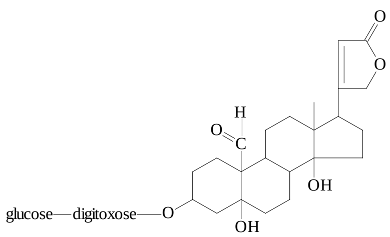
The characteristic constituents are cardenolides based on strophanthidin aglycone. The principal cardenolides include helveticoside and erizimoside (= glucohelveticoside). The seeds contain glucosinolates, sterols and fatty oil. Flavonoids occur mostly in the aerial parts of the plant.



strophanthidin



helveticoside



erizimoside (= glucohelveticoside)

Figure 5.186-188
The structure of strophanthidin, helveticoside and erizimoside (= glucohelveticoside).

Uses

Formerly the drug was used for the treatment of mild cardiac insufficiency. At present the plant is not frequently used.

Leonuri cardiacae herba

Plant

Leonurus cardiaca L. – Motherwort (Lamiaceae)

This perennial plant is native to Mediterranean countries, Europe and Asia.

Figure 5.189
Motherwort (*Leonurus cardiaca* L.)

Drug

Leonuri cardiacae herba (Motherwort, Ph. Eur.)

The drug consists of the whole or cut, dried flowering aerial parts of *Leonurus cardiaca* L. It contains minimum 0.2% of flavonoids, expressed as hyperoside, and calculated with reference to the dried drug.

Figure 5.190
Leonuri cardiacae herba (Motherwort)

Constituents

The characteristic constituents of the drug are bufadienolides. They are glycosides of scillarenin and 5,6-dehydro-scillarenin. Other constituents include diterpenes (e.g. marrubiin), iridoids (e.g. ajugoside), flavonoids, stachidrin (dimethyl-pirrolidinium-2-carboxilate) and triterpenes such as ursolic and oleanolic acid.

scillarenin 5,6-dihydro-scillarenin

Figure 5.191-192
The structure of scillarenin and 5,6-dehydro-scillarenin.

Uses

The drug can be used for the treatment of mild cardiac insufficiency and nervous heart complaints. *Leonuri cardiacae herba* may be combined with *Crategi folium cum flore* (hawthorn leaf and flower) in herbal teas.

Dosage

Adult and elderly daily dose: 4 g of the drug as an infusion.

Scillae bulbus

Plant

Urginea maritima (L.) Baker – Squill (Liliaceae)

Squill occurs wild as an aggregate of at least six species of varying chromosome number. The plant is native to Mediterranean countries and West Asia. White squill can be found in Spain, Portugal, Sardinia, Malta, Cyprus and Greece; red squill is native to Algeria and Marocco.

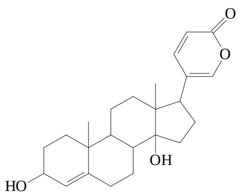
Drug

Scillae bulbus (Squill bulb)

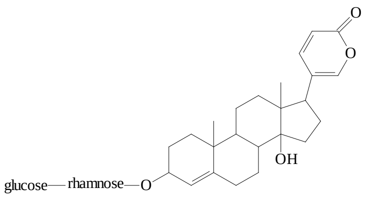
The drug consists of the dried sliced bulbs of *Urginea maritima* (L.) Baker, from which the membranous outer scales have been removed.

Constituents

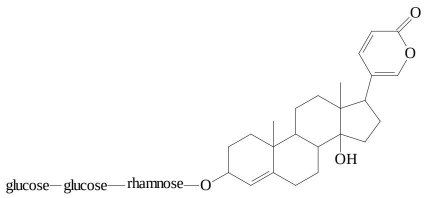
The characteristic constituents of the drug are bufadienolides. In white squill there is a mixture of 15 bufadienolides: the aglycone is scillarenin and the principal glycosides are scillaren A, glucoscillaren A and proscillaridin A. In red squill the principal glucosides are scillirozide and glucoscillirozide, their aglycone part is scillirosidine.



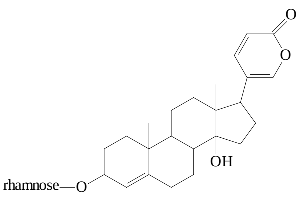
scillarenin



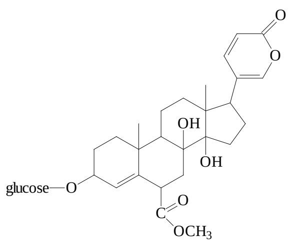
scillaren A



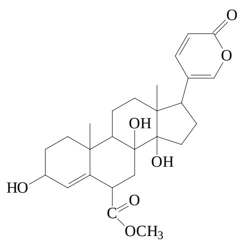
glucoscillaren A



proscillaridin A



scillirozide



scillirosidine

Figure 5.193-198
The structure of scillarenin, scillaren A, glucoscillaren A, proscillaridin A, scillirozide and scillirosidine.

Uses

In pharmaceutical industry white squill is used principally. Scillaren A and proscillaridin A can be absorbed from the gastrointestinal tract (almost in 25%), therefore these compounds are administered orally. The therapeutic indications include aorta-insufficiency, angina pectoris, oedema associated with nephritis. In small doses the drug provokes mild gastric irritation causing a reflex secretion from the bronchioles, therefore it can be used as an expectorant, but in large doses it causes vomiting.

The drug should not be used without medical advice.

Hellebori radix (et rhizoma)

Plant

Helleborus niger L. – Black hellebore (Ranunculaceae)

This perennial plant is indigenous to Central Europe. In Hungary *Helleborus* species are protected.

Figure 5.199
Black hellebore (*Helleborus niger* L.)

Drug

Hellebori radix (*et rhizoma*) (Black hellebore root et rhizome)

The drug consists of the whole or cut, dried roots and rhizomes of *Helleborus niger* L.

Figure 5.200
Hellebori radix (*et rhizoma*) (Black hellebore root et rhizome)

Constituents

The characteristic constituents of the drug are bufadienolides. The principal constituent is hellebrin which is the glycoside of the aglycone hellebrigenin. The drug also contains steroidal saponins, but their structure has not been identified yet.

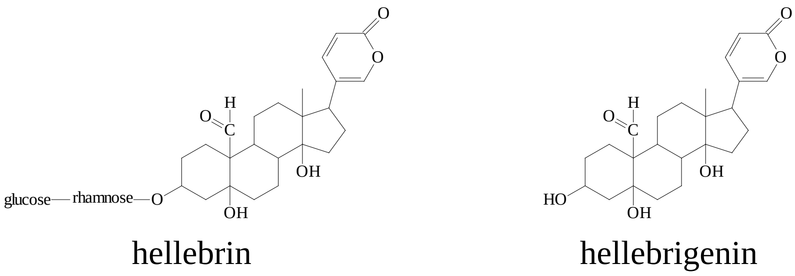


Figure 5.201-202
The structure of hellebrin and hellebrigenin.

Uses

The bufadienolides of the drug have a digitalis-like action. The aglycone hellebrigenin is the bufadienolide analogue of strophanthidin. The drug which has cardiotonic as well as abortifacient properties is considered dangerous and is now obsolete in ordinary medicine. The drug is used principally in veterinary medicine: *Hellebori rhizoma* is placed into the ears of pigs, sheep or in the chest of cows, where the drug causes inflammation, and it increases the resistance of these animals against different infections (so called stimulus therapy).

Chapter 6
Drugs containing alkaloids of ornithine, lysine and phenylalanine origin

Definition of alkaloids

Old definition: Alkaloids are the end products of plant metabolism; they are organic heterocyclic bases containing N-atom and having strong physiological action.

In the meantime it has been justified that alkaloids occur also in animals (e.g. salamanders, frogs, insects, sea animals, etc.), as well as fungi and bacteria.

New definition: Alkaloids are cyclic organic compounds, which contain the N-atom in the state of negative oxydation grade; and occur in various living organisms in limited quantities.

Classification of alkaloids

Compared with most other classes of natural compounds, alkaloids are characterized by a great structural diversity and there is no uniform classification for alkaloids. They are often divided into the following major groups:

- "True alkaloids", which contain N-atom in a heterocycle and originate from amino acids. Their characteristic examples are atropine, nicotine and morphine. This group also includes some alkaloids which beside nitrogen containing heterocycle contain terpene (e.g. evonine) or peptide fragments (e.g. ergotamine). This group also includes piperidine alkaloids (e.g. coniine), although they do not originate from amino acids.
- "Protoalkaloids", which contain N-atom outside the heterocycle, but in the form of amino group; they also originate from amino acids (e.g. mescaline, ephedrine).
- Polyamine alkaloids: they are derivatives of putrescin, spermidine and spermine.
- Peptide and cyclopeptide alkaloids.
- Pseudoalkaloids. Their biosynthesis does not start from amino acids:
- Terpene alkaloids (e.g. aconitine);
- Steroid alkaloids (tomatidine, solanidine).

Another possibility for classification

One of the well-established classifications is based on the **chemical structures** of alkaloids. According to this classification there are two main classes:

- Nonheterocyclic or atypical alkaloids, sometimes called „protoalkaloids" or biological amines.
- Heterocyclic or typical alkaloids, divided into 14 groups according to their ring structure.

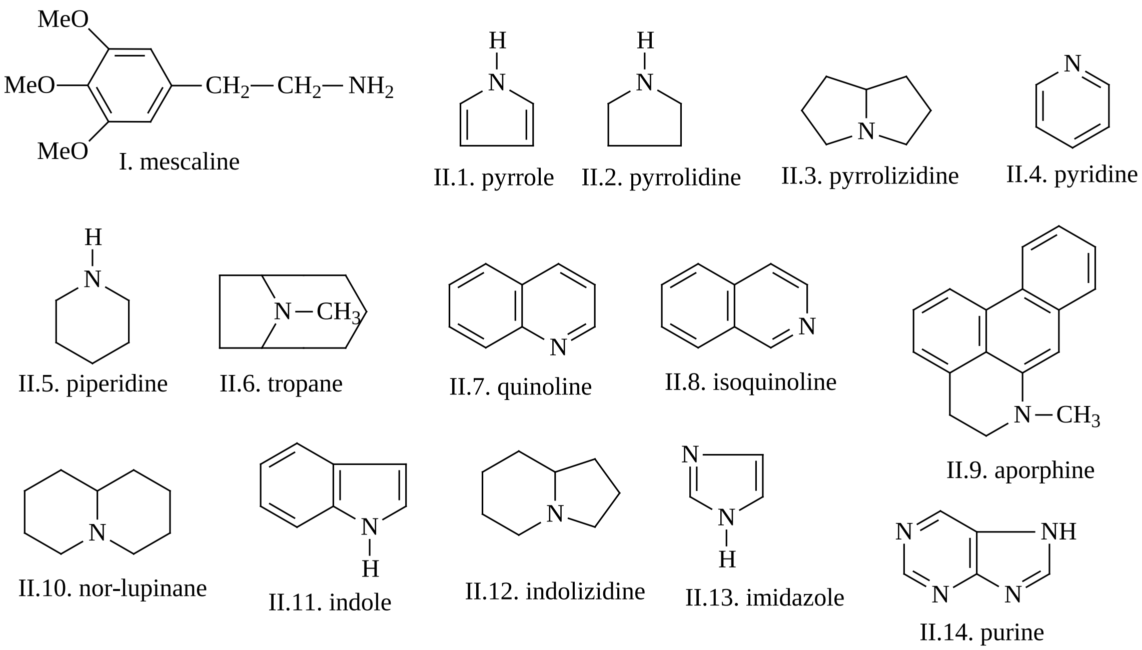


Figure 6.1
The most important groups of alkaloids based on their structure.

Alkaloids occur in both plants and animals. The plant species in the following plant families can produce alkaloids with various structures: Magnoliaceae, Lauraceae, Menispermaceae, Berberidaceae, Ranunculaceae, Papaveraceae, Fabaceae, Rutaceae, Loganinaceae, Apocynaceae, Gentianaceae, Rubiaceae, Boraginaceae, Solanaceae, Asteraceae, Liliaceae, Amaryllidaceae, Orchidaceae, etc.

Most important properties of alkaloids

Most alkaloids are crystalline substances which form salts with various acids, such as malic acid, succinic acid, fumaric acid, meconic acid and citric acid. In plants alkaloids may exist in the free state, as salts or as N-oxides. A few, for example nicotine and coniine are oxygen-free and are liquids. There are some coloured alkaloids such as berberine (yellow) or sanguinarine (copper-red), but alkaloids are generally colourless. Usually the free bases cannot be dissolved in water but are readily dissolved in organic solvents. Salts are soluble in water but sparingly soluble in organic solvents. Of course there are some exceptions (e.g. caffeine, colchicine). They have a variety of applications and medicinal uses, which will be detailed at the description of each plant drug.

Extraction: Extraction methods of alkaloids vary depending on the scale and purpose of the process, as well as the nature of the raw material. Most alkaloids are present in the form of salts formed with organic acids in the source plants. Generally, drugs are soaked with the mixture of ammonia and 70% alcohol (3:7). Base extraction is achieved by processing the raw material with alkaline solutions (e.g. ammonia) and extracting the alkaloid bases with organic solvents, such as 1,2-dichloroethane, chloroform, diethyl ether or benzene. The most frequent extraction techniques are: Soxhlet, extraction with shaker, extraction with ultrasonic water-bath and extraction with acid progress.

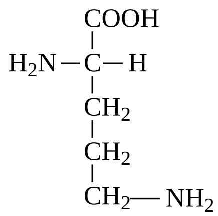
Tests for alkaloids: Most alkaloids are precipitated from neutral or slightly acidic solutions by Mayer's reagent (potassiomercuric iodide solution), by Wagner's reagent (solution of iodine in potassium iodide), by solution of tannic acid, by Hager's reagent (a saturated solution of picric acid) and by Dragendorff's reagent (solution of potassium bismuth iodide). Purine-derivative alkaloids (e.g. caffeine) can be detected by murexide test.

6.2 Alkaloids formed from ornithine

Alkaloids formed from ornithine (**Figure 6.2**) can be found in species belonging to the plant families of Solanaceae, Convolvulaceae, Boraginaceae, Asteraceae, Fabaceae and Erythroxylaceae.

Biosynthesis starting from ornithine can result in the formation of two main types of alkaloids, the group of tropane- and ecgonine-alkaloids, and the group of pyrrolizidine-alkaloids (**Figure 6.3**).

Another biosynthesis pathway from ornithine (through the formation of putrescine and other intermediers) can lead to the formation of alkaloids with pyrrolizidine-skeleton. Farfarae folium (*Tussilago farfara*), Echinaceae radix (*Echinacea purpurea*) and Petasitidis folium (*Petasites hybridus*) also contain pyrrolizidine alkaloids, but their use in phytotherapy is not attributed to their alkaloid content.



ornithine (α,δ-diamino-valerianic acid)

Figure 6.2
The structure of ornithine

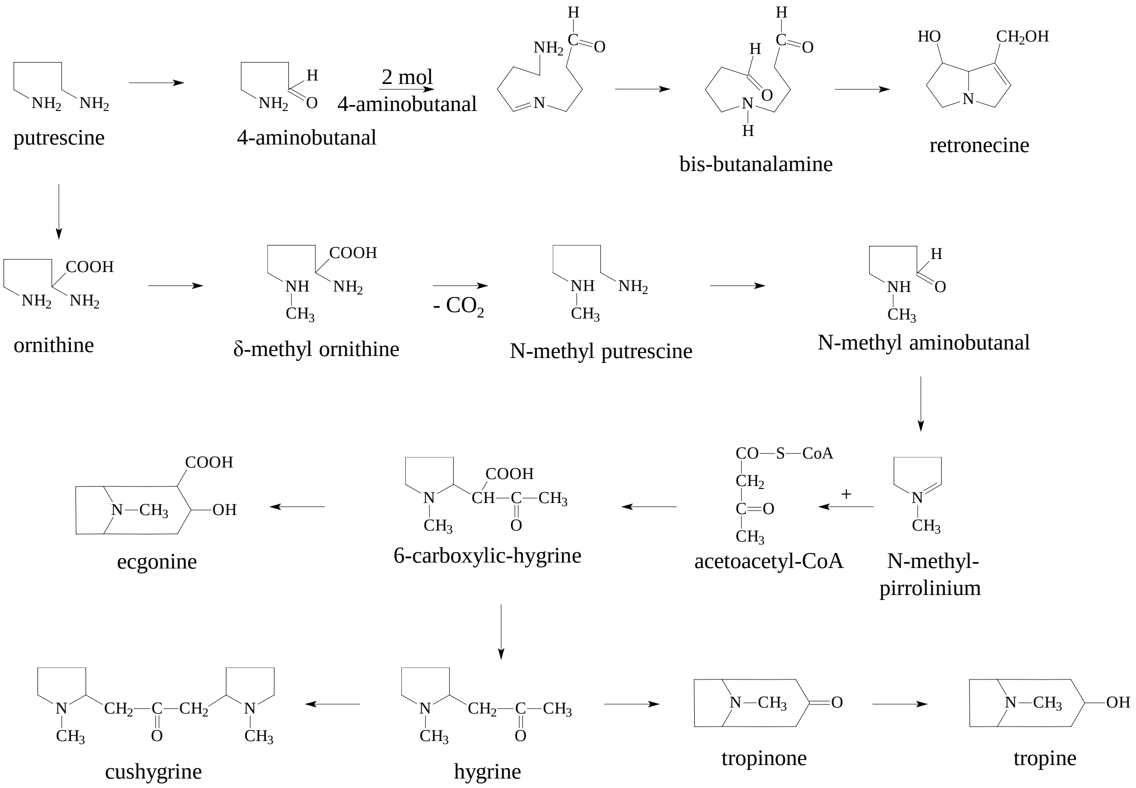


Figure 6.3
Some ornithine-derived alkaloids

Drugs

Belladonnae folium

Plant

Atropa belladonna L. –Belladonna (Deadly nightshade) (Solanaceae)

This perennial herbaceous shrub is native to Europe, West-Asia, Caucasus and North-Africa.

Figure 6.4
Belladonna /Deadly nightshade (*Atropa belladonna* L.)

Drug

Belladonnae folium (Belladonna leaf, Ph. Eur.). **Other drugs:** *Belladonnae folii extractum siccum normatum* (Belladonna leaf dry extract, standardized, Ph. Eur.), *Belladonnae pulvis normatus* (Belladonna, prepared, Ph. Eur.), *Belladonnae folii tinctura normata* (Belladonna leaf tincture, standardised, Ph. Eur.)

Belladonna leaf consists of the dried leaf or of the dried leaf and flowering, and occasionally fruit-bearing tops of *Atropa belladonna* L. It contains not less than 0.30% of total alkaloids, calculated as hyoscyamine with reference to the drug dried at 100°C to 105°C. The alkaloids consist mainly of hyoscyamine together with small quantities of hyoscine (scopolamine).

Belladonna leaf has a slightly nauseous odour.

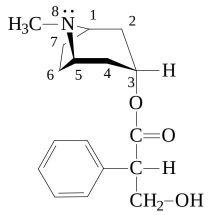
Standardised belladonna leaf dry extract is produced from Belladonna leaf. It contains not less than 0.95% and not more than 1.05% of total alkaloids, calculated as hyoscyamine, with reference to the dried extract. The extract is produced from the drug and ethanol (70% *V/V*) using an appropriate procedure. The drug is a hygroscopic brown or greenish powder.

Prepared belladonna is belladonna leaf powder adjusted if necessary by adding powdered lactose or belladonna leaf powder with a lower alkaloid content to contain 0.28% to 0.32% of total alkaloids, calculated as hyoscyamine with reference to the dried drug. It has slightly nauseous odour.

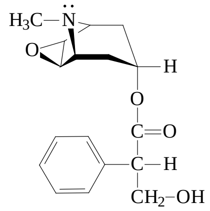
Tincture is produced from Belladonna leaf. It contains 0.027% to 0.033% of total alkaloids, calculated as hyoscyamine. The alkaloids consist mainly of hyoscyamine together with small quantities of hyoscine. The tincture is produced from 1 part of the powdered drug and 10 parts of ethanol (70% *V/V*) by a suitable procedure.

Constituents

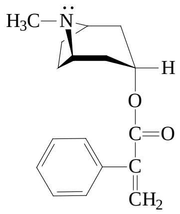
The characteristic constituents of the leaves are tropane alkaloids (0.3-0.6%), e.g. atropine, L-hyoscyamine, apoatropine, L-scopolamine and cuscohygrine. [Atropine = ester of tropine (3α-hydroxy-tropane) formed with racemic tropic acid (α-phenyl-β-hydroxy-propionic acid)]. These alkaloids can also be found in the root of the plant (in amount of 0.3-0.9%). Other constituents of the leaves are flavonoids (quercetin, kaempferol) and coumarins such as scopoletin.



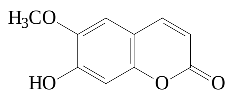
Atropin(e) = ester of tropine (3α-hydroxy-tropane) formed with racemic tropic acid (α-phenyl-β-hydroxy-propionic acid).



L-scopolamin(e)
(= 6,7-epoxide of L- hyosciamin(e)



apoatropine



scopoletin

Figure 6.5-8
The structure of atropine (DL-hyoscyamine), apoatropine, L-scopolamine and scopoletin.

Uses

In pharmaceutical industry pure crystalline atropine and its derivatives are used. Atropine and its preparations such as *Tinctura belladonnae* and *Extractum belladonnae siccum* are used in the case of hyperacidity and stomach ulcer. Atropine (and the diluted aqueous solution of atropine-sulphate) is used in ophthalmology as a mydriatic drug because it can dilate the pupils of the eyes. Its application is strictly prohibited in the case of glaucoma. Atropin is used in tablets as spasmolytic, in injections against bile stones (cholelithiasis) and kidney stones (nephrolithiasis). It is an analgesic drug in the case of painful menstruation (accompanied with cramps). The drug acts on the central nervous system in the case of neurovegetative dystony and neurastheny. Its overdosage causes psychomotoric restlessness, excitement and hallucination. Side effects include xerostomia, hoarseness, visual disorders. Overdose of atropin can lead to death, therefore the drug and its products should not be used without medical advice!

Hyoscyami folium

Plant

Hyoscyamus niger L. – Hyoscyamus (Henbane) (Solanaceae)

This annual or biennial plant is native to Europe, but it is also cultivated.

Figure 6.9
Hyoscyamus/Henbane (*Hyoscyamus niger* L.)

Drug

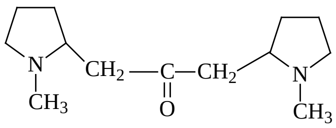
Hyoscyami folium (Hyoscyamus leaf).

Hyoscyamus leaf consists of the dried leaves or the dried leaves and flowering tops of *Hyoscyamus niger* L. It is required to contain not less than 0.05% of total alkaloids calculated as hyoscyamine. The British Pharmacopoeia description refers to petiolate as well as sessile leaves, the first-year biennial leaves being thus admitted.

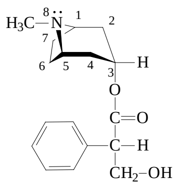
Figure 6.10
Hyoscyami folium (Hyoscyamus leaf)

Constituents

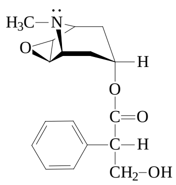
The main characteristic constituents of the leaves are tropane alkaloids (0.03-0.25%), with L-hyoscyamine and L-scopolamine (ratio 1.2:1), atropine, apoatropine and cuscohygrine. L-hyoscyamine is the principal alkaloid in the seeds. Other constituents of the leaves are flavonoids (e.g. rutin) and coumarins in traces.



cuscohygrine



L-hyosciamin(e)



L-scopolamine

Figure 6.11-13

The structure of L-hyoscyamine, L-scopolamine and cuscohygrine.

Uses

Hyoscyamus leaf is used similarly to Belladonna leaf, but its dose should be set higher, because of the lower alkaloid-content. Earlier the drug was used in asthma cigarettes. The drug and its products should not be used without medical advice!

Stramonii folium

Plant

Datura stramonium L. – Datura/Thornapple (Solanaceae)

This plant is native to Europe, but it is also cultivated.

Figure 6.14
Datura/Thornapple (*Datura stramonium* L.)

Drug

Stramonii folium (Stramonium leaf, Ph. Eur.). **Other Drug** *Stramonii pulvis normatus* (Stramonium, prepared, Ph. Eur.)

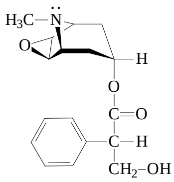
Stramonium leaf consists of the dried leaf or of the dried leaf, flowering tops and occasionally, fruit-bearing tops of *Datura stramonium* L. and its varieties. It contains not less than 0.25% of total alkaloids, calculated as hyoscyamine with reference to the drug dried at 100°C to 105°C. The alkaloids consist mainly of hyoscyamine with varying proportions of hyoscine (scopolamine). Stramonium leaf has an unpleasant odour.

Prepared stramonium is stramonium leaf powder adjusted, if necessary, by the addition of powdered lactose or stramonium leaf of lower alkaloid content to contain 0.23% to 0.27% of total alkaloids, calculated as hyoscyamine with reference to the dried drug. It is a greyish-green powder with an unpleasant odour.

Figure 6.15
Stramonii folium (Stramonium leaf)

Constituents

The main characteristic constituents of the leaves are tropane alkaloids (0.2-0.6%) with L-hyoscyamine and L-scopolamine. The ratio of these two compounds is variable, in the older leaves this ratio is 2:1, but in the younger leaves L-scopolamine content is higher. Other alkaloids include atropine, apoatropine and cuscohygrine. These alkaloids can be found in every part of the plant, therefore it is very toxic. Other constituents of the leaves are flavonoids (e.g. rutin) and coumarins (scopoletin and umbelliferon).


L-scopolamine

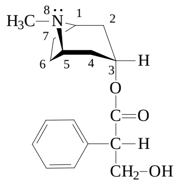

L-hyosciamin(e)

Figure 6.16-17
The structure of L-hyoscyamine and L-scopolamine.

Uses

The drug has spasmolytic action, and can be used in the treatment of asthma, cough and chronic laryngitis. The powder of stramonium leaves mixed with the powder of henbane leaves and impregnated with KNO_3 was used earlier in asthma-cigarettes. The drug and its products should not be used without medical advice!

Cocae folium

Plant

Erythroxylum coca Lam. – Coca (Erythroxylaceae)

The plant is a shrub cultivated in Bolivia, Peru, Columbia and Java.

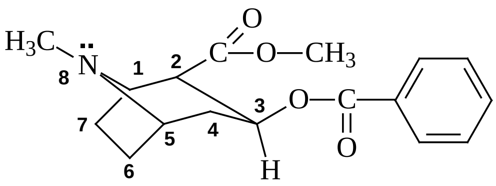
Drug

Cocae folium (Coca leaf)

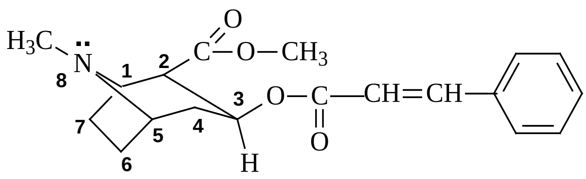
Coca leaf consists of the dried leaves of *Erythroxylum coca* Lam.

Constituents

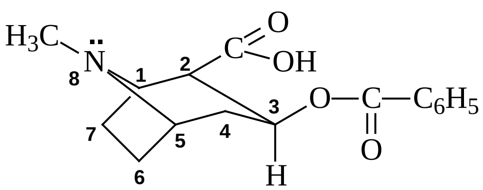
The main characteristic constituents of the leaves are tropane alkaloids (0.7-2.5%) of which cocaine, cinnamylcocaine and α-truxilline are the most important.These alkaloids occur in different proportions in different commercial varieties. Other alkaloids include tropacocaine, benzoylecgonine and β-truxilline.



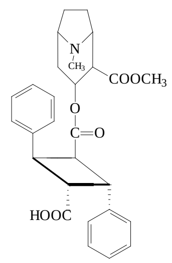
cocaine



cinnamylcocaine



benzoylecgonine



α-truxilline

Figure 6.18-21
The structure of cocaine, cinnamylcocaine, benzoylecgonine and α-truxilline.

Uses

Pure cocaine was used earlier as a local anaesthetic, today its use is restricted to otolaryngology. Cocaine is a dangerous drug, its use without medical control is illegal and prohibited. It stimulates the central nervous system, decreases the sensation of hunger, increases the efficiency of muscles and causes euphoria. Its long term use causes dependence, its overdose causes somatic and senile insanity.

Nicotianae folium

Plant

Nicotiana tabacum L. – Tobacco (Solanaceae)

This plant is cultivated worldwide.

Figure 6.22
Tobacco (*Nicotiana tabacum* L.)

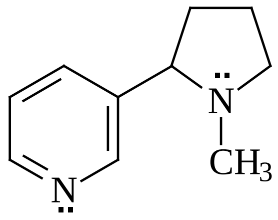
Drug

Nicotianae folium (Tobacco leaf)

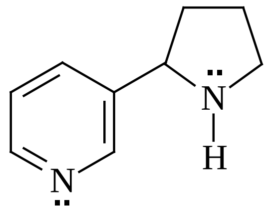
Tobacco leaf consists of the dried leaves of *Nicotiana tabacum* L. or other cultivated species (e.g. *N. rustica* L.)

Constituents

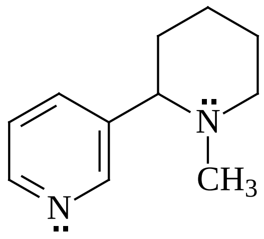
The main characteristic constituents of the leaves are alkaloids (0.05-10%). The principal tobacco alkaloids have a pyridine moiety associated with either a pyrrolidine ring (ornithine-derived) or a piperidine ring (lysine-derived). The former group is represented by nicotine and the latter by anabasine. Tobacco leaf contains nornicotine as well. Other constituents are flavonoids and coumarins.



nicotine



nornicotine



anabasine

Figure 6.23-25
The structure of nicotine, nornicotine and anabasine.

Uses

Since nicotine is strongly toxic (50-100 mg of pure nicotine causes death), tobacco and its alkaloids are not significant constituents for the pharmaceutical industry. However, nicotine is used for the synthesis of nicotinic acid and nicotinamide. A recent pharmaceutical introduction is that of nicotine chewing-gum, nasal spray or patch, intended to help smokers who want to give up smoking.

The health-deteriorating effect of smoking is well-known; 1 g of tobacco leaf contains 5-10 mg of nicotine, which can cause arrhythmia, atherosclerosis, gastritis, chronic bronchitis, stomach ulcer, vascular spasms, vasoconstriction in the limbs, necrosis of the limbs, cancer of throat, oesophagus, lung and stomach.

Pulmonariae herba

Plant

Pulmonaria officinalis L. – Pulmonaria (Boraginaceae)

This plant is native to Europe mainly in oak-forests.

Figure 6.26
Pulmonaria (*Pulmonaria officinalis* L.)

Drug

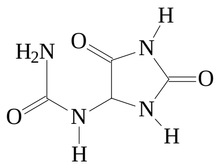
Pulmonariae herba (Pulmonaria)

The drug consists of the dried flowering aerial parts of *Pulmonaria officinalis* L.

Figure 6.27
Pulmonariae herba (Pulmonaria)

Constituents

The drug contains pyrrolizidine alkaloids, mucilage, silicic acid, flavonoids, chlorogenic acid, rosmarinic acid and allantoin.



allantoin

Figure 6.28
The structure of allantoin.

Uses

Today the drug is principally used in ethnomedicine. It has expectorant and cough-reliever effect. But it should be highlighted that the internal use of the drug does not recommended because of pyrrolizidine alkaloids.

Symphyti radix

Plant

Symphytum officinale L. – Comfrey (Boraginaceae)

The plant occurs in Europe in wet meadows and marshy areas.

Figure 6.29
Comfrey (*Symphytum officinale* L.)

Drug

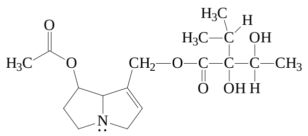
Symphyti radix (Comfrey root)

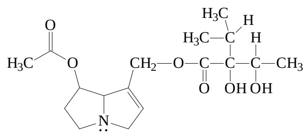
The drug consists of the dried rhizomes and roots of *Symphytum officinale* L.

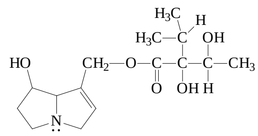
Figure 6.30
Symphyti radix (Comfrey root)

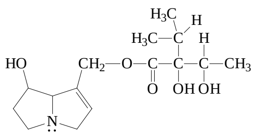
Constituents

The drug contains pyrrolizidine alkaloids (0.05-0.08%) with 1,2-unsaturated necine ring structures, almost entirely in the form of their N-oxides, e.g. 7-acetylintermedine, 7-acetyllycopsamine together with smaller amounts of intermedine, lycopsamine and symphytine. Comfrey root also contains allantoin (0.6-4.7%), mucilage, phenolic acids such as rosmarinic acid, salicylic acid and caffeic acid, triterpene saponins (based on the aglycon of hederagenin) such as symphytoxide A, and lithospermic acid.


acetylintermedine


acetyllycopsamine


intermedine


lycopsamine

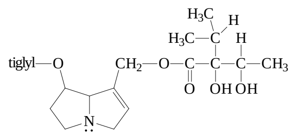

symphytine

Figure 6.31-35
The structure of 7-acetylintermedine, 7-acetyllycopsamine, intermedine, lycopsamine and symphytine.

Uses

The therapeutic indications include the treatment of strains, contusions, distorsions, osteoarthritis, epicondylitis, tendovaginitis and periarthritis. The drug and its preparations can be used only externally.

Dosage

Ointments or other preparations containing up to 35% of root extract (1:2, ethanol 60% V/V), applied 3-4 times daily. Comfrey root preparations should be applied only to intact skin.

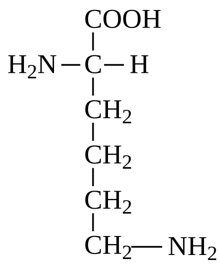
Its use is not recommended for more than 4-6 weeks per year (if the daily application contains between 10 μg and 100 μg of pyrrolizidine alkaloids).

Pregnancy and lactation

No human data are available. In accordance with general medical practice the product should not be used during pregnancy and lactation without medical advice.

6.3 Alkaloids formed from lysine

Lysine (**Figure 6.36**) and its associated compounds give rise to a number of alkaloids, some of which are analogous to the ornithine group. Although in some cases, such as the quinolizidine lupin alkaloids, lysine is incorporated via a symmetrical precursor, e.g. cadaverine; in the majority of examples (anabasine, sedamine) the incorporation is asymmetric. In general, for the simple α-substituted piperidines, the C-2 of lysine becomes the point of attachment of the α-side-chain. Lysine-derived alkaloids occur in the plant families of Piperaceae, Crassulaceae, Fabaceae, Punicaceae, Apiaceae, Solanaceae, Lobeliaceae and Arecaceae.



lysine
(α,ε-diamino-capronic acid)

Figure 6.36
The structure of lysine.

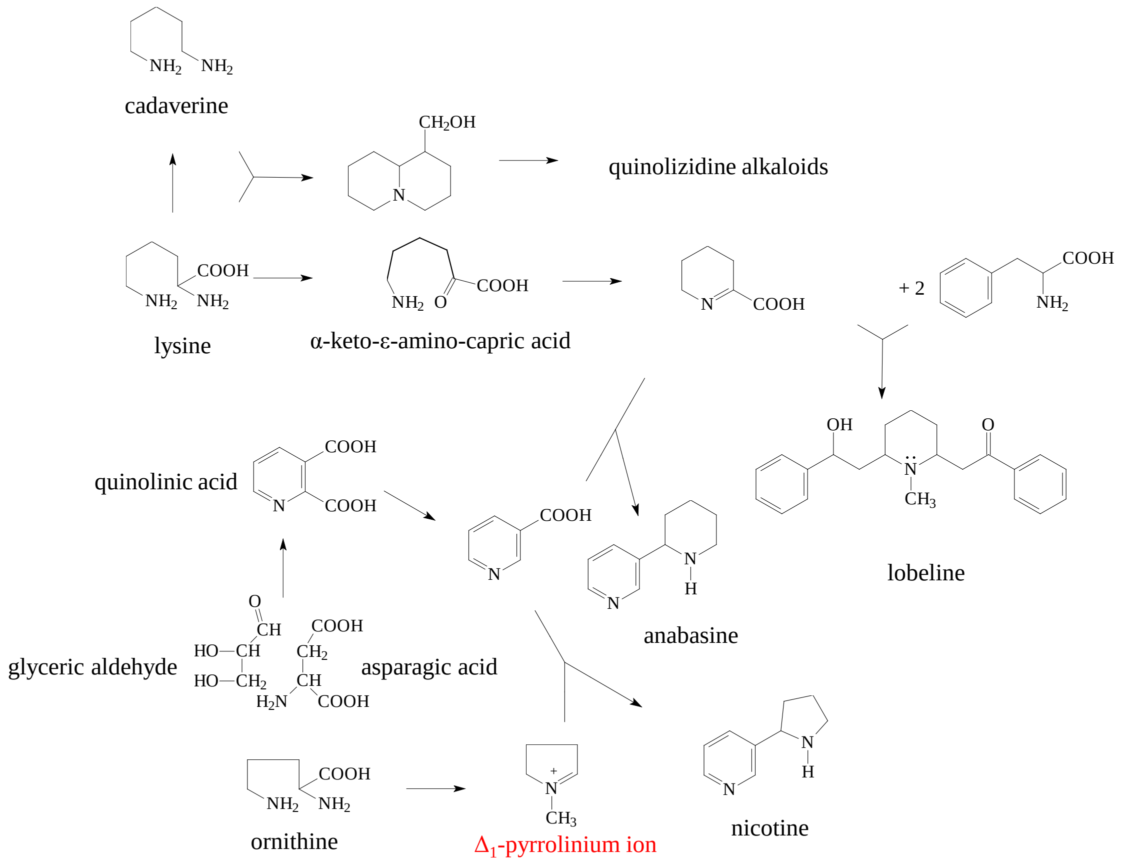


Figure 6.37
Biosynthesis of some lysine-derived alkaloids and nicotine.

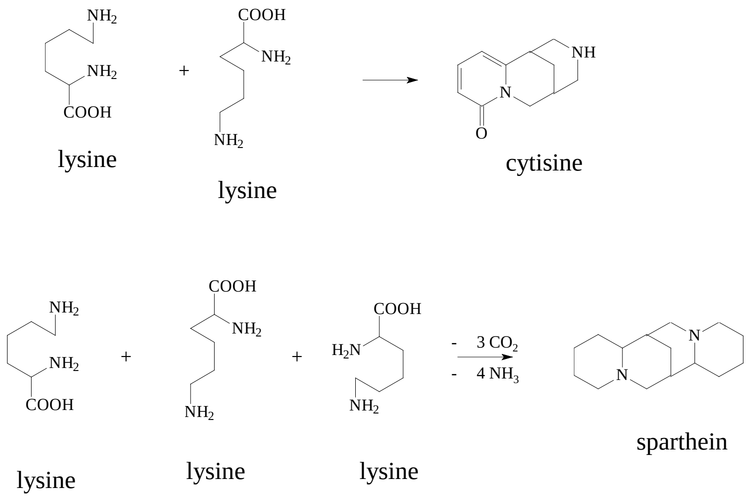


Figure 6.38
Formation of quinolizidine alkaloids from lysine.

Drugs

Lobeliae herba

Plant

Lobelia inflata L. – Lobelia (Lobeliaceae)

This annual plant is indigenous to the eastern USA and Canada. It is also cultivated in the USA and the Netherlands.

Figure 6.39
Lobelia (*Lobelia inflata* L.)

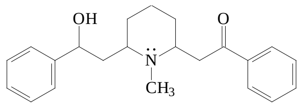
Drug

Lobeliae herba (Lobelia)

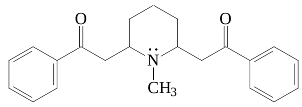
The drug consists of the dried aerial parts of *Lobelia inflata* L.

Constituents

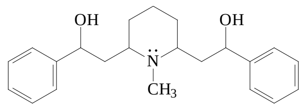
The drug contains a mixture of alkaloids (0.2-0.6%), the principal alkaloid being lobeline, while other related alkaloids include lobelanine, lobelanidine, lobinine and isolobinine.



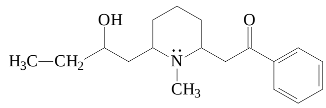
lobeline



lobelanine



lobelanidine



lobinine

Figure 6.40-43
The structure of lobeline, lobelanine, lobelanidine and lobinine.

Uses

Lobelia or the pure constituent lobeline are used in spasmodic asthma and chronic bronchitis. Lobeline stimulates the respiratory system, and it is used in the case of gas-, CO- and narcotic-poisonings. It is also included in some antismoking preparations. In the form of injection lobeline hydrochloride is used in the resuscitation of new-born infants. The drug has a paralytic effect in toxic doses. The drug and its preparations should not be used without medical advice.

Laburni semen (Cytisi semen)

Plant

Laburnum anagyroides Medic. – Laburnum (Fabaceae)

This shrub or small tree is native to Europe.

Figure 6.44
Laburnum (*Laburnum anagyroides* Medic.)

Drug

Laburni semen (Laburnum seed)

The drug consists of the dried, ripe seeds of *Laburnum anagyroides* Medic.

Figure 6.45
Laburni semen (Laburnum seed)

Constituents

The drug contains a mixture of alkaloids, the principal quinolizidine alkaloid being cytosine, and additional alkaloids include N-methyl-cytisine, sparteine and the pyrrolizidine laburnine.

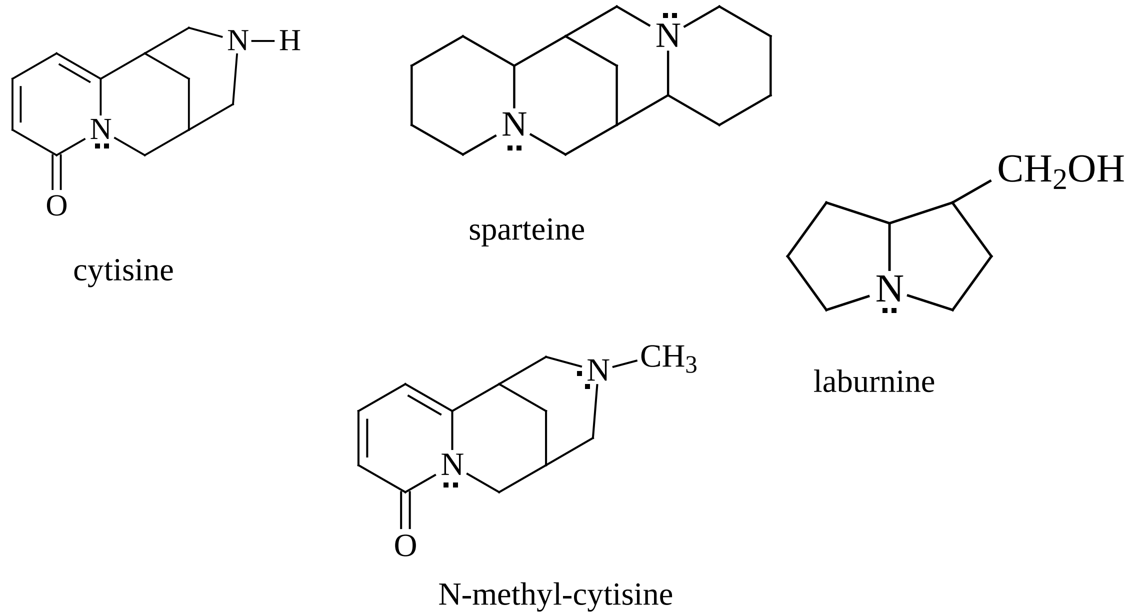


Figure 6.46-49
The structure of cytisine, N-methyl-cytisine, sparteine and laburnine.

Uses

The drug is used for the isolation of cytisine, which stimulates the respiratory system; it is used against the paralysis of respiration. The drug and its preparations should not be used without medical advice.

Sarothamni scoparii herba

Plant

Sarothamnus scoparius (L.) Wimm. – Broom (Fabaceae)

Broom is a perennial shrub native to Europe.

Figure 6.50
Broom [*Sarothamnus scoparius* (L.) Wimm.]

Drug

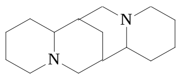
Sarothamni scoparii herba (Broom)

The drug consists of the dried flowering aerial parts of *Sarothamnus scoparius* (L.) Wimm.

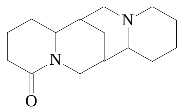
Figure 6.51
Sarothamni scoparii herba (Broom)

Constituents

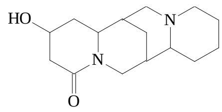
The drug contains a mixture of alkaloids (0.8-1.5%), the principal quinolizidine alkaloid is sparteine and additional alkaloids are lupanine, 4-hydroxylupanine, 13-hydroxylupanine and 17-oxosparteine. Other constituents include amines such as dopamine, flavonoids, e.g. scoparin and kaempferol, coumarins and small amounts of essential oil.



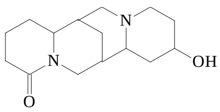
sparteine



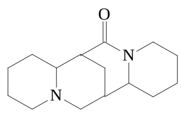
lupanine



4-hydroxylupanine



13-hydroxylupanine



17-oxosparteine

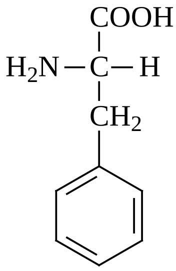
Figure 6.52-56
The structure of sparteine, lupanine, 4-hydroxylupanine,
13-hydroxylupanine and 17-oxosparteine.

Uses

The drug is used for the isolation of sparteine, which has antiarrhythmic action. It decreases the excitability of the stimulus-leader system in the heart, decreases or stops ventricle-fibrillation. It increases blood pressure and has diuretic activity. Spartein or the drugs containing this compound can only be used under medical supervision. The usage of this drug is not recommended for pregnant women, and for patients suffering from high blood pressure.

6.4 Alkaloids formed from phenylalanine

Phenylalanine (**Figure 6.57**) with tyrosine and dihydrophenylalanine and their corresponding decarboxylation products are the precursors of a large number alkaloids, e.g. protoalkaloids, benzylisoquinolines, protoberberines, ipecacuanha alkaloids, as well as the morphine- and rhoeadine-type alkaloids. These alkaloids occur in the plant families of Berberidaceae, Ranunculaceae, Papaveraceae, Fumariaceae, Rubiaceae, Solanaceae and Liliaceae.



phenylalanine
(α-amino-β-phenyl-propionic acid)

Figure 6.57
The structure of phenylalanine.

Drugs

Capsici fructus

Plants

Capsicum annuum L. var. minimum (Miller) Heiser or *Capsicum frutescens* L. – Paprika/Capsicum (Solanaceae)

Paprika is native to Middle-America, Mexico, but it is also widely cultivated, e.g. in Hungary.

Figure 6.58
Paprika (*Capsicum annuum* L.)

Drug

Capsici fructus (Capsicum, Ph.Eur.)

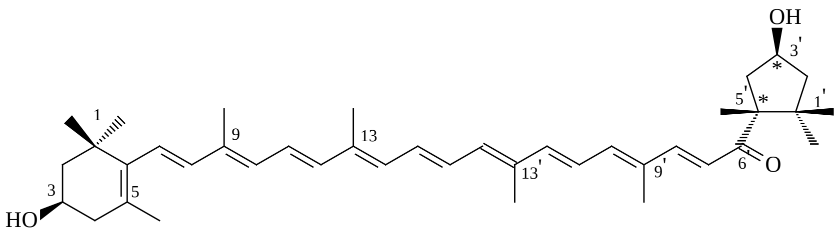
The drug consists of the dried ripe fruits of *Capsicum annuum* L. var. *minimum* (Miller) Heiser and small-fruited varieties of *Capsicum frutescens* L. It contains minimum 0.4% of total capsaicinoids expressed as capsaicin, and calculated with reference to the dried drug.

It has extremely pungent taste.

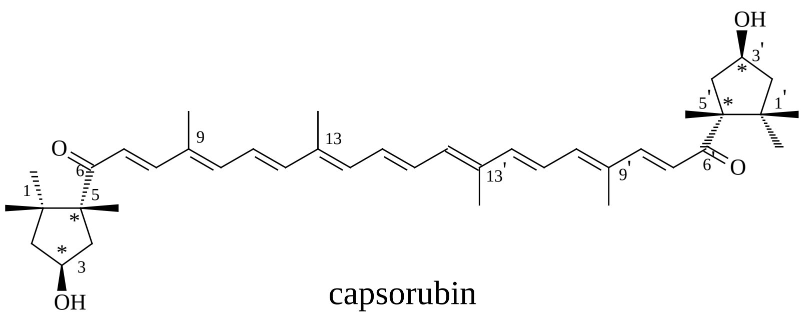
Figure 6.59
Capsici fructus (Capsicum)

Constituents

The main active constituents are capsaicinoids, principally capsaicin (63-77%), dihydrocapsaicin (20-32%) and nordihydrocapsaicin and small amounts of homodihydrocapsaicin. The fruit also contains carotenoids such as capsanthin, capsorubin, β-cryptoxanthin, zeaxanthin, lutein and β-carotene, flavonoids and ascorbic acid (vitamin C).



capsanthin



capsorubin

Figure 6.60-65
The structure of capsaicin, dihydrocapsaicin, nordihydrocapsaicin, homodihydrocapsaicin, capsanthin and capsorubin.

Uses

The drug and its preparations are used medically for external purposes (not more than 10 days). The therapeutic indications are relief of muscle pain, e.g. backache, treatment of pain in osteoarthritis and rheumatoid arthritis, treatment of neuralgias such as the pain following herpes zoster and painful diabetic neuropathy and treatment of pruritus of varying aetiology, such as in prurigo nodularis or associated with psoriasis, haemodialysis or contact with water.

Dosage

Adults and children over 12 years of age: in liquid or semi-solid forms: preparations containing extracts corresponding to 0.025%-0.075% of capsaicinoids, 3-4 times daily. In plasters: extracts corresponding to 10-40 μg of capsaicinoids per cm^2.

Capsicum preparations should not be used on broken skin or wounds and in the case of known hypersensitivity to capsaicinoids.

Special warnings and precautions for use

The drug should not be applied to mucosa or near the eyes. It is recommended not to scratch the site of application to avoid damaging the skin. Treatment should be discontinued if excessive warmth is experienced. Hands should be washed with soap and water after handling products.

Interaction with other medicaments

Capsicum should not be used together with other external products, e.g. other rubefacient or pain relieving gels at the same application site.

Undesirable effects

Capsicum preparations usually cause hyperaemia with marked erythema. This reaction is part of the normal pharmacological effect and generally subsides within a short time. Skin hypersensitivity reactions such as urticaria and vesiculation may occur. In such cases treatment should be discontinued.

Pregnancy and lactation

No human data are available. In accordance with general medical practice the product should not be used during pregnancy and lactation without medical advice.

Ephedrae herba

Plant

Ephedra distachya L. – Ephedra/Common horse-tail (Ephedraceae)

The plant is native to Europe. In Asia, mainly in China other *Ephedra* species occur (*E. sinica*, *E. equisetina*). In India and Pakistan the species of *E. intermedia* and *E. gerardina* can be found.

Figure 6.66
Ephedra (*Ephedra distachya* L.)

Drug

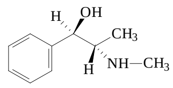
Ephedrae herba (Ephedra)

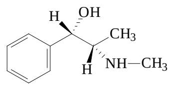
The drug consists of slender, more or less broken aerial stems which are woody and usually branch only at the base.

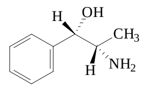
Figure 6.67
Ephedrae herba (Ephedra)

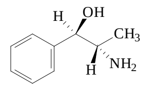
Constituents

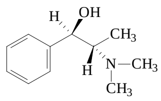
The main active constituents are protoalkaloids (0.5-2%) such as (-)-ephedrine, (+)-pseudoephedrine, (+)-norpseudoehedrine, (-)-norephedrine, (-)-methylephedrine and (+)-methylpseudoephedrine. Other constituents include flavonoids and tannins.


(-)-ephedrine


(+)-pseudoephedrine


(+)-norpseudoehedrine


(-)-norephedrine


(-)-methylephedrine

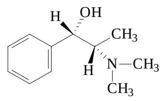

(+)-methylpseudoephedrine

Figure 6.68-73
The structure of (-)-ephedrine, (+)-pseudoephedrine, (+)-norpseudoehedrine, (-)-norephedrine, (-)-methylephedrine and (+)-methylpseudoephedrine.

Uses

The main effective substance of the drug is (-)-ephedrine, which is a sympathomimetic, exerting spasmolytic effect on bronchus-muscles, therefore it can be used in the case of asthma bronchiale, in conditions resulting from allergy and bronchitis. Due to its vasoconstrictive action, it can be used in the case of cold as a component of nasal drops. The drug and its products should not be used without medical advice.

Papaveris fructus sine seminibus

Plant

Papaver somniferum L. – Poppy (Papaveraceae)

Different varieties of the plant are widely cultivated, but in some countries permission is required for cultivation.

Figure 6.74
Poppy (*Papaver somniferum* L.)

Drug

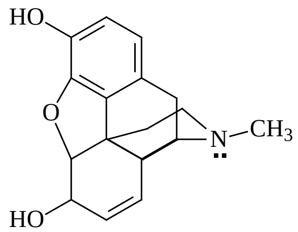
Papaveris fructus sine seminibus (Poppy capsule without seeds)

The drug consists of the dried, ripe fruits (capsules) without seeds of *Papaver somniferum* L.

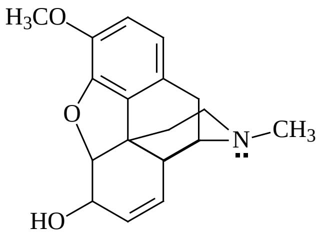
Figure 6.75
Papaveris fructus sine seminibus (Poppy capsule without seeds)

Constituents

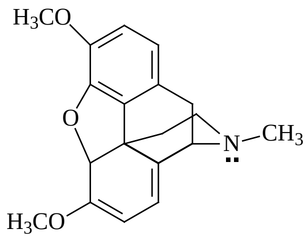
The main active constituents are the mixture of approx. 30 alkaloids; the main component is morphine (0.015-0.018%). The additional alkaloids (0.035-0.23%) include codeine, thebaine, papaverine, narcotine and narceine. The isolation of morphine from dried poppy straw was patented by a Hungarian pharmacist, János Kabay in 1930.



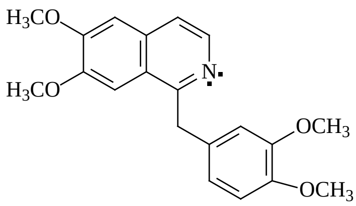
morphine



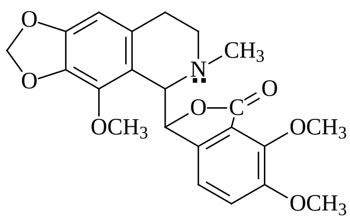
codeine



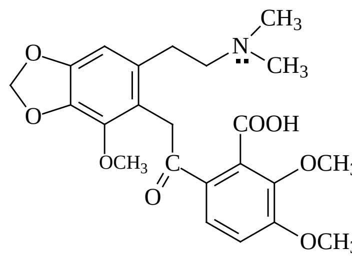
thebaine



papaverine



narcotine



narceine

Figure 6.76-81
The structure of morphine, codeine, thebaine, papaverine, narcotine and narceine.

Uses

The drug is used for the extraction of morphine and the main additional alkaloids in the pharmaceutical industry.

Opium crudum

Plant

Papaver somniferum L. – Poppy (Papaveraceae)

Opium is produced after incision of the green, unripe capsules of poppy. The incision must not penetrate into the interior of the capsule. The latex, which is at first white, rapidly coagulates and turns brown. Each capsule is cut several times at intervals of 2 or 3 days. After collection the latex is placed in a tilted vessel so that the dark fluid which is not required may drain off. By exposure to air opium acquires a suitable consistency for packing.

Drug

Opium crudum (Opium, raw, Ph. Eur.). **Other Drug** *Opii pulvis normatus* (Opium, prepared, Ph. Eur.)

Raw opium is intended only as starting material for the manufacture of galenical preparations. It is not dispensed as such. Raw opium is the air-dried latex obtained by incision from the unripe capsules of *Papaver somniferum* L. It contains not less than 10.0% of morphine and not less than 2.0% of codeine, both calculated with reference to the drug dried at 100°C to 105°C. Raw opium has a characteristic odour and a blackish-brown colour. It consists of masses of various sizes, which tend to be soft and shiny and, after drying, become hard and brittle.

Opii pulvis normatus is raw opium powdered, and dried at a temperature not exceeding 70°C. It contains:

- morphine: 9.8% to 10.2% (drug dried at 100-105°C for 4 h)
- codeine: minimum 1.0% (drug dried at 100-105°C for 4 h).

Content adjusted if necessary by adding a suitable excipient or raw opium powder.

Opium prepared is a yellowish-brown or dark brown powder.

Constituents

The main active constituents are the mixture of alkaloids; the main component is morphine. The additional alkaloids include codeine, thebaine, papaverine, narcotine and narceine. Other constituents are different organic acids, e.g. meconic acid, fumaric acid, malic acid and succinate acid, sugars, amino acids and water.

Uses

The drug is used for the extraction of morphine and the main additional alkaloids in the pharmaceutical industry. A number of pharmaceutical products contain opium or its extract, e.g. Tinctura opii, Pulvis opii et ipecacuanhae, Pulvis opii, Extractum opii, Opium concentratum.Tinctura and Pulvis opii can be used in the case of diarrhoea as consequence of acute infection._Pulvis opii et ipecacuanhae has expectorant, diaphoretic and cough-reliever effects in the case of cold. Extractum opii and Opium concentratum are substituting agents of morphine._Morphine can be used for the alleviation of strong pains (e.g. in the case of cancer) and as a narcotic drug, but it causes euphoria and dependency. It is one of the most dangerous drugs if used illegally._Codeine and narcotine are cough-relievers, papaverine has a spasmolytic action.

Chelidonii herba

Plant

Chelidonium majus L. – Greater celandine (Papaveraceae)

The plant is native to Europe.

Figure 6.82
Greater celandine (*Chelidonium majus* L.)

Drug

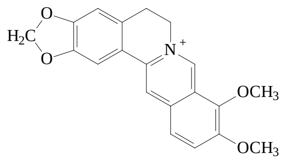
Chelidonii herba (Greater celandine)

The drug consists of the dried, whole or cut aerial parts of *Chelidonium majus* L. collected during flowering. It contains minimum 0.6% of total alkaloids, expressed as chelidonine, calculated with reference to the dried drug.

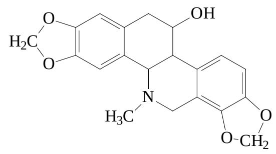
Figure 6.83
Chelidonii herba (Greater celandine)

Constituents

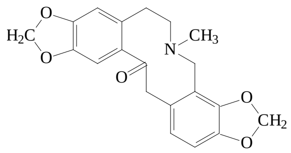
The main active constituents are benzylisoquinoline alkaloids (0.01-1%) of the berberine, protoberberine, and benzophenanthridine types, the principal alkaloids being chelidonine together with protopine, sanquinarine, chelerythrine, etc. Over 20 alkaloids have been identified in the drug. Other substances include cholin, methylamin, thyramin, chelidonic acid, citric acid, malic acid, succinic acid, derivatives of caffeic acid and flavonoids.



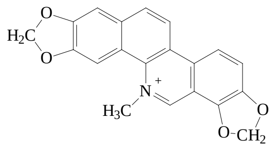
berberine



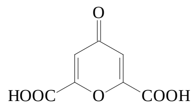
chelidonine



protopine



sanquinarine



chelidonic acid

Figure 6.84-88

The structure of berberine, chelidonine, protopine, sanquinarine and chelidonic acid.

Uses

The therapeutic indications of the drug include the symptomatic treatment of mild to moderate spasms of the upper gastrointestinal tract, minor gall bladder disorders and dyspeptic complaints such as bloating and flatulence. The freshly obtained yellow latex of the plant can be employed for removal of warts, because alkaloids of this latex have strong antiviral, antibacterial action and they inhibit cell division.

Dosage

Daily dose for adults and children over 12 years: 1-4 g of the drug as a tea infusion. 125-700 mg of standardized hydroalcoholic extracts corresponding to 9-24 mg of total alkaloids, calculated as chelidonine. Tincture (1:10): 2-4 ml, 3 times daily. Fluid extract (1:1): 1-2 ml, 3 times daily. In long-term use for more than 4 weeks, checks on liver enzyme activity are recommended.

Overdose: Abdominal pain, gastrointestinal cramps, urinary urgency, drowsiness and haematuria may result due to the alkaloids. In this case, treatment must be stopped immediately.

For removal of warts the yellow latex flowing out of the freshly harvested plant can be used or the tincture (1:1, 96% V/V) prepared from the fresh or dried herb.

Contra-indications

Patients with biliary obstruction or existing or previous liver diseases should not use the drug and its preparations internally. In case of gallstones, the drug and its preparations should not be used without medical advice.

Undesirable effects

Mild gastrointestinal disturbances, such as nausea or diarrhoea, stomach upset sometimes occur. In rare cases, hepatic inflammation and an increased liver enzyme activity and serum bilirubin have been reported, but this is reversible on discontinuation of therapy.

Pregnancy and lactation

No data are available. In accordance with general medical practice the product should not be used during pregnancy and lactation without medical advice.

Fumariae herba

Plant

Fumaria officinalis L. – Fumitory (Fumariaceae)

The plant is native to Europe.

Figure 6.89
Fumitory (*Fumaria officinalis* L.)

Drug

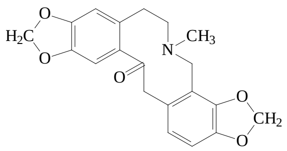
Fumariae herba (Fumitory, Ph. Eur.)

The drug consists of the whole or fragmented, dried aerial parts of *Fumaria officinalis* L. harvested in full bloom. It contains not less than 0.4% of total alkaloids, expressed as protopine and calculated with reference to the dried drug.

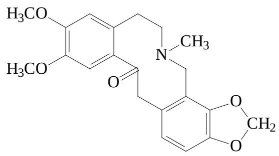
Figure 6.90
Fumariae herba (Fumitory)

Constituents

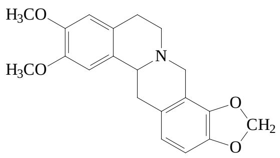
The main active constituents are isoquinoline alkaloids (0.3-1.3%) of the protopine, spirobenzylisoquinoline and protoberberine types, the principal ones being protopine and fumarophycine together with cryptopine, sinactine and fumaritine. Over 20 alkaloids have been identified. Other constituents are flavonoids (e.g. rutin), aliphatic acids such as fumaric and malic acids and hydroxycinnamic acid derivatives (e.g. coumaric acid, caffeic acid and ferulic acid).



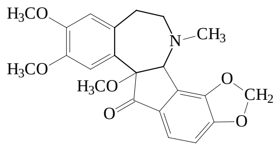
protopine



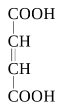
cryptopine



sinactine



fumaritine



fumaric acid

Figure 6.91-95

The structure of protopine, cryptopine, sinactine, fumaritine and fumaric acid.

Uses

The therapeutic indications of the drug include the treatment of digestive complaints such as stomach ache, nausea, vomiting, feeling of fullness and flatulence due to hepatobiliary disturbance. The smooth muscle-relaxing effect of the drug extract has been demonstrated on isolated rat duodenum.

Dosage

Daily dose for adults: 4-6 g of the drug as an aqueous extract or infusion. Liquid extract (1:1, ethanol 25% V/V) or tincture (1:5, ethanol 45% V/V).

Contra-indications

Patients with biliary obstruction should not use the drug and its preparations internally. In case of gallstones, the drug and its preparations should not be used without medical advice.

Pregnancy and lactation

No data are available. In accordance with general medical practice the product should not be used during pregnancy and lactation without medical advice.

Berberidis radicis cortex

Plant

Berberis vulgaris L. – Barberry (Berberidaceae)

This shrub is native to Europe.

Figure 6.96
Barberry (*Berberis vulgaris* L.)

Drug

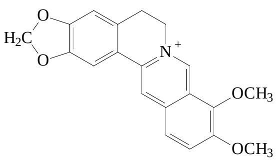
Berberidis radicis cortex (Barberry root-bark)

The drug consists of the whole or fragmented, dried root-bark or partly the roots of *Berberis vulgaris* L.

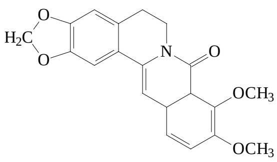
Figure 6.97
Berberidis radicis cortex (Barberry root-bark)

Constituents

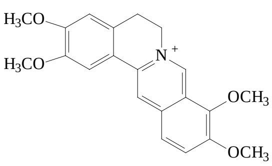
The main active constituents are alkaloids (8%), the principal one being berberine. Additional alkaloids are oxyberberine, palmatine, jatrorrhizine, etc.



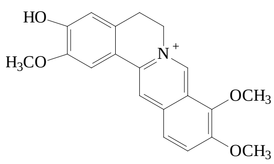
berberine



oxyberberine



palmatine



jatrorrhizine

Figure 6.98-101
The structure of berberine, oxyberberine, palmatine and jatrorrhizine.

Uses

The extract prepared from the drug has antibacterial, cholagogue and smooth muscle-relaxing effects. The drug is principally used in ethnomedicine and homoeopathy. It can be used in the treatment of digestive complaints such as stomach ache, nausea, vomiting, feeling of fullness and flatulence due to hepatobiliary disturbance, but these effects have not been proved by clinical studies.

Dosage

Daily dose for adults: 2 g of the drug as an infusion.

Contra-indications

Patients with biliary obstruction should not use the drug and its preparations internally. In case of gallstones, the drug and its preparations should not be used without medical advice.

Pregnancy and lactation

No data are available. In accordance with general medical practice the product should not be used during pregnancy and lactation without medical advice.

Hydrastis rhizoma

Plant

Hydrastis canadensis L. – Goldenseal (Ranunculaceae)

This small perennial plant is indigenous to the woods of eastern Canada and eastern USA. Today it can be cultivated, too, mainly in the USA and Europe.

Drug

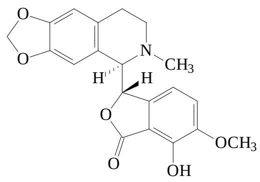
Hydrastis rhizoma (Goldenseal rhizome, Ph. Eur.)

The drug consists of the whole or cut, dried rhizome and root of *Hydrastis canadensis* L.

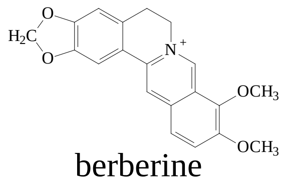
It contains minimum 2.5% of hydrastine and minimum 3.0% of berberine, calculated with reference to the dried drug.

Constituents

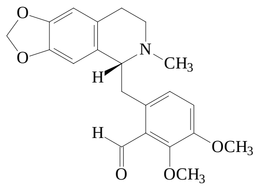
The main active constituents are alkaloids (2.5-6%), e.g. hydrastine, berberine and canadine.



hydrastine



berberine



canadine

Figure 6.102-104
The structure of hydrastine, berberine and canadine.

Uses

The extract prepared from the drug has antibacterial, cholagogue, smooth muscle-relaxing and sedative effects. The drug is principally used for the treatment of digestive complaints such as dyspepsia, gastritis, feeling of fullness and flatulence. Hydrastine hydrochloride has been used in various forms to control uterine haemorrhage.

Dosage

Daily dose for adults: 0.5-1 g of the drug as an infusion.

Contra-indications

Patients with hypertonia should not use the drug and its preparations.

Pregnancy and lactation

The drug and its products must not be used during pregnancy and lactation.

Colchici tuber

Plant

Colchicum autumnale L. – Autumn crocus or meadow saffron (Liliaceae)

This perennial plant is native to Europe.

Figure 6.105
Autumn crocus or meadow saffron (*Colchicum autumnale* L.)

Drug

Colchici tuber (Colchicum corm)

The drug consists of the dried corm collected during or directly after the flowering period of *Colchicum autumnale* L.

Constituents

The main active constituents are colchicine-type alkaloids (0.1-0.6%), the main alkaloids being colchicine (60%) and demecolcine. Further alkaloids are artefacts developed during drying and storage.

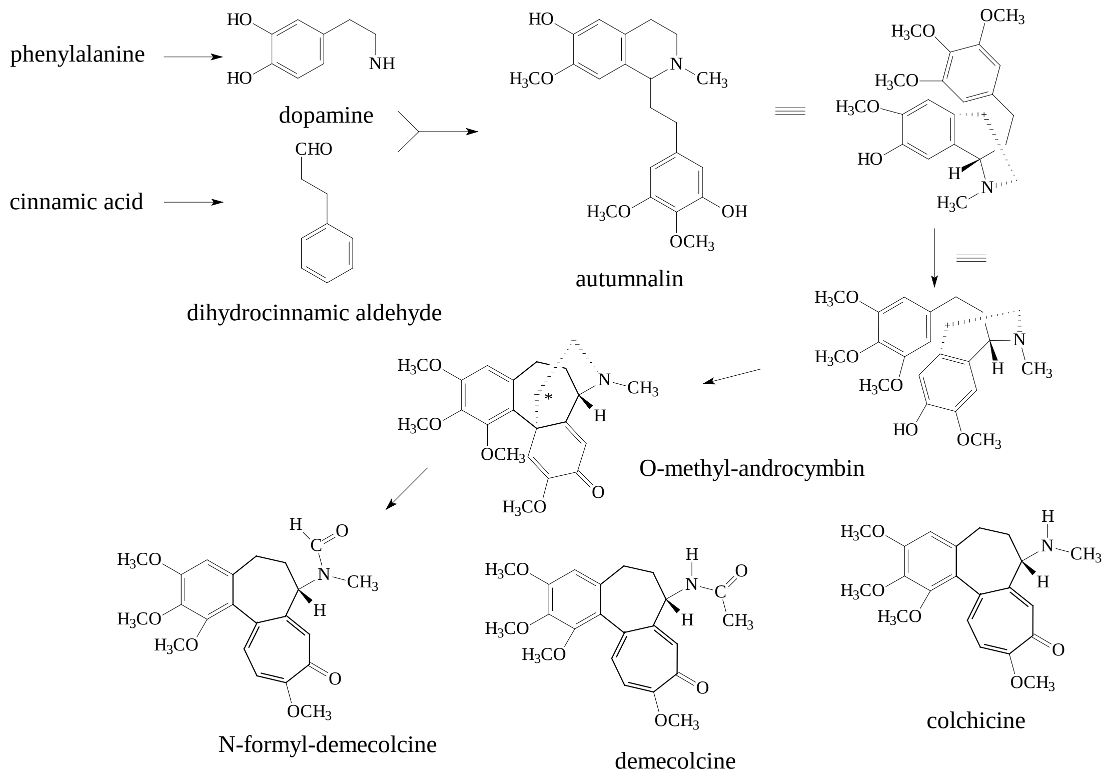


Figure 6.106
The biosynthesis of demecolcine and colchicine.

Uses

Pure colchicine has cytostatic effect, therefore it is used in biological experiments to produce polyploidy or multiplication of the chromosomes in a cell nucleus. Colchicum preparations are also used to relieve gout, but must be employed under medical supervision. *Pure colchicine is highly toxic*! The less toxic demecolcine can be used in cancer therapy (chemotherapy).

Dosage

Daily dose for patients with gout: 1 mg of colchicum preparations, maximum dose 4-8 mg.

Pregnancy and lactation

The drug and its products must not be used during pregnancy and lactation.

Ipecacuanhae radix

Plant

Cephaelis ipecacuanha (Brot.) Rich. and *C. acuminata* Karsten – Matto Grosso and Costa Rica Ipecacuanha (Rubiaceae)

Cephaelis ipecacuanha is a shrub found in Brazil, mainly in the moist and shady forests of Matto Grosso and Minas Geraes. It is also cultivated in Malaya and Burma. *C. acuminata* is found in Columbia, Nicaragua and Costa Rica.

Drug

Ipecacuanhae radix (Ipecacuanha root, Ph. Eur.). **Other drugs:** *Ipecacuanhae extractum fluidum normatum* (Ipecacuanha liquid extract, standardised, Ph. Eur.), *Ipecacuanhae tinctura normata* (Ipecacuanha tincture, standardised, Ph. Eur.), *Ipecacuanhae pulvis normatus* (Ipecacuanha, prepared, Ph. Eur.)

Ipecacuanha root consists of the fragmented and dried underground organs of *Cephaelis ipecacuanha* (Brot.) A.Rich., known as Matto Grosso ipecacuanha, or of *Cephaelis acuminata* Karsten, known as Costa Rica ipecacuanha, or of a mixture of both species. It contains not less than 2.0% of total alkaloids, calculated as emetine with reference to the dried drug. The principal alkaloids are emetine and cephaëline. Ipecacuanha root has a slight odour.

Standardised liquid extract produced from *Ipecacuanha root*. It contains minimum 1.80% and maximum 2.20% of total alkaloids, calculated as emetine. The extract is produced from the herbal drug and solvent of suitable strength by an appropriate procedure. It is a dark-brown liquid.

Tincture produced from *Ipecacuanha root*. It contains 0.18% (*m/m*) to 0.22% (*m/m*) of total alkaloids, calculated as emetine. The tincture is produced by a suitable procedure from the herbal drug and ethanol of suitable strength. It is a yellowish-brown liquid.

Prepared ipecacuanha is ipecacuanha root powder adjusted, if necessary, by the addition of powdered lactose or ipecacuanha root powder with a lower alkaloid content to contain 1.9% to 2.1% of total alkaloids, calculated as emetine with reference to the dried drug. It is a light grey to yellowish-brown powder with a slight odour.

Figure 6.107
Ipecacuanhae radix (Ipecacuanha root)

Constituents

The main active constituents are isoquinoline derivative alkaloids (2-3.5%), principally with emetine and cephaëline. These alkaloids derive from the condensation of dopamine with loganin (an iridoid compound). Additional alkaloids are psychotrine, psychotrine methylether and emetamine. Other constituents include starch, iridoid glucoside and calcium oxalate.

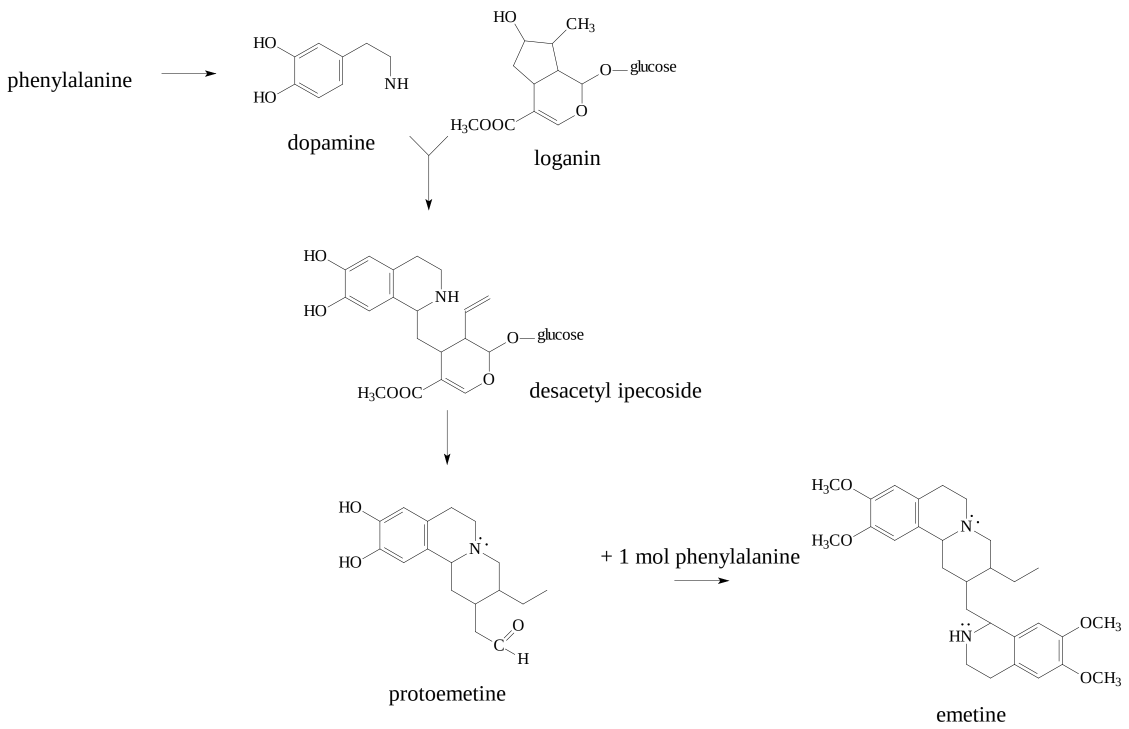


Figure 6.108
The biosynthesis of emetine.

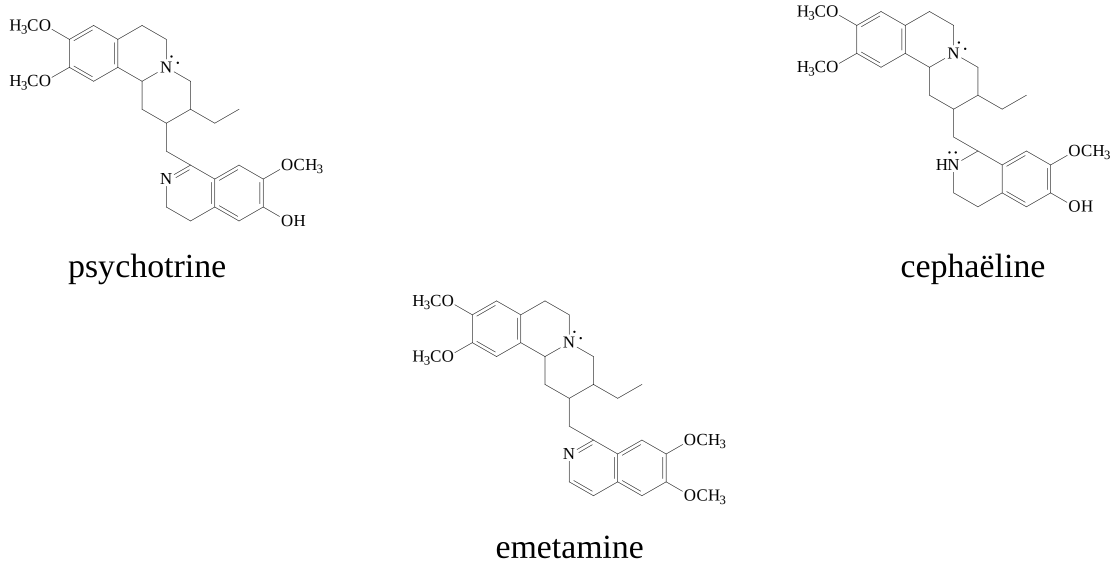


Figure 6.109-111
The structure of cephaëline, psychotrine and emetamine.

Uses

Ipecacuanha is used as an expectorant and emetic and in the treatment of amoebic dysentery. The action of emetine and cephaëline is dose-dependent. In low doses they have expectorant activity, but in higher doses they possess emetic effect. Psychotrine is a selective inhibitor of the human immunodeficiency virus. The drug and its preparations should not be used without medical advice.

Dosage

Single dose: for babies (from 3 months to 1 year): 0.01 g; from 1 year to 3 years: 0.015 g; from 3 years to 6 years: 0.02 g; from 6 years to 9 years: 0,025 g; from 9 years to 12 years: 0.03 g; for adults: 0.05 g.

Pregnancy and lactation

The drug and its products must not be used during pregnancy and lactation.

Boldi folium

Plant

Peumus boldus Mol. –Boldo (Monimiaceae)

Peumus boldus is a dioecious, evergreen shrub or a small tree, which is native to Chile, Peru and Marocco. It is cultivated in Italy.

Figure 6.112
Boldo (*Peumus boldus* Mol.)

Drug

Boldi folium (Boldo leaf, Ph. Eur.)

Boldo leaf consists of the whole or fragmented dried leaf of *Peumus boldus* Molina. The whole drug contains not less than 20.0 ml/kg and not more than 40.0 ml/kg and the fragmented drug not less than 15.0 ml/kg of essential oil. It contains not less than 0.1% of total alkaloids, expressed as boldine, calculated with reference to the anhydrous drug. Boldo leaf has an aromatic odour especially when rubbed.

Figure 6.113
Boldi folium (Boldo leaf)

Constituents

The main characteristic constituents are isoquinoline alkaloids of the aporphine and noraporphine types (0.25-0.5%), the major alkaloids being boldine and isoboldine. Other constituents are essential oil (2-3%) containing monoterpenes such as p-cymene, linalool, ascaridole, 1,8-cineole, etc. and flavonoids (especially glycosides of rhamnetin, isorhamnetin and kaempferol).

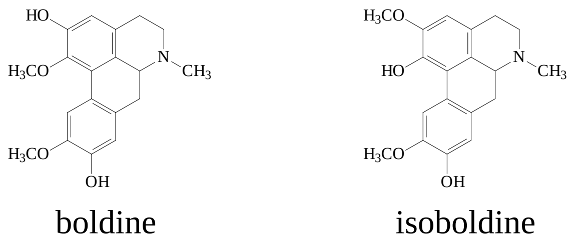


Figure 6.114-115
The structure of boldine and isoboldine.

Uses

The therapeutic indications of the drug include the treatment of minor hepatobiliary dysfunction and the symptomatic treatment of mild digestive disturbances.

Dosage

Adult daily dose: 2-5 g of the drug as a tea infusion. 0.2-0.6 g of the crude drug or equivalent hydroethanolic extract. Tincture (1:5, ethanol 80% V/V): 1-3 ml, fluid extract (1:1, ethanol 80% V/V): 0.5-1 ml.

The drug and its preparations should not be used for more than 4 weeks.

Contra-indications

Patient with biliary obstruction should not use the drug. *The essential oil of the plant must not be used in therapy due to its toxic ascaridole content.*

Pregnancy and lactation

The drug and its products must not be used during pregnancy and lactation. Very high doses of a dry ethanolic boldo leaf extract (800 mg/kg/day) have been reported to cause abortifacient and teratogenic effects in rats.

Curare

Plants

Chondrodendron tomentosum Ruiz. et Pavon (Menispermaceae), *Strychnos toxifera* Schomburgk ex Bentham (Loganiaceae)

Chondrodendron tomentosum is a liana found in the rain forests by the river Amasonas. The drug used to be traded in the “tube” of bamboo-cane (*Bambusa sp.*), therefore it was called “Tube-curare”. Because of its botanical origin its synonym name is “Menispermaceae-curare”, too. *Strychnos toxifera* is also a liana found in Brazil, Peru, Ecuador, Venezuela and Columbia. The drug was packed in gourds, therefore it was called „Calabash-curare”.

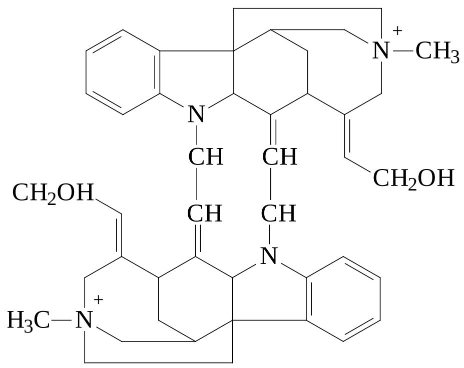
Drug

Curare (Curare)

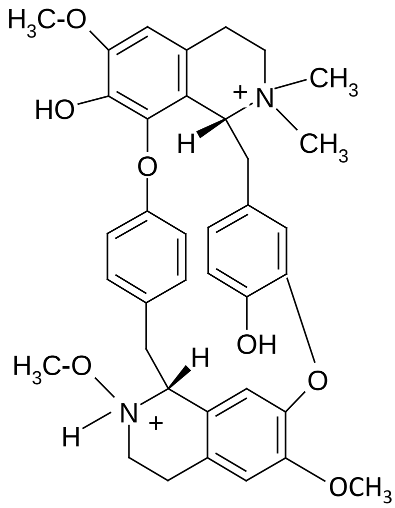
Curare is a brown or black, bitter paste. Tube-curare is the concentrated aqueous extract of the bark or leaves of *Chondrodendron tomentosum* Ruiz. et Pavon. Calabash-curare is prepared similarly from *Strychnos toxifera* Schomburgk ex Bentham.

Constituents

Tube-curare contains principally (+)-tubocurarine (dimer alkaloid, bisbenzylisoquinoline type), (-)-curine and (+)-chondrocurarine. Calabash-curare contains a mixture of approx. 40 alkaloids with principally C-toxiferine (dimer alkaloid).



C-toxiferine



(+)-tubocurarine

Figure 6.116-117
The structure of (+)-tubocurarine and C-toxiferine.

Uses

Curare is now little used except as a source of alkaloids. Tubocurarine chloride is used to secure muscular relaxation in surgical operations and in certain neurological conditions. The action of C-toxiferine is 20-50 times stronger than that of (+)-tubocurarine. Curare was used as an arrow poison by the indigenous inhabitants.

Chapter 7
Drugs containing alkaloids of tryptophan and histidine origin

7.1 Alkaloids formed from tryptophan

With a few minor exceptions, tryptophan (**Figure 7.1**) and its decarboxylation product, tryptamine, give rise to the large class of indole alkaloids. The alkaloids biosynthesised from tryptophan occur not only in plants, but also in fungi. In the synthesis of these alkaloids terpenoids are often involved, as well.

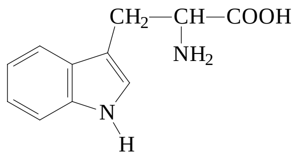


Figure 7.1
The structure of tryptophan.

Drugs

Secale cornutum

Fungus

Claviceps purpurea (Fries) Tulasne (Clavicipitaceae)

Drug

Secale cornutum (Ergot)

The drug is the overwintering form of the fungus (*Claviceps purpurea*), which grows on the ears of cereals (e.g. rye). The drug is 1.5-4 cm long, 2-5 mm thick, dark-purple, or brownish-black, a slightly bent sclerotium.

Figure 7.2
Secale cornutum (Ergot)

Constituents

The drug contains a mixture of approx. 30 alkaloids (0.05-1%). Classification of ergot-alkaloids: amides, peptide-alkaloids, clavin-alkaloids. Besides the alkaloids, the drug contains amines, anthraquinone-derivatives and fatty oils in ~40%. The most important ergot-alkaloids are the derivatives of lysergic (D-lysergic) acid: ergometrine, ergotamine, ergocristine. Diethylamide of lysergic acid (LSD = Lisergsäure-diethylamide) can be prepared by partial synthesis from lysergic acid. It has hallucinogenic action and it is a dangerous illegal drug. In the molecule of ergocristine, an isopropyl-group is connected to the oxasolidin(one)-ring instead of CH_3-group.

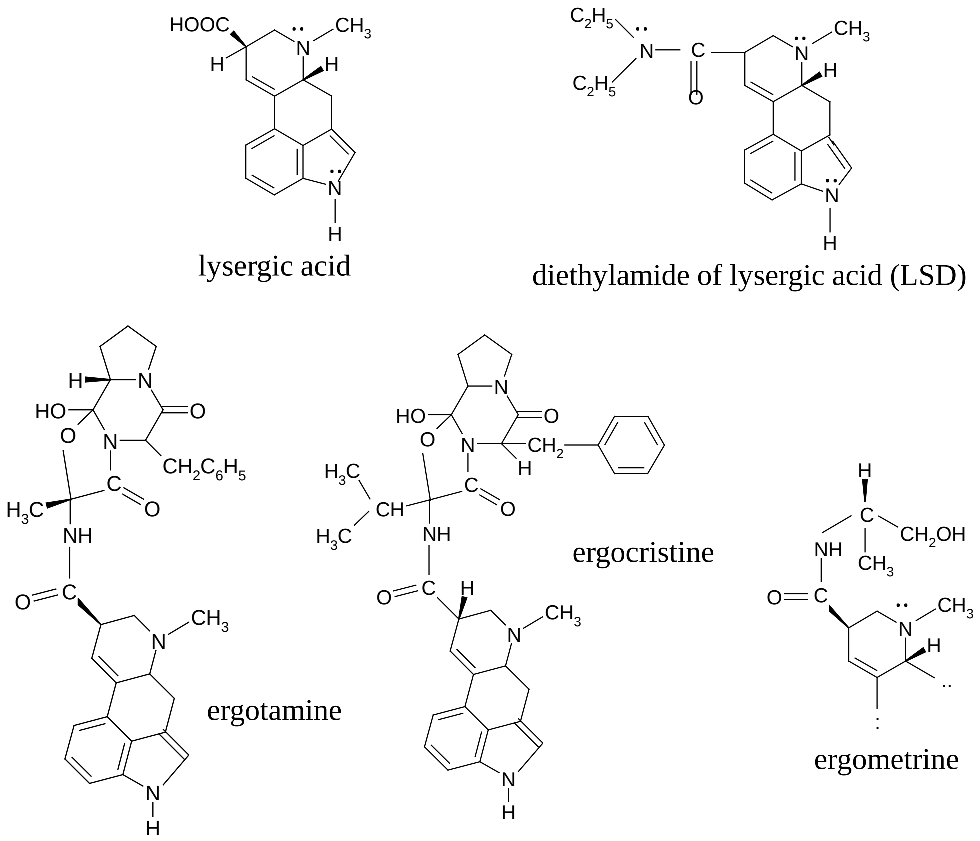


Figure 7.3-7
The structure of lysergic acid, LSD, ergometrine, ergotamine and ergocristine.

Uses

The amide- and peptide alkaloids are used for pharmaceutical purposes. The action of ergometrine is similar to that of oxytocine; it has myometrium-contractive action; it can be used at delivery. The most important pharmacological effect of ergotamine is its vasoconstrictor action, therefore it is used for the alleviation of bleeding after delivery and for treatment of migraine. The dihydro-derivatives of ergotoxine-alkaloids (mixture of many alkaloids) can be used to decrease blood pressure.

Rauwolfiae radix

Plant

Rauwolfia serpentina (L.) Benth et Hook – Rauwolfia (Apocynaceae)

The plant is native to India, Pakistan and South-Vietnam.

Figure 7.8
Rauwolfia [*Rauwolfia serpentina* (L.) Benth et Hook]

Drug

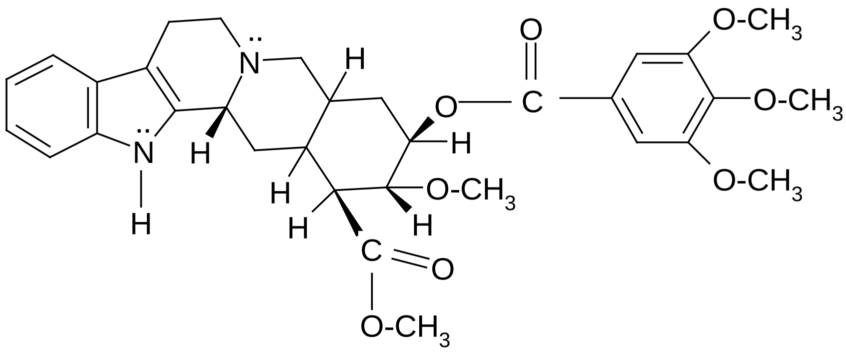
Rauwolfiae radix (Rauwolfia root, DAB)

The drug consists of the dried roots and rhizomes of *Rauwolfia serpentina* (L.) Benth et Hook.

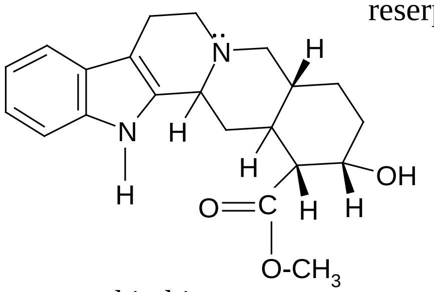
Figure 7.9
Rauwolfiae radix (Rauwolfia root)

Constituents

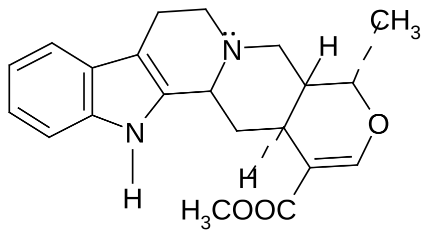
It contains a mixture of ~ 50 alkaloids (alkaloid content: 1.5-3 %). The most important alkaloids of the drug are reserpine, yohimbine and aymalicine.



reserpine



yohimbine



aymalicine

Figure 7.10-12
The structure of reserpine, yohimbine and aymalicine.

Uses

Reserpine has sedative and hypotensive action; it can be used for reducing anxiety, stress, agression and in the treatment of chronic schizophrenia. Aymalicine increases the blood supply of the brain. Yohimbine can be employed as an aphrodisiac.

Vincae minoris herba

Plant

Vinca minor L. – Lesser periwinkle (Apocynaceae)

The evergreen plant occurs in Europe and also in Hungary.

Figure 7.13
Lesser periwinkle (*Vinca minor* L.)

Drug

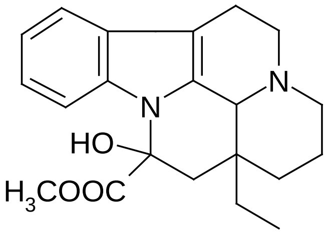
Vincae minoris herba (Lesser periwinkle)

The drug consists of the flowering part of *Vinca minor* L.

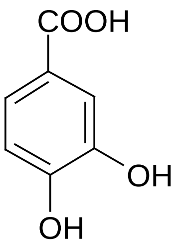
Figure 7.14
Vincae minoris herba (Lesser periwinkle)

Constituents

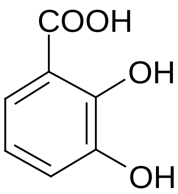
The drug contains a mixture of ~40 alkaloids (0.25-1%); the main alkaloid is vincamine (25-65% of the total alkaloid content). Further characteristic substances include loganin, derivatives of benzoic acid and of cinnamic acid, glycosides of these compounds, flavonoids (kaempferol and quercetin) and ursolic acid.



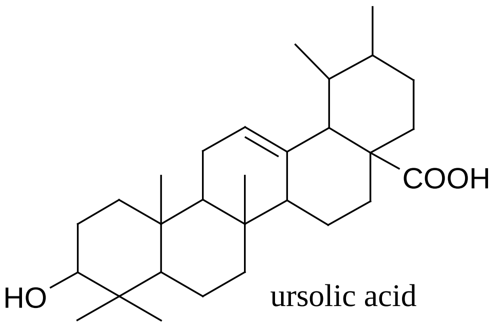
vincamine



3,4-dihydroxy-benzoic acid



2,3-dihydroxy-benzoic acid



ursolic acid

Figure 7.15-18
The structure of vincamine, 3,4-dihydroxy-benzoic acid, 2,3-dihydroxy-benzoic acid and ursolic acid

Uses

Vinca minor is an industrial medicinal plant, used for the preparation of vincamine. Vincamine exerts a hypotensive action, dilates the blood vessels of the brain, increases its blood and oxygen supply. From vincamine the ethylester of apovincaminic acid (Cavinton®) can be prepared by semisynthetic way. Cavinton® dilates the cerebral blood vessels; it can be used in the insufficiency of cerebral blood circulation.

In traditional medicine the drug is used in the case of the disorders of cerebral blood circulation, against amnesia, forgetfulness, decrease of the intellectual ability. In the case of hypertonia it can be used for lowering blood pressure.

Catharanthi herba

Plant

Catharanthus roseus (L.) G. Don – Madagascar periwinkle (Apocynaceae)

This plant is native to Madagascar, but it is also widespread in many tropical and subtropical countries.

Figure 7.19
Madagascar periwinkle [*Catharanthus roseus* (L.) G. Don]

Drug

Catharanthi herba (Madagascar periwinkle)

The drug consists of the flowering part of the evergreen sub-shrub of *Catharanthus roseus* (L.) G. Don.

Constituents

The drug contains a mixture of ~ 90 alkaloids (alkaloid content is ~0.7%); the main alkaloids are vinblastine and vincristine.

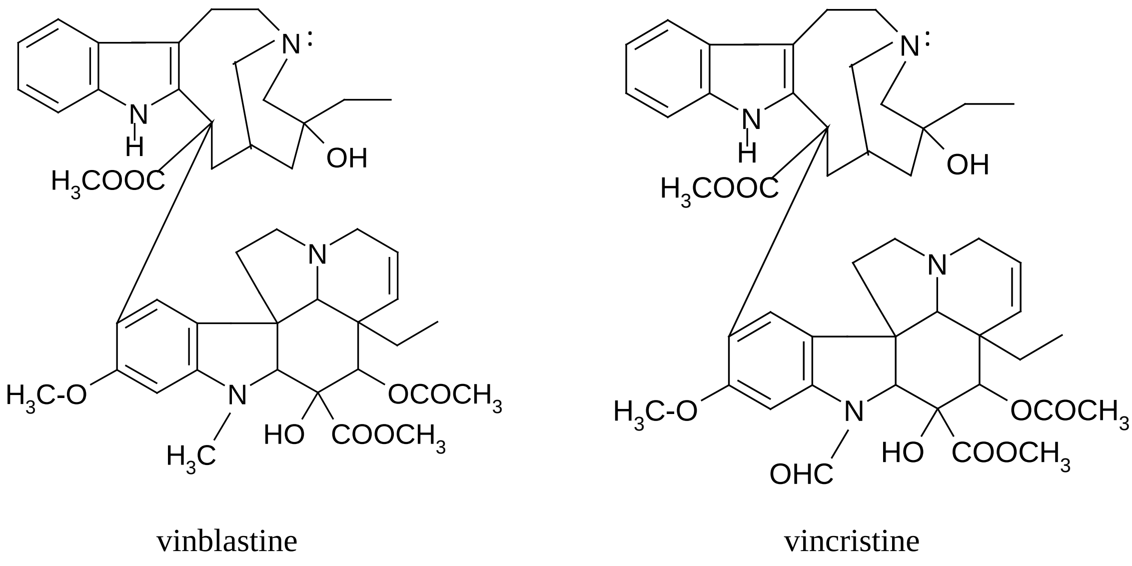


Figure 7.20-21
The structure of vinblastine and vincristine.

Uses

The drug is used for the preparation of vinblastine and vincristine in the pharmaceutical industry. These compounds have mitosis inhibiting action; they can be used in cancer therapy as cytostatics, particularly in the case of leukemia and lymphogranulomatosis (Hodgkin-disease).

Strychni semen

Plant

Strychnos nux-vomica L. – Nux vomica (Loganiaceae)

The plant is native to India, Sri Lanka (Ceylon) and North-Australia.

Drug

Strychni semen (= Nux vomica) (Nux vomica seed, Ph. Hg. VII.)

The drug consists of the dried, ripe seeds of the small tree or shrub of *Strychnos nux-vomica* L.

Constituents

The drug contains a mixture of alkaloids (2.5-4%) such as strychnine, brucine (1:1) and several other alkaloids. Further effective substances include loganin and chlorogenic acid.

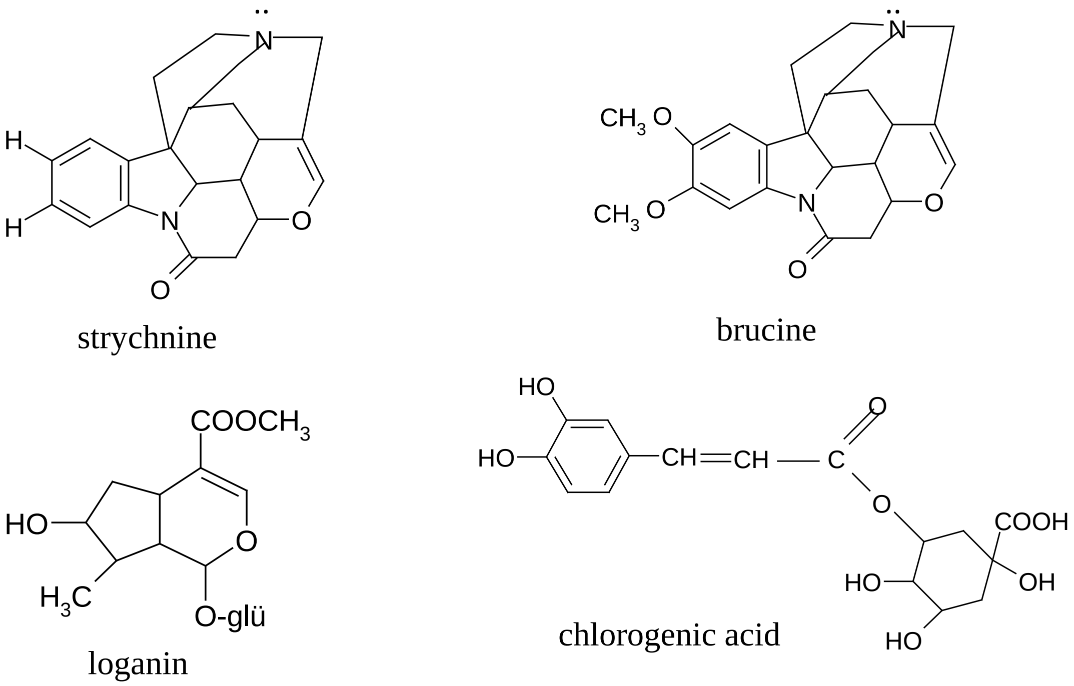


Figure 7.22-25
The structure of strychnine, brucine, loganin and chlorogenic acid.

Uses

Strychnine, which is a very bitter substance, increases the muscle tension. It can be used in the case of reconvalescence, exhaustion and after stroke to increase the sensibility of the sense organs, and for treatment of paralysis. The alkaloid content was formerly used as a circulatory stimulant in such cases as surgical shock, but its use is now limited to that of a respiratory stimulant in certain cases of poisoning.

Cinchonae cortex

Plant

Cinchona pubescens Vahl (= *C. succirubra* Pavon ex Klotzsch) – Red cinchona (Rubiaceae)

The plant is native to the eastern slopes of the Andes mountain at the height of 1500-2500 m: Venezuela, Bolivia; it can also be found in Zaire and in Malaysia.

Drug

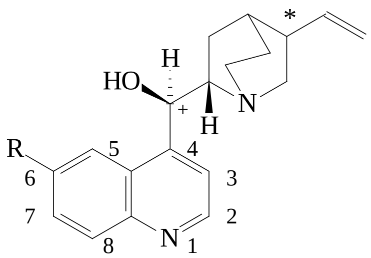
Cinchonae cortex (Cinchona bark, Ph. Eur.) = *Chinae succirubrae cortex*

The drug consists of the whole or cut, dried bark of *Cinchona pubescens* Vahl (*Cinchona succirubra* Pavon), of *C. calisaya* (Weddell), of *C. ledgeriana* (Moens ex Trimen) or of their varieties or hybrids. It contains minimum 6.5% of total alkaloids, of which 30% to 60% consists of quinine-type alkaloids calculated with reference to the dried drug. Cinchona bark has an intense bitter, somewhat astringent taste.

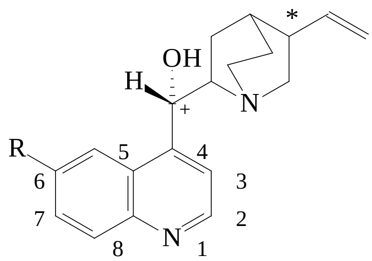
Figure 7.26
Cinchonae cortex (Cinchona bark)

Constituents

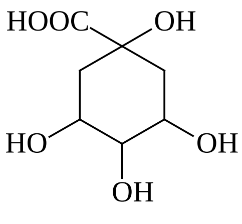
The drug contains a mixture of different alkaloids (6-7% alkaloid-content); its main alkaloids are quinine, quinidine, cinchonine, cinchonidine. Further characteristic substances of the drug include tannins, triterpenes and quinic acid.



Quinine: R = OCH_3
Cinchonidine: R = H



Quinidine: R = OCH_3
Cinchonine: R = H



quinic acid

Figure 7.27-29
The structure of quinine, quinidine, cinchonine, cinchonidine and quinic acid.

Uses

The mentioned alkaloids are effective against malaria; quinine is antipyretic, chinidine has antiarrhythmic action. Pure quinine is used in the therapy against malaria and as fever reducer, pure chinidin against disorders of cardiac rhythm. The tincture prepared from this drug is appetizing.

Physostigmae semen

Plant

Physostigma venenosum Balf. – Calabar bean (Fabaceae)

This plant is native to tropical West-Africa; it was newly introduced to India and Brasilia.

Drug

Physostigmae semen = Calabar semen (Calabar bean)

The drug consists of the seeds of *Physostigma venenosum* Balf.

Constituents

The drug contains a mixture of several alkaloids (alkaloid content is 0.1-0.5%); its main alkaloids are physostigmine and eseroline.

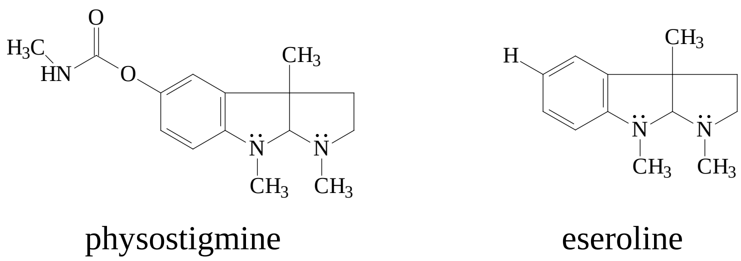


Figure 7.30-31
The structure of physostigmine and eseroline.

Uses

Physostigmine has a parasympathomimetic effect, it can be used in ophthalmology for constricting the pupil, and to treat glaucoma. Physostigmine salicylate is used for contracting the pupil of the eye, often to combat the effect of mydriatics. With Alzheimer’s disease it has shown some evidence of inducing a slight improvement in intellectual and cognitive performance. It is used in the veterinary medicine against flatulence.

Uncariae tomentosae radix

Plant

Uncaria tomentosa (Willd.) DC. – Cat’s claw (Rubiaceae)

The plant is native to Middle- and South-America (Peru).

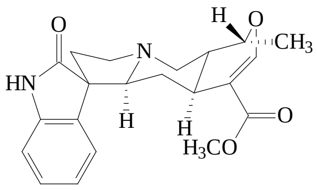
Drug

Uncariae tomentosae radix (Cat’s claw root)

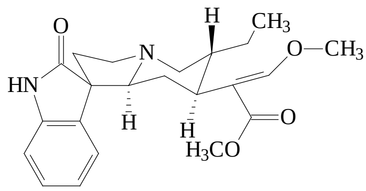
The drug consists of the dried roots of *Uncaria tomentosa* (Willd.) DC.

Constituents

The drug contains a mixture of different indole alkaloids (0.1-0.5%) (with tetra- and pentacyclic ring systems): pteropodin, rinchophylline, mitraphylline. Other constituents are saponins, oleanolic acid and ursolic acid.



pteropodin



rinchophylline

Figure 7.32-33
The structure of pteropodin and rinchophylline.

Uses

The drug has antirheumatic, antiviral and immunostimulant actions, and is also used as a pharmaceutical raw material. It can be used in the treatment of joint diseases and rheuma. **The drug and its preparations should not be used during pregnancy and lactation!**

Passiflorae herba

Plant

Passiflora incarnata L. – Passion flower (Passifloraceae)

The plant is native to America and Europe (Italy, Greece).

Drug

Passiflorae herba (Passion flower, Ph. Eur.)

Passion flower consists of the fragmented or cut, dried aerial parts of *Passiflora incarnata* L. It may also contain flowers and/or fruits. It contains not less than 1.5 per cent of total flavonoids expressed as vitexin, calculated with reference to the dried drug.

Figure 7.34
Passiflorae herba (Passion flower)

Constituents

The drug contains traces of β-carboline alkaloids, e.g. harmol, harmalol and harman. Other characteristic constituents are flavonoids, mainly C-glycosides of apigenin and luteolin such as isovitexin, isoorientin and their 2”-β-D-glucosides, and maltol (possibly is an artefact) and traces of essential oil.

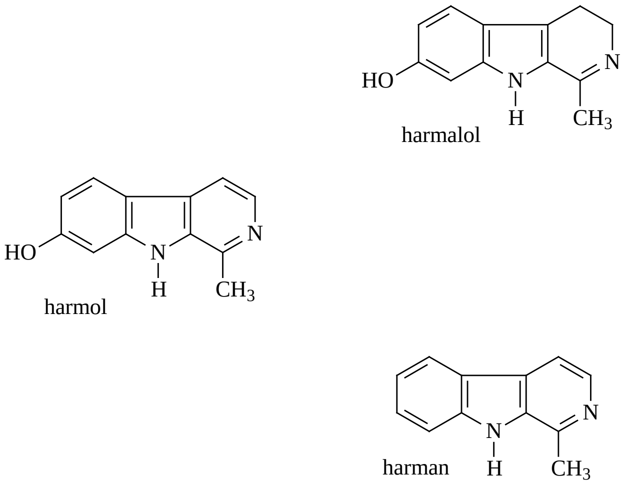


Figure 7.35-37
The structure of harmol, harmalol and harman.

Uses

The therapeutic indications include tenseness, restlessness and irritability with difficulty in falling asleep.

Dosage

Adult single dose: 0.5-2 g of the drug as an infusion, 3-4 times daily. The drug should not be recommended under 12 years of age.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

7.2 Alkaloids formed from histidine

Alkaloids biosynthesized from histidine (**Figure 7.38**) are not widely distributed in plants.

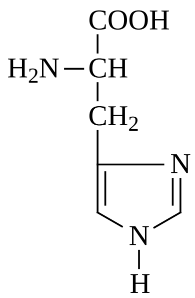


Figure 7.38
The structure of histidine.

Imidazole alkaloids can be formed from histidine. The most important pharmaceutical examples of this group are *Pilocarpus* alkaloids, pilocarpine being used as an ophthalmic cholinergic drug.

Drug

Jaborandi folium

Plant

Pilocarpus jaborandi Holmes, *P. microphyllus* Stapf, P. *pennatifolius* Lemaire (Rutaceae)

These plants are native to the neotropical region of South America, mainly in Brazil.

Drug

Jaborandi folium (Jaborandi leaf)

The drug consists of the dried leaves of *Pilocarpus* species.

Constituents

The drug contains a mixture of alkaloids (alkaloid content is 0.5-7%) having a lactone ring; its main alkaloid is pilocarpine. Further alkaloids include iso-pilocarpine, pilocarpidin, (+)-pilosine and (+)iso-pilosine. It also contains essential oils (comprising mainly terpinene and dipentene) and tannins.

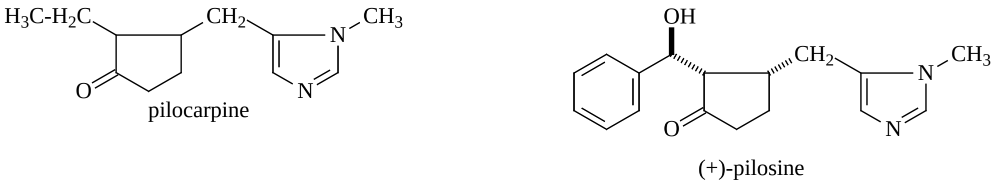


Figure 7.39-40
The structure of pilocarpine and pilosine.

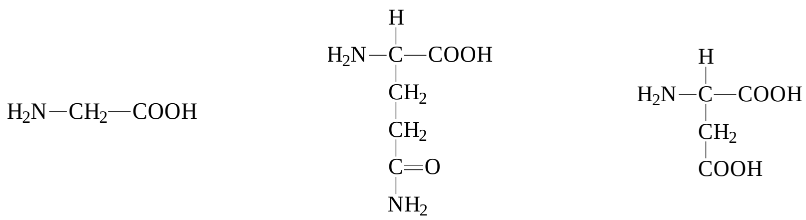
Uses

The drug is used as an industrial drug. Pure pilocarpine is applied as a parasympathomimetic. It is used mostly in ophthalmology; it can cause contraction of the pupils (its action being antagonistic to that of atropine). In the case of glaucoma pilocarpine decreases the internal pressure of the eye and the pain.

Chapter 8
Purine-containing drugs, drugs containing specific amino acid derivatives

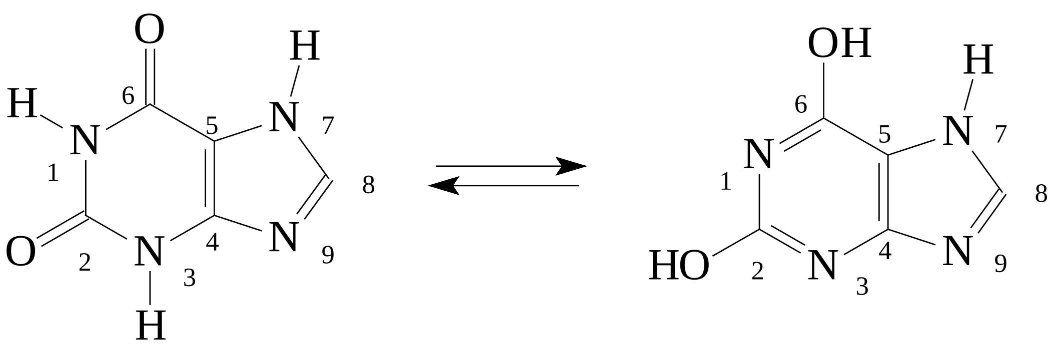
8.1 Alkaloids having purine skeleton

The fundamental compound of purine-alkaloids is: **xanthine** (2,6-dihydroxy-purine). It is formed from one molecule of **glycine**, one molecule of **glutamine** and one molecule of **aspartic acid**.



glycine | glutamine (monoamide of α-amino-glutaric acid | aspartic acid

Figure 8.1
The structure of glycine, glutamine, aspartic acid and xanthine.



xanthine (lactam-form) | xanthine (lactim-form)

Figure 8.2
The lactim and lactam form of xanthine.

The most important purine-alkaloids include **caffeine** (1,3,7-trimethyl-xanthine), **theophylline** (1,3-dimethyl-xanthine) and **theobromine** (3,7-dimethyl-xanthine).

Drugs

Coffeae semen

Plants

Coffea arabica L., *C. liberica* Buill. ex Hiern (Rubiaceae)

These plants are native to Ethiopia; and are cultivated in South-America (Brazil, Columbia), Middle-America, Angola, Liberia, South-Arabia, South-India, Ceylon (Sri-Lanka), Java and Sumatra.

Figure 8.3
Coffee shrub (*Coffea arabica* L.)

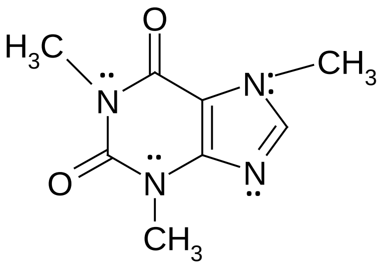
Drug

Coffeae semen (Coffee bean)

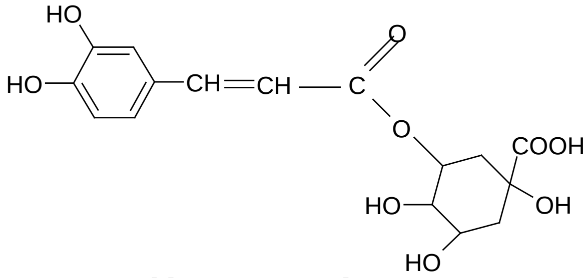
The drug consists of the roasted beans of the cultivated shrub of *Coffea arabica* L.

Constituents

The drug contains caffeine (0.3-2.5%), theophylline, theobromine and other additional alkaloids in traces. Other effective substances are the following: chlorogenic acid (3-5%); diterpenes, fatty oils, proteins and niacine. In roasted coffee ~300 compounds can be identified by gas chromatography (GC).



caffeine
(1,3,7-trimethyl-xanthine)



chlorogenic acid

Figure 8.4-5
The structure of caffeine and chlorogenic acid.

Uses

Caffeine stimulates the central nervous system, increases the pulse rate, the blood supply of the brain, the muscles, the heart, the kidney and the skin; it increases the mental capacity. Caffeine inhibits sleep, decreases the tiredness of striated muscles, increases blood pressure and the action of analgesics. It can be used as a component of analgesics, in sobering up intoxicated persons, in barbiturate-intoxications. Caffeine has diuretic effect. Its use is not recommended in the case of hypertonia, stomach ulcer and in patients with different heart diseases.

Theae folium

Plant

Camellia sinensis (L.) O. Kuntze – Tea shrub (Theaceae)

This plant is native to South-China, Cambodia, India; it is cultivated in Sri Lanka (Ceylon), Indonesia, Japan, Middle-Africa, Georgia, Pakistan, Argentina, Brazil and Peru.

Drug

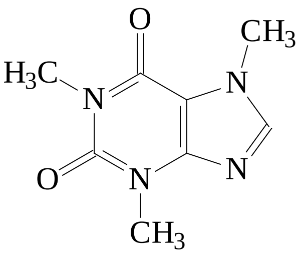
Theae (nigrae) folium = black tea leaves; *Theae viridis folium* = green tea leaves

The drug consists of the young leaves of the cultivated shrub of *Camellia sinensis* (L.) O. Kuntze.

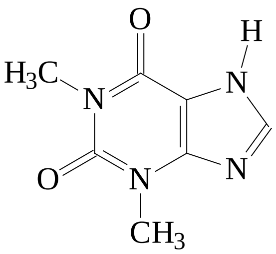
Figure 8.6
Theae viridis folium (Green tea leaves)

Constituents

The drug contains caffeine (2.5-4.5%), theophylline (0.02-0.04%) and theobromine (0.05%). Caffeine occurs in tea leaves in free state or partly connected to tannins (catechol, epicatechol, gallocatechol and epigallocatechol). Caffeine level is higher in green tea than in black tea. The drug's volatile oil content is 0.5-1%. Further characteristic substances of the drug are flavonoids and saponins.



caffeine



theophylline

Figure 8.7-8
The structure of theophylline and caffeine.

Uses

The drug acts as a stimulant; the caffeine-content of one cup of tea is ~20 mg.

Cacao semen

Plant

Theobroma cacao L. – Cocoa (Sterculiaceae)

The plant is native to Middle- and South-America. It is cultivated in Ghana, Kamerun, Brazil and in other countries.

Drug

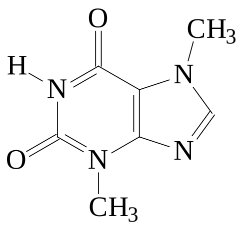
Cacao semen (Cocoa seed)

The drug consists of the roasted seeds without seed-coat of *Theobroma cacao* L.

Figure 8.9
Cacao semen (Cocoa seed)

Constituents

The drug contains theobromine (1-2 %), caffeine (0.2-0.3 %), theophylline (in traces), tannins (5 %) and fats (50-60 %).



theobromine

Figure 8.10
The structure of theobromine.

Uses

Cocoa powder is used for preparation of cacao (cocoa)-drink and chocolate. Cacao/cocoa-butter is also used for producing chocolate; in pharmacy it is the basic material of ointments, creams and suppositories.

Colae semen

Plant

Cola acuminata (Beauv.) Schott et Endl., *C. nitida* (Vent.) Schott et Endl., *C. ballayi* Cornu, *C. verticillata* (Schumach. Et Thunn.) Stapf (Sterculiaceae)

These plants are native to tropical West-Africa; they are cultivated in Brazil, the Caribic Islands and in India.

Drug

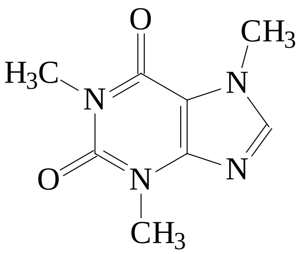
Colae semen (Cola, Ph. Eur.)

Cola consists of the whole or fragmented dried seeds, freed from the testa, of *Cola nitida* (Vent.) Schott et Endl. (*C. vera* K. Schum.) and its varieties, as well as of *Cola acuminata* (P. Beauv.) Schott et Endl. (*Sterculia acuminata* P. Beauv.). It contains not less than 1.5 per cent of caffeine, calculated with reference to the dried drug.

Figure 8.11
Colae semen (Cola)

Constituents

The drug contains caffeine (0.6-3%), theobromine (0.1%) and tannins (2.4%). In the fresh drug caffeine is bound to tannins, but during drying and storing these compounds are decomposed, and caffeine will be present in its free state. 100 ml Coca-cola contains 0.01-0.03 g of caffeine.



caffeine

Figure 8.12
The structure of caffeine.

Uses

The drug acts as a stimulant; it can be used as the raw material of cola drinks.

Guarana

Plant

Paullinia cupana H. B. Kunth (Sapindaceae)

The plant is native toVenezuela and Brazil.

Drug

Guarana (Guarana)

The drug consists of the dry paste prepared from the seeds of the climbing shrub of *Paullinia cupana* H. B. Kunth.

Constituents

The drug contains caffeine (2.5-8%), catechols and tannins (~ 25%).

Uses

A drink is prepared from this drug, which is a stimulant. The drug can be used in preparations against headache.

Mate folium

Plant

Ilex paraguariensis St. Hill. – Maté (Aquifoliaceae)

The plant is native to Paraguay, Uruguay, South-Brazil and North-Argentina.

Drug

Mate folium (Maté leaf, DAC)

The drug consists of the dried and cured leaves of the tree of *Ilex paraguariensis* St. Hill.

Figure 8.13
Mate folium (Maté leaf)

Constituents

The plant contains caffeine (0.5-1.5%), chlorogenic acid (12%), volatile oils (0.3%) and flavonoids.

Uses

In the above mentioned countries of South-America mate tea is a national tea drink.

8.2 Alkaloids having terpenoid skeleton

The skeletons of these alkaloids are of terpenoid origin, but the origin of the N-atom is often unknown.

Pseudoalkaloids

- monoterpene alkaloids (*Valeriana* species)
- sesquiterpene alkaloids (*Nuphar* species)
- diterpene alkaloids (*Aconitum* species)
- steroid alkaloids (*Veratrum*- and *Solanum*-species)

Drugs

Aconiti tuber

Plant

Aconitum napellus L. – Aconite (Ranunculaceae)

The plant is native to the high mountains of Europe and Asia.

Figure 8.14
Aconite (*Aconitum napellus* L.)

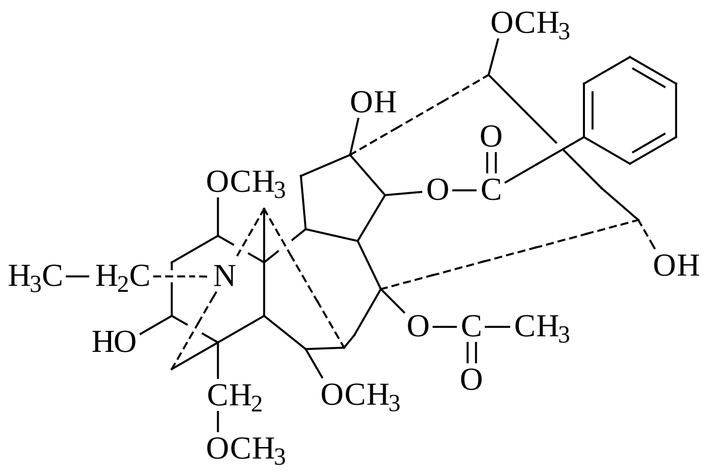
Drug

Aconiti tuber (= radix)

The drug consists of the dried roots of the perennial plant of *Aconitum napellus* L.

Constituents

The drug contains a mixture of alkaloids (0.2-3%); its main alkaloid being aconitine, which is an easily hydrolizable diester (acetyl- and benzoylester) having a very complicated chemical structure.



aconitine

Figure 8.15
The structure of aconitine.

Uses

The drug is only used in the case of neuralgia and chronic arthritis in homoeopathy. Aconitine is one of the strongest poisons of plant origin. Lethal dose: 2-5 mg. It causes respiratory paralysis and cardiac collapse.

Veratri rhizoma et radix

Plant

Veratrum album L. – Veratrum (Liliaceae)

The plant occurs in central and southern Europe and also in Hungary.

Figure 8.16
Veratrum (*Veratrum album* L.)

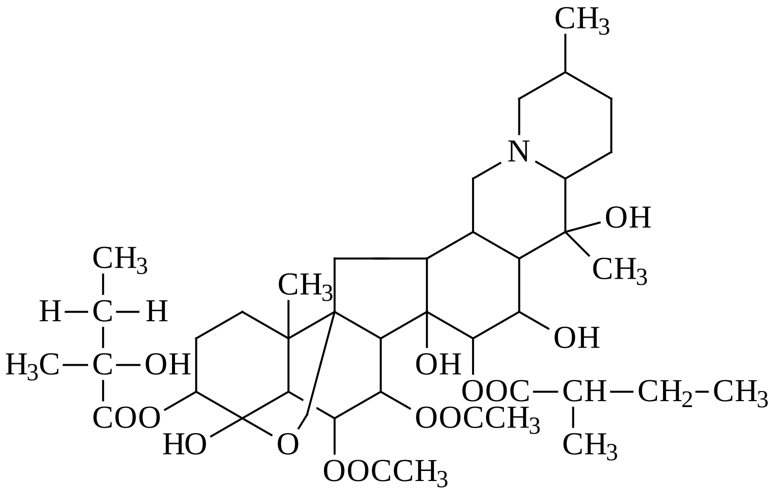
Drug

Veratri rhizoma et radix (Veratrum rhizome and root, Ph. Hg. VII.)

The drug consists of the dried rhizomes and roots of *Veratrum album* L.

Constituents

The drug contains protoveratrine A and B, as main alkaloids; it also contains several additional alkaloids and alkaloid-glycosides.



protoveratrine A

Figure 8.17
The structure of protoveratrine A.

Uses

The compounds mentioned above have hypotensive and vasodilator effect, similarly to cardenolides. The drug is used by the pharmaceutical industry to isolate the active alkaloids.

Dulcamarae fructus et stipes (= Solani herba)

Plant

Solanum dulcamara L. - Nightshade (Solanaceae)

The plant occurs in Asia, Europe and also in Hungary.

Figure 8.18
Nightshade (*Solanum dulcamara* L.)

Drug

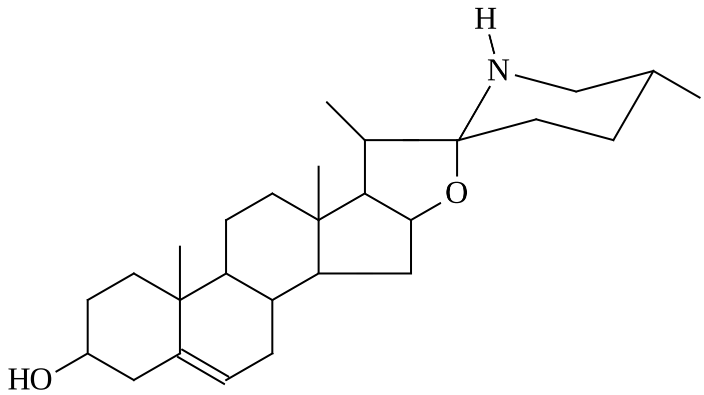
Dulcamarae fructus et stipes (Nightshade fruit and stalk)

The drug consists of the dried fruits together with fruit stalks of *Solanum dulcamara* L.

Figure 8.19
Dulcamarae fructus et stipes (Nightshade fruit and stalk)

Constituents

The main constituents are steroid glycoalkaloids and steroid saponins.



solasodine

Figure 8.20
The structure of solasodine.

Uses

In traditional medicine the drug is used in the case of rheuma, gout (arthritis), different dermatological diseases, e.g. eczema and psoriasis.

Today it is a basic material of the pharmaceutical industry, because pregnadienolone acetate can be prepared by partial synthesis from the aglycones, which can be formed after hydrolysis of steroid glycoalkaloids and of steroid saponins. Pregnadienolone acetate is the starting material of all steroid hormones, contraceptives, corticosteroids (having anti-inflammatory action) and a number of other medicines.

8.3 Drugs containing specific amino acid derivatives

In plants, a variety of substances including alkaloids, different amines, betains, guanidin-derivatives, alliin-derivatives and glucosinolates can be derived from amino acids.

Drugs

Allii sativi bulbus

Plant

Allium sativum L. - Garlic (Alliaceae)

With a history of human use of over 7,000 years, garlic is native to central Asia, and has long been a staple in the Mediterranean region, as well as a frequent seasoning in Asia, Africa, and Europe. It was known to the ancient Egyptians, and has been used for both culinary and medicinal purposes.

Figure 8.21
Garlic (*Allium sativum* L.)

Drugs

Allii sativi bulbi pulvis (Garlic powder, Ph. Eur.), *Allium sativum ad preparationes homoeopathicas* (Ph. Eur.)

Garlic powder is produced from the bulbs of *Allium sativum* L., cut, freeze-dried or dried at a temperature not exceeding 65°C and powdered. It contains not less than 0.45 per cent of allicin, calculated with reference to the dried drug. The mother tincture of *Allium sativum* L. is prepared by maceration of the cut drug using alcohol of a suitable concentration.

Figure 8.22
Allii sativi bulbus (Garlic bulb)

Constituents

The carefully dried, powdered material contains about 1% of alliin ([(+)-S-allyl-L-cysteine sulphoxide] as the main sulphur-containing amino acid. Other characteristic compounds include (+)-S-methyl-L-cysteine sulphoxide, S-allyl-cysteine, ubiquitous amino acids, steroids and adenosine. In the presence of the enzyme alliinase, alliin will be converted to allicin (1 mg of alliin is considered to be equivalent to 0.45 mg of allicin). Allicin is the precursor of different transformation products, including ajoenes, vinyldithiines, oligosulphides and polysulphides depending on the condition applied. Material derived from garlic by steam distillation or extraction in an oily medium containing various allicin transformation products.

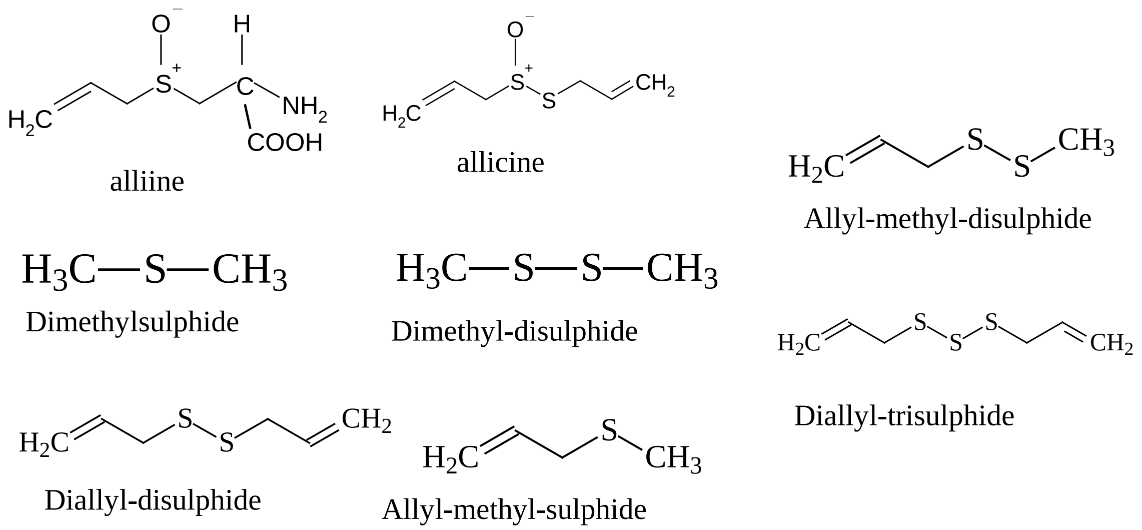


Figure 8.23-30
The structures of alliin, allicin, dimethylsulphide, dimethyl-disulphide, diallyl-disulphide, allyl-methyl-sulphide, allyl-methyl-disulphide, diallyl-trisulphide.

Uses

Therapeutic indications of garlic include prophylaxis of atherosclerosis, treatment of elevated blood lipid levels insufficiently influenced by diet, treatment of high blood pressure and garlic also can be used in the case of upper respiratory tract infections.

Dosage

Prophylaxis of atherosclerosis or treatment of elevated blood lipid levels

Adults: The equivalent of 6-10 mg of alliin (approx. 3-5 mg of allicin) daily, typically contained in one clove of garlic or in 0.5-1.0 g of dried garlic powder.

Upper respiratory tract infections

Adults: 2-4 g of dried bulb or 2-4 ml of tincture (1:5, 45% ethanol), three times daily

Interaction with other medicaments

Garlic may have antiplatelet properties. It might therefore be expected to increase the risk of bleeding with conventional antiplatelet drugs and other drugs that have antiplatelet adverse effects. In two cases interactions have been observed in patients on warfarin who had used garlic products.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Allii ursini folium

Plant

Allium ursinum L. – Wild Garlic/Ramson (Alliaceae)

This plant is native to Europe, North-Asia and Hungary (mostly in Transdanubia). In Hungary the plant is protected; leaves can be collected with official permission, but the bulbs should not be collected. The leaves of *A. ursinum* are easily mistaken for lily of the valley (*Convallaria majalis*), but the latter plant is toxic, and may cause fatal poisoning. A good means of positively identifying ramson is grinding the leaves between one's fingers, which should produce a garlic-like smell.

Figure 8.31
Wild garlic (*Allium ursinum* L.)

Drug

Allii ursini folium (Wild garlic leaf)

The drug consists of the dried leaves of *Allium ursinum* L.

Figure 8.32
Allii ursini folium (Wild garlic leaf)

Constituents

The chemical composition of this plant is similar to that of garlic. The characteristic compounds include allicin (formed from alliin), sulphides, disulphides, ascorbic acid (vitamin C), γ-L-glutaminyl-peptides, flavonoids, prostaglandins (in traces) and lectins.

Uses

Wild garlic has antibacterial effect, mostly used in the treatment of intestinal infections; it has weak antihypertonic, antiarteriosclerotic action and cardioprotective action.

Dosage

see garlic

Allii cepae bulbus

Plant

Allium cepa L. - Onion (Alliaceae)

The plant is native to Iran, Egypt, Europe, Mexico and cultivated all over the world.

Figure 8.33
Onion (*Allium cepa* L.)

Drug

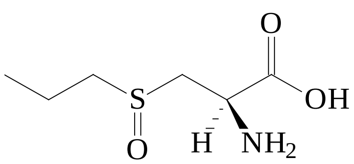
Allii cepae bulbus (Onion)

The drug is the fresh bulb of *Allium cepa* L.

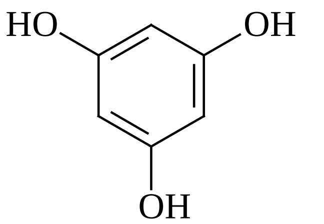
Figure 8.34
Allii cepae bulbus (Onion)

Constituents

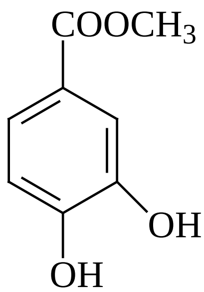
The bulb contains approx. 0.01% essential oil with alliin-derivatives (methyl and propyl alliin). Other constituents are cepaenes, quercetine (4%; mainly in the scale leaves), flavonoids (e.g. kaempferol glycosides), phloroglucine, sugars, oligosaccharides, glycosides of oleanolic acid, vitamins and selenium.



S-propyl-L-cysteine-sulfoxide



phloroglucine



protocatechu acid-methylester

Figure 8.35-37
The structure of S-propyl-L-cysteine-sulphoxide, phloroglucine and protocatechu acid-methylester.

Uses

Onion is an appetizer. The drug has antibacterial activity. It can be used particularly in the case of a runny nose, common cold and tracheitis.

Dosage

see garlic

Bursae pastoris herba

Plant

Capsella bursa pastoris (L.) Medic. - Shepherd's-purse (Brassicaceae)

It is native to eastern Europe and Asia, but is naturalized and considered a common weed in many parts of the world.

Figure 8.38
Shepherd's-purse (*Capsella bursa pastoris* (L.) Medic.)

Drug

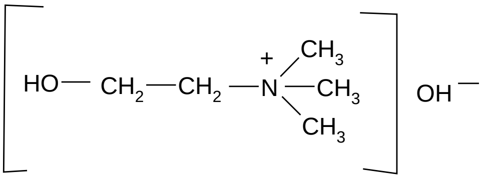
Bursae pastoris herba (Shepherd's-purse)

The drug is the flowering shoot of *Capsella bursa pastoris* (L.) Medic.

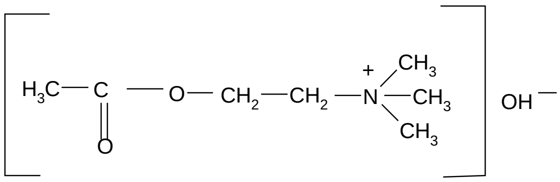
Figure 8.39
Bursae pastoris herba (Shepherd's-purse)

Constituents

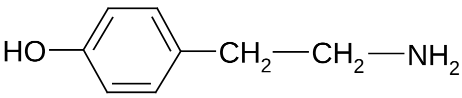
The characteristic compounds of the drug are cholin, acetylcholin, thyramine, flavonoids (luteolin, kaempferol, quercetin and their derivatives), polypeptides.



cholin



acetylcholin



thyramine (parahydroxyphenyl-ethylamine)

Figure 8.40-42
The structure of cholin, acetylcholin and thyramine (parahydroxyphenyl-ethylamine).

Uses

The drug exerts a haemostatic and diuretic action. It slightly decreases blood pressure, and can be used in the case of menorrhagia.

Dosage

5 g of the drug is used for preparing a tea infusion (150 ml). 10-15 g is the daily dose.

Galegae herba

Plant

Galega officinalis L. - Goat's rue (Fabaceae)

It is native to Europe and Asia, but it can be cultivated, as well.

Figure 8.43
Goat's Rue (*Galega officinalis* L.)

Drug

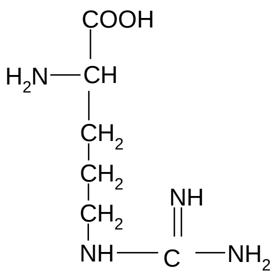
Galegae herba (Goat's rue)

The drug is the upper part of the flowering branches of the shrub of *Galega officinalis* L.

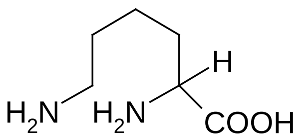
Figure 8.44
Galegae herba (Goat's rue)

Constituents

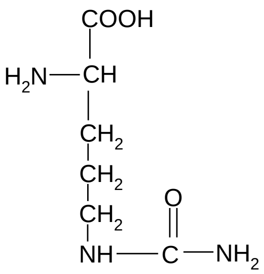
The main active compounds of the drug are lysine, arginine, citrulline and derivatives of guanidine (e.g. galegin). Other relevant compounds are alkaloids (peganin), saponins, and flavonoids (kempferol, quercetin, luteolin).



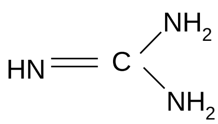
arginine (α-amino-δ-guanidino-valerianic acid)



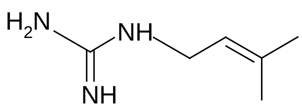
lysine (α,ε-diamino-capronic acid)



citrulline
(α-amino-δ-ureido-valerianic acid)



guanidine
(imino-carbamide)



galegin

Figure 8.45-49
The structure of arginine, lysine, citrulline, guanidine and galegin.

Uses

The drug has been traditionally used in the treatment of mild diabetes (not severe cases, in old patients). From galegin anti-diabetic medicines were developed.

Dosage

2 g of the drug is used for preparing infusion (150 ml). 6 g is the recommended daily dose.

Phaseoli legumen

Plant

Phaseolus vulgaris L. - Bean (Fabaceae)

It is cultivated all over the world.

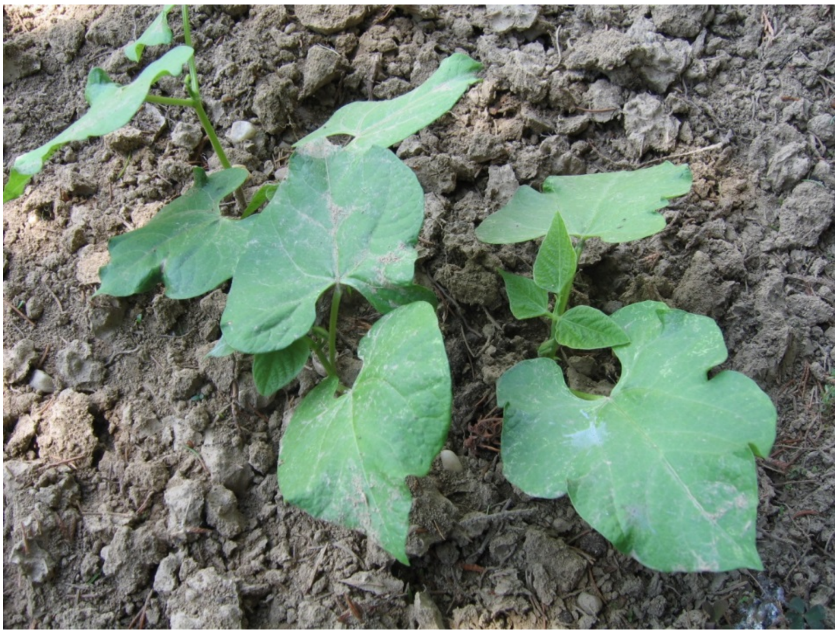


Figure 8.50
Bean (*Phaseolus vulgaris* L.)

Drug

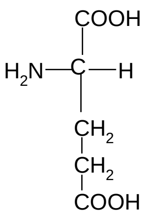
Phaseoli legumen (Bean pod)

The drug is the pod (without seeds) of the dried crop of the cultivated varieties.

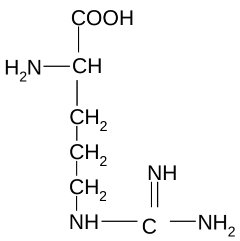
Figure 8.51
Phaseoli legumen (Bean pod)

Constituents

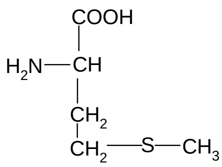
The main active compounds of the drug are amino acids, e.g. glutaminic acid, arginine, proline, asparaginic acid and methionin. Other characteristic compounds are flavonoids, e.g. kaempferol, quercetin and their glycosides (rutin), saponins, chromium salts, silicic acid (H_2SiO_3).



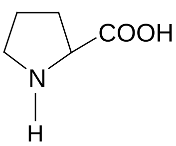
glutaminic acid
(α-amino-glutaric acid)



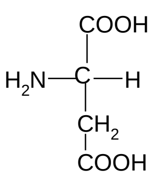
arginine
(α-amino-δ-guanidino-valerianic acid)



methionin
(α-amino-γ-methylmercapto-butyric -acid)



proline
(pyrrolidin-2-carboxylic acid = 2-carboxy-pyrrolidin)



asparaginic acid
(amino-succinic acid)

Figure 8.52-56
The structure of glutaminic acid, arginine, proline, asparaginic acid and methionine.

Uses

The drug is used mainly in traditional medicine, due to its diuretic and antidiabetic activity.

Dosage

2.5-5 g of the drug is used for preparing infusion (150 ml). 5-10 g is the recommended daily dose.

Chapter 9
Drugs containing cyanogenic glycosides and glucosinolates

9.1 Cyanogenic glycosides

In 1830 the cyanogenic glycoside manihotoxin was isolated from *Manihot utilissima* (cassava). In the same year amygdalin was obtained from bitter almonds, linamarin from linseed and phaseolunatin from a bean, *Phaseolus lunatus*. Cyanogenic glycosides belong to the products of secondary plant metabolism. Over 2500 plant species involving about 110 families (e.g. Rosaceae, Fabaceae, Linaceae, Asteraceae) are estimated to be cyanogenic. The presence or absence of hydrogen cyanide (HCN) has taxonomic importance and is used as a character for separating the subfamilies of Rosaceae. The release of HCN is related to the cyanogenic glycoside content of the plants. Cyanogenic glycosides can be hydrolysed by enzymatic or spontaneous hydrolysis (this process is cyanogenesis). HCN can inactivate the cytochrome oxidase enzyme, therefore in high doses it can block the central nervous system (CNS).

The production of HCN depends on both the rate of biosynthesis of cyanogenic glycosides and on the existence (or absence) of its degrading enzymes. Amino acids are the precursors of the biosynthesis of cyanogenic glycosides. Amino acids are hydroxylated, then the N-hydroxylamino acids are converted to aldoximes, which are turned into nitriles. The latter compounds are hydroxylated to alpha-hydroxynitriles and then they are glycosilated to cyanogenic glycosides (**Figure 9.1**). The generation of HCN from cyanogenic glycosides (**Figure 9.2**) is a two-step process involving deglycosilation and the cleavage of the molecule (regulated by beta-glucosidase and alpha-hydroxynitrilase). The tissue level compartmentalisation of cyanogenic glycosides and their hydrolysing enzymes prevents large-scale hydrolysis in intact plant tissue. The actual level of cyanogenic glycosides is determined by various factors, including both developmental and ecological ones.

These compounds are composed of an alpha-hydroxynitrile type aglycone and of a sugar moiety (mostly D-glucose). The most well-known cyanogenic glycosides include linamarin, lotaustralin, prunasin and amygdalin (mandelonitrile-β-gentiobioside) (**Figure 9.3**). In plants they have defensive roles against pest insects.

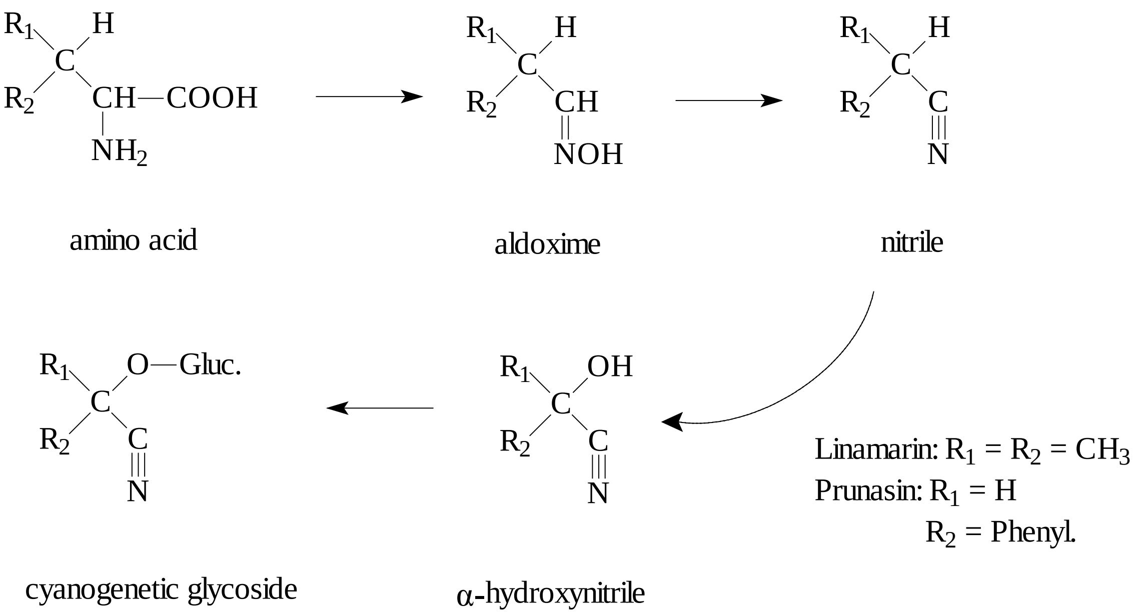


Figure 9.1
Biosynthetic pathway for cyanogenic glycosides.

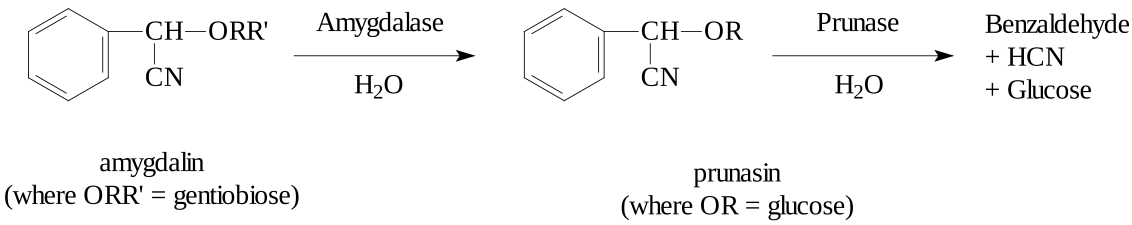
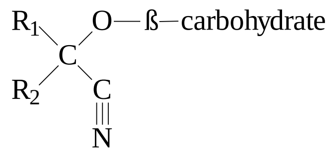


Figure 9.2
The generation of HCN from cyanogenic glycosides.



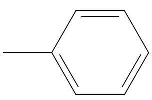
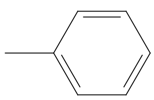
glucoside	R_1	R_2	carbohydrate
linamarin	$-CH_3$	$-CH_3$	glucose
lotaustralin	$-C_2H_5$	$-CH_3$	glucose
prunasin		-H	glucose
amygdalin		-H	gentiobiose

Figure 9.3
The structures of some well-known cyanogenic glycosides.

Drugs

Amygdalae amarae semen

Plant

Prunus dulcis var. *amara* – Bitter almond (Rosaceae)

Bitter almond is native in subtropical regions of China, Asia Minor, the Mediterranean Basin, Europe and California.

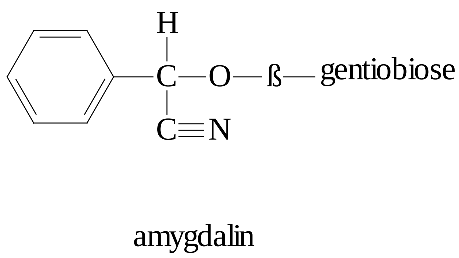
Drugs

Amygdalae amarae semen, Amygdalae oleum virginale (Ph. Eur.), *Amygdalae oleum raffinatum* (Ph. Eur.)

Virgin almond oil is the fatty oil obtained by cold expression from the ripe seeds of *Prunus dulcis* (Miller) D.A. Webb var. *dulcis* or *Prunus dulcis* (Miller) D.A. Webb var. *amara* (D.C.) Buchheim or a mixture of both varieties. Refined almond oil is the fatty oil from the ripe seeds of the same varieties, obtained by cold expression, followed by rectification. A suitable antioxidant may be added. Almond oil is a yellow, clear, liquid, slightly soluble in alcohol, miscible with light petroleum. It solidifies at about −18°C and has a relative density of about 0.916.

Constituents

The main components of bitter almond are cyanogenic glycosides (amygdalin 1-8% and prunasin). The seeds contain essential oil, 30% protein and 35-60% fatty oils (fatty acids: palmitic acid, palmitoleic acid, stearic acid, oleic acid, linoleic acid).



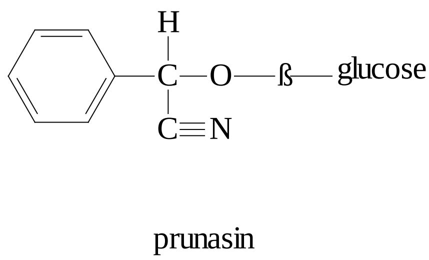


Figure 9.4
The structure of amygdalin and prunasin.

Uses

Bitter almond seeds are used for producing vegetable oil and aroma in food industry. Sweet almond oil is used in body lotions as emollient (softening effect on the skin).

Bitter almond oil can be used as a solvent for certain kinds of drugs, e.g. preparation of oily injections in pharmaceutical industry.

Bitter almond seeds may be toxic because of their cyanogenic glycoside content. The consumption of 10 or 60 seeds may cause fatal poisoning in the case of children or adults, respectively.

Lini semen

Plant

Linum usitatissimum L. - Flax (Linaceae)

Flax has long been cultivated for its fibres and seeds in a number of countries (South America, India, USA, Canada, Europe).

Figure 9.5
Flax (*Linum usitatissimum* L.)

Drugs

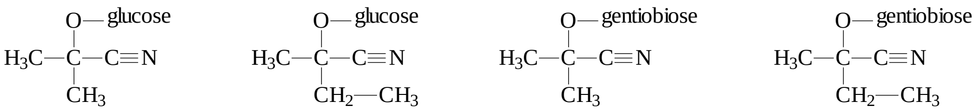
Lini semen (Linseed, Ph. Eur.), *Lini oleum virginale* (Linseed oil, virgin, Ph. Eur.)

Linseed consists of the dried ripe seeds of *Linum usitatissimum* L. Virgin oil is obtained by cold expression from ripe seeds of *Linum usitatissimum* L. A suitable antioxidant may be added. The oil is a clear, yellow or brownish-yellow liquid, on exposure to air turning dark and gradually thickening. When cooled, it becomes a soft mass at about −20 °C. It is very slightly soluble in alcohol, miscible with light petroleum. Relative density: about 0.931.

Figure 9.6
Lini semen (Linseed)

Constituents

The seeds contain 0.1-1.5% of cyanogenic glycosides such as linustatin and neolinustatin. Other relevant components include 3-9% of mucilage polysaccharides composed mainly of galacturonic acid, xylose, galactose and rhamnose units. The seeds contain 30-45% fatty oil mainly consisting of triglycerides of linolenic (40-60%), linoleic and oleic acids. Other constituents include 25% of protein, sterols, lignans (secoisolariciresinol) and a serine proteinase inhibitor.



linamarin lotaustralin linustatin neolinustatin

Figure 9.7-10
The structures of linamarin, lotaustralin, linustatin and neolinustatin.

Uses

Linseed has a mild laxative effect. Internally the seeds can be used in the management of constipation, irritable bowel syndrome (IBS), diverticular disease, and in the case of symptomatic short-term treatment of gastritis and enteritis.

Dosage

Internal use

Adults and children over 12 years of age

As a laxative: 5 g of whole, finely-cracked or freshly crushed seeds, soaked in water and taken with a glassful of liquid three times daily. The effect starts 18-24 hours later.

As a demulcent for gastritis and/or enteritis: for a mucilaginous preparation soak 5-10 g of whole linseed in 150 ml water and strain after 20-30 minutes.

External use

30-50 g of crushed or powdered seeds as a warm poultice or warm compress (for abscesses, furuncles, and in the case of eczema and psoriasis)

Children from 6 to 12 years of age: half the adult dose

Children under 6 years of age: to be treated under medical supervision only

Because of the gradual mode of action of bulk-forming laxatives, treatment should be continued for a minimum of 2-3 days to ensure optimum benefit. If abdominal pain occurs, or if there is no response after 48 hours, use of linseed should be discontinued and medical advice must be sought.

Linseed (whole, finely-cracked or freshly crushed) should be soaked and taken with at least 10-fold amounts of liquid, otherwise intestinal obstruction may occur.

Contra-indications

Atonic and obstructive ileus, subileus or conditions likely to lead to intestinal obstruction. Acute abdominal pain of any origin (e.g. appendicitis)

Interaction with other medicaments

The absorption of other medications taken at the same time may be delayed. Patients with diabetes should be aware of a potential delay in glucose absorption.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Overdose

In spite of its cyanogenic glycoside content, single doses of up to 150-300 g of powdered linseed are not toxic.

9.2 Glucosinolates

Glucosinolates are a class of organic compounds that contain sulphur and nitrogen and are derived from glucose and an amino acid (**Figure 9.11**). They occur as secondary metabolites in almost all plants of the order Brassicales including the families Brassicaceae and Cappar(id)aceae; but also in some other orders, for example, in Violales and Euporbiales. About 120 different glucosinolates are known to occur naturally in plants.

From this group of compounds sinigrin and sinalbin were isolated in crystalline form from black and white mustards. These and similar glycosides have since been isolated from many plants, particularly those used as condiments (e.g. horseradish) or in folk medicine. They are volatile compounds and have a characteristic smell and hot taste.

Glucosinolates are water-soluble anions and belong to the glucosides. Every glucosinolate contains a central carbon atom, which is bound via a sulphur atom to the thioglucose group (making a sulphated aldoxime) and via a nitrogen atom to a sulphate group. In addition, the central carbon atom is bound to a side group; different glucosinolates have different side groups, and it is the variation in the side chain that is responsible for the variation in the biological activities of these plant compounds.

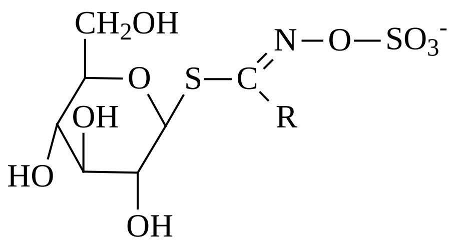


Figure 9.11
The general structure of a glucosinolate.

They are synthesized from certain amino acids: the so-called aliphatic glucosinolates are derived mainly from methionine, but also from alanine, leucine, isoleucine or valine. Aromatic glucosinolates include indolic glucosinolates, such as glucobrassicin, derived from tryptophan, and others derived from phenylalanine, its chain-elongated homologue homophenylalanine, and sinalbin derived from tyrosine.

Plants contain the enzyme myrosinase, which, in the presence of water, cleaves off the glucose group from a glucosinolate. The remaining molecule then quickly converts to an isothiocyanate, a nitrile, or a thiocyanate; these are the active substances that serve as defence for the plant. Glucosinolates are also called mustard oil glycosides. The standard product of the reaction is isothiocyanate (mustard oil); the other two products mainly occur in the presence of specialised plant proteins that alter the outcome of the reaction (**Figure 9.12**). To prevent damage to the plant itself, the myrosinase enzyme and glucosinolates are stored in separate compartments of the cell and occur together only in case of physical injury.

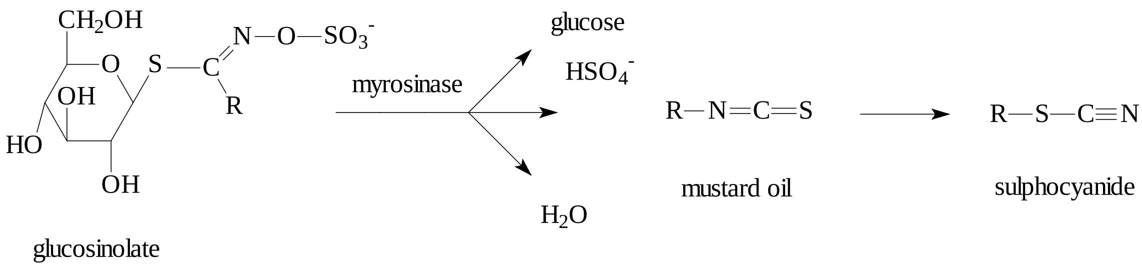


Figure 9.12
The action of myrosinase (β-thioglucosidase).

Mustard oil has a strong antibacterial activity against different microorganisms, and has rubefacient effect. Internally the drugs containing mustard oil can be used for treating respiratory diseases, e.g. hay fever. Externally this compound is used in the form of plasters to treat rheumatic complaints. The chemopreventive effects of the glucosinolates present in cruciferous vegetables (e.g. broccoli, cabbage) have already been reported. Glucosinolates are well known for their toxic effects in both humans and animals at high doses.

Drugs

Sinapis nigrae semen

Plant

Brassica nigra (L.) Koch – Black mustard (Brassicaceae)

It is cultivated in Hungary, and native in Europe, North Africa, Caucasus and the Indian subcontinent.

Drug

Sinapis nigrae semen (Black mustard seed)

The drug consists of the dried ripe seeds of *Brassica nigra* (L.) Koch.

Figure 9.13
Sinapis nigrae semen (Black mustard seed)

Constituents

The seeds contain 1-5% of sinigrin (glucoside of allyl isothiocyanate), sinapin (pseudoalkaloid), 30% of fatty oil, small amounts of mucilage.

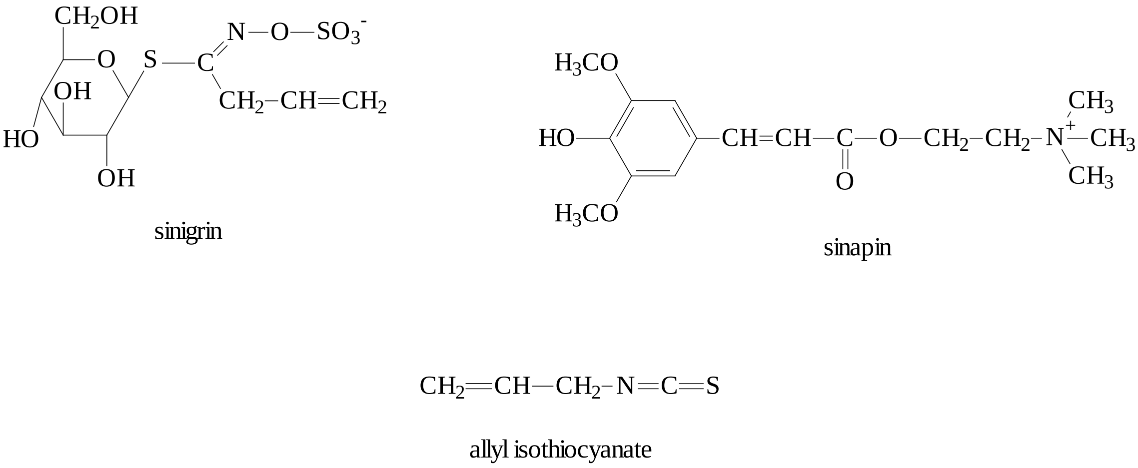


Figure 9.14-16
The structure of sinigrin, sinapin and allyl isothiocyanate.

Uses

Mustard has been traditionally used, particularly in the form of plasters, as a rubefacient, in the case of rheumatic pains. Allyl isothiocyanate (volatile mustard oil) can be used for preparation of liniments or ointments to treat rheuma. In an aqueous medium sinigrin will be converted to allyl isothiocyanate, which has strong antibacterial activity against e.g. *Staphylococcus aureus* and *Escherichia coli* in high dilution.

Mustard is a spice, and in this form can be used for treating digestive problems.

In veterinary medicine, mustard is applied as a stomachic and diuretic medicinal plant.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Chapter 10
Drugs containing phenylpropanoid and phloroglucin derivatives

10.1 Phenylpropanoid derivatives

Phenolic compounds probably constitute the largest group of plant secondary metabolites. They are widespread in nature, and can be found in most classes of natural compounds having aromatic moieties. They range from simple structures with one aromatic ring to highly complex polymeric substances, for example tannins and lignins. Phenols are important compounds of some medicinal plants, which are used as coloring agents, antioxidants, flavourings and aromatizers. Phenylpropanoids are mostly derived from *p*-coumaric acid (*p*-hydroxycinnamic acid). These compounds are located in various essential oils. They have alcoholic, aldehyde and carboxylic acid groups, e.g. eugenol (= phenolic phenylpropane). Medicinal plants containing phenylpropanoid derivatives are widely used in phytotherapy. It should be noted that some compounds (e.g. *trans*-isoasarone, *trans*-isoeugenol methyl ether and *trans*-isoelemicin in the rhizome of *Asarum europeum* L.) should not be used for medicinal purposes because of their toxic effect.

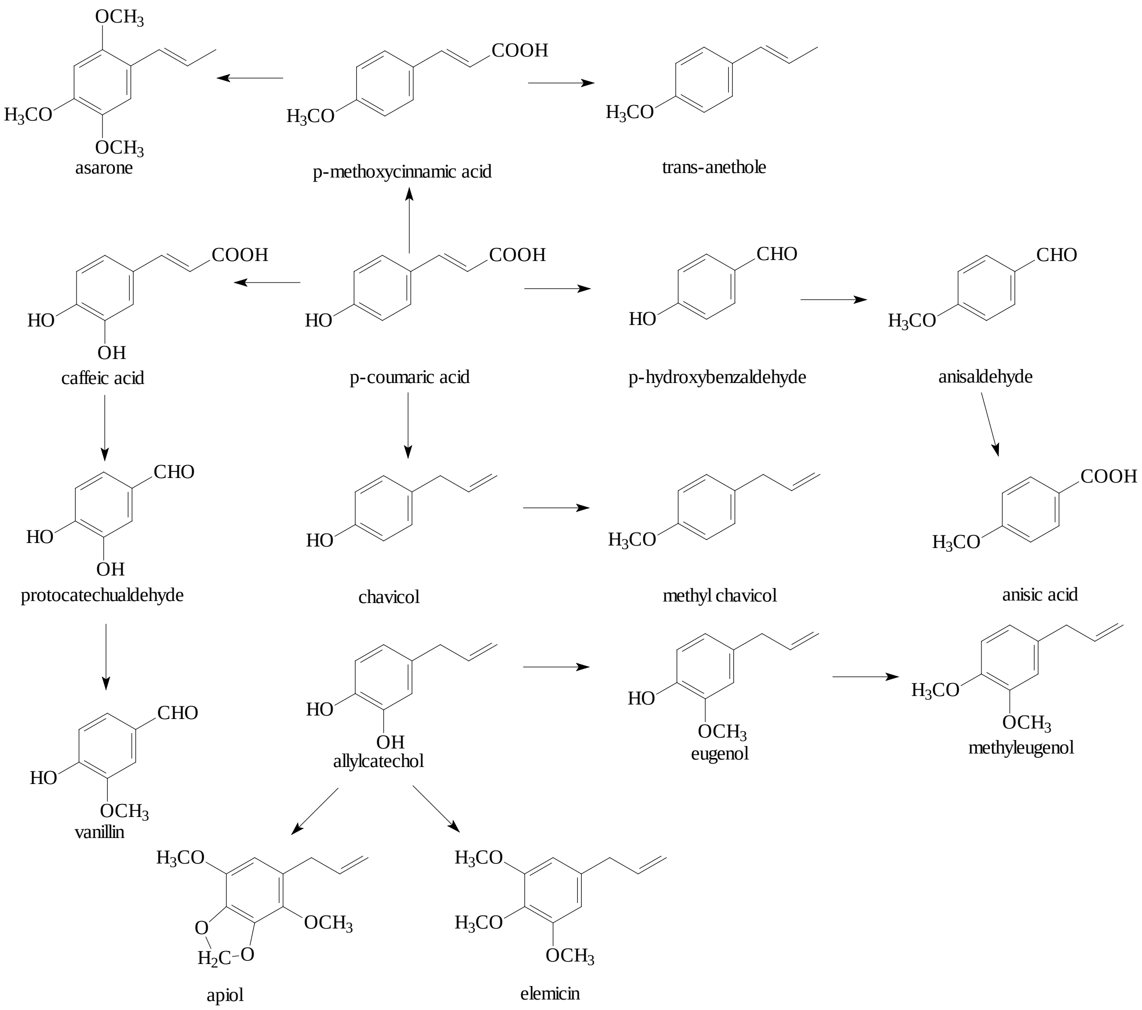
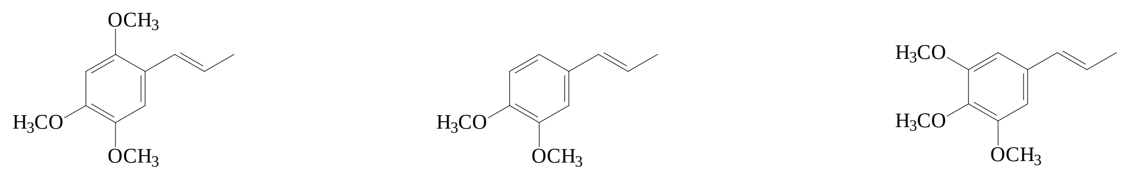


Figure 10.1
Biosynthesis of some cinnamic acid derivatives.



trans-isoasarone *trans*-isoeugenol methyl ether *trans*-isoelemicin

Figure 10.2
The structure of *trans*-isoasarone, *trans*-isoeugenol methyl ether and *trans*-isoelemicin.

Drugs

Cinnamomi cortex

Plant

Cinnamomum zeylanicum Nees. – Cinnamon (Lauraceae)

The plant is native to India, Ceylon and cultivated (Java, Sumatra, South America).

Figure 10.3
Cinnamon (*Cinnamomum zeylanicum* Nees.)

Drug

Cinnamomi cortex (Cinnamon bark, Ph. Eur.). **Other drugs:** *Cinnamomi zeylanici corticis aetheroleum* (Cinnamon bark oil, Ph. Eur.), *Cinnamomi corticis tinctura* (Cinnamon bark tincture, Ph. Eur.), *Cinnamomi zeylanici folii aetheroleum* (Cinnamon leaf oil, Ph. Eur.)

Cinnamon consists of the dried bark, freed from the outer cork and the underlying parenchyma, of the shoots grown on cut stock of *Cinnamomum zeylanicum* Nees. It contains not less than 12 ml/kg of essential oil. Cinnamon has a characteristic, aromatic odour.

Figure 10.4
Cinnamomi cortex (Cinnamon bark)

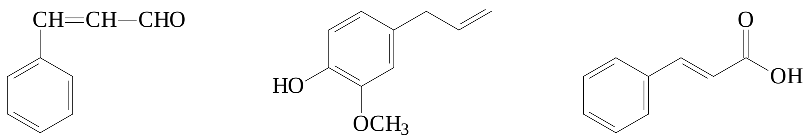
Ceylon cinnamon bark oil is obtained by steam distillation of the bark of the shoots of *Cinnamomum zeylanicum* Nees. A clear, mobile, light yellow liquid becoming reddish over time, with a characteristic odour reminiscent of cinnamic aldehyde.

The tincture is produced from 1 part of the drug and 5 parts of ethanol (70 per cent *V/V*) by an appropriate procedure. *Appearance*: clear, brownish-red liquid, with a characteristic odour.

Cinnamon leaf oil is obtained by steam distillation of the leaves of *Cinnamomum zeylanicum* Nees. It is a clear, mobile, reddish-brown to dark brown liquid, with a characteristic odour reminiscent of eugenol.

Constituents

Cinnamon contains up to 4% of essential oil consisting principally of cinnamaldehyde (60-75%) together with cinnamyl acetate and eugenol. Other compounds of the oil are β-caryophyllene, linalool and 1,8-cineole. The essential oil of the leaf contains 70% of eugenol. Other constituents include pentacyclic diterpenes (the pesticide cinnzeylanol), oligomer procyanidins and phenolcarboxylic acids (caffeic acid, ferulic acid, sinapinic acid).



cinnamaldehyde eugenol *trans*-cinnamic acid

Figure 10.5-7
The structure of cinnamaldehyde, eugenol and *trans*-cinnamic acid.

Uses

The drug has antimicrobial effect. Therapeutic indications include dyspeptic complaints such as gastrointestinal spasm, bloating and flatulence; loss of appetite and diarrhoea. Cinnamon oil can be used by inhalation in case of respiratory mycoses. Externally the drug and its oil are used in foot bath (because of antiseptic property). *In vitro* and a few *in vivo* studies demonstrated the antidiabetic activity of cinnamon. The leaf essential oil is used in cosmetic industry (in soaps, creams, perfumes).

Dosage

Adult and elderly daily dose: 1.5-4 g of dried bark or as an infusion; 0.5-1.0 ml of fluid extract (1:1, 70% ethanol); 2-4 ml of tincture.

Children: for infantile diarrhoea, proportion of adult dose according to age and body weight in alcohol-free preparations.

Overdose: Cinnamon bark oil and cinnamaldehyde in doses over 0.2 g/day (equivalent to 15-20 g of crude drug) have irritant properties.

Contra-indications

Patients with known allergy to cinnamon, cinnamon bark oil or cinnamaldehyde, and in case of gastric and duodenal ulcers.

Pregnancy and lactation

Only limited data available. In accordance with general medical practice, cinnamon and its preparations should not be used internally during pregnancy and lactation without medical advice.

Caryophylli flos

Plant

Syzygium aromaticum (L.) Merill et Perry – Clove (Myrtaceae)

The plant is native to Indonesia, Madagascar, Mauritius and Maluku Islands.

Drug

Caryophylli flos (Clove, Ph. Eur.). **Other Drug** Caryophylli floris aetheroleum (Clove oil, Ph. Eur.)

Clove consists of the whole flower buds of *Syzygium aromaticum* (L.) Merill et L. M. Perry (*Eugenia caryophyllus* (C. Spreng.) Bull. et Harr.) dried until they become reddish-brown. It contains not less than 150 ml/kg of essential oil. Clove has a characteristic, aromatic odour.

Figure 10.8
Caryophylli flos (Clove)

Clove oil is obtained by steam distillation from the dried flower buds of *Syzygium aromaticum* (L.) Merill et L. M. Perry (*Eugenia caryophyllus* C. Spreng. Bull. et Harr.). A clear, yellow liquid which becomes brown when exposed to air, miscible with methylene chloride, toluene and fatty oils.

Constituents

Clove contains up to 20% of essential oil consisting principally of eugenol (80-95%) together with approx. 3% acetyleugenol. The oil also contains sesquiterpenes (α- and β-caryophyllene) and small quantities of esters, ketones and alcohols. Other constituents include flavonoids (quercetin and kaempferol glycosides), tannins (e.g. gallotannin), syringic acid and triterpenes.

acetyleugenol eugenol

Figure 10.9-10
The structure of eugenol and acetyleugenol.

Uses

Clove has antibacterial, antifungal, antiviral, local anesthetic and spasmolytic activities. In dentistry it is used as a disinfectant and anaesthetization of the canal in teeth. The drug is applied in mouthwashes, in case of inflammation of the mouth and the throat. Internally clove can be used in case of digestive problems. It is a taste corrigent. The drug is used as a stimulant aromatic, as a spice and for the preparation of the volatile oil.

Clove stem oil is produced in Tanzania and in Madagascar; it is used mainly in the flavouring and perfumery industries. Clove leaf oil is distilled in Madagascar, Tanzania and in Indonesia, and is used for the isolation of eugenol.

Dosage

Adult and elderly daily dose: 3-5 g of dried drug or as an infusion.

For the symptomatic treatment of minor inflammations in the mouth or the throat:

Mouthwashes corresponding to 1-5% essential oil. Apply several times daily.

The use in children and adolescents under 18 years of age is not recommended. Not to be used for more than 1 week.

For the temporary relief of toothache due to a dental cavity:

Undiluted essential oil or solutions in a strength up to 50% or gels in a strength of 20%. Repeat administration after 20 minutes, then every 2 hours if necessary. Not to be used for more than 1 week. Application: A small piece of cotton wool should be soaked in the undiluted oil or in a diluted solution; semi-solid dosage forms should be placed on a cotton bud. Cotton bud or cotton wool should be accurately directed to the decayed part of the tooth.

The use in children and adolescents under 18 years of age is not recommended.

Overdose: No case of overdose from oromucosal or dental use has been reported. However, after oral administration of 5-10 ml of clove oil in children below 2 years of age, life threatening conditions were observed. Overdose may lead to CNS depression, urinary abnormalities, anion gap acidosis, deterioration of liver function, coma, seizure and low blood glucose levels. Treatment should be supportive and symptomatic; there have been reports in the literature that N-acetylcysteine has been successfully used as an antidote.

Contra-indications

Patients with known allergy to clove, clove oil or cinnamaldehyde should not use these drugs.

Pregnancy and lactation

No data available. In accordance with general medical practice, clove and its preparations should not be used internally during pregnancy and lactation without medical advice.

Zingiberis rhizoma

Plant

Zingiber officinale Roscoe – Ginger (Zingiberaceae)

The plant is grown in many parts of the world, including Jamaica, China, India and Africa. Jamaica ginger, once the traditional pharmaceutical ginger, has been largely replaced by other sources. It was introduced into Europe by the Phoenician traders.

Figure 10.11
Ginger (*Zingiber officinale* Roscoe)

Drug

Zingiberis rhizoma (Ginger, Ph. Eur.)

Ginger consists of the dried, whole or cut rhizome of *Zingiber officinale* Roscoe, with the cork removed, either completely or from the wide flat surfaces only. Whole or cut, it contains not less than 15 ml/kg of essential oil, calculated with reference to the anhydrous drug. Ginger has a characteristic aromatic odour and a spicy and burning taste.

Figure 10.12
Zingiberis rhizoma (Ginger)

Constituents

Essential oil (0.25-3%) contains monoterpenes (mainly geranial), and sesquiterpenes (mainly β-sesquiphellandrene, *ar*-curcumene, α-zingiberene). Pungent principles (4-7.5% w/w) consist of the gingerols (e.g. 6-gingerol, zingerone), shogaols (e.g. 6-shogaol) and related phenolic ketone derivatives. Other constituents include diarylheptenones, diterpenes, 6-gingesulphonic acid, monoacyldigalactosyl glycerols, coumaric acid, ferulic acid, fatty acids and sterols. Gingerols: they will be converted into dehydro derivatives (shogaols) during storage. Their ratio (gingerols:shogaols) determines the freshness of the drug.

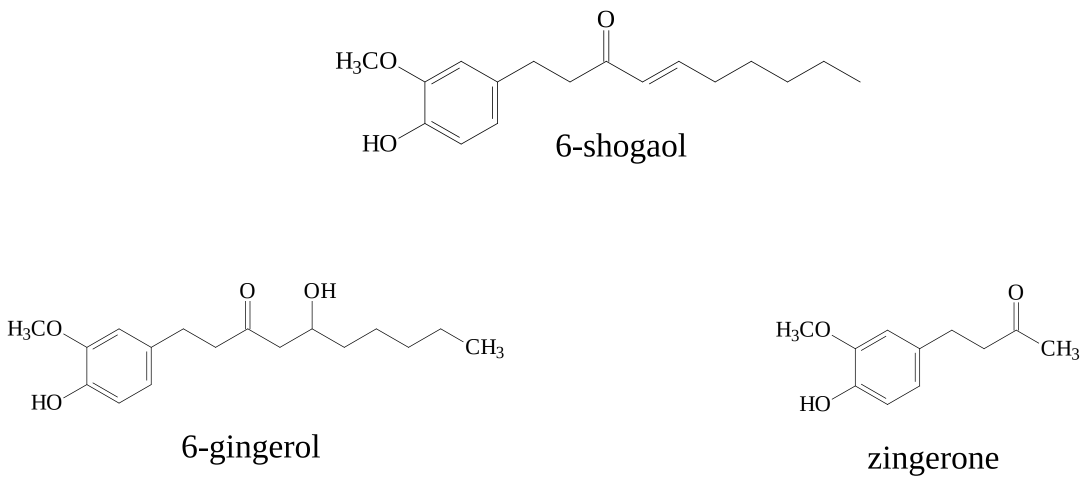


Figure 10.13-15
The structure of 6-gingerol, zingerone and 6-shogaol.

Uses

Therapeutic indications include the prophylaxis of nausea and vomiting in motion sickness, the management of digestive disorders and as a postoperative antiemetic for minor day-case surgical procedures. Ginger is used in food, liqueur and perfume industries.

Dosage

Adult and children over 6 years: 0.5-2 g of the powdered drug daily in single or divided doses; for the prophylaxis of motion sickness, 30 minutes before travel.

Undesirable effect

Heartburn has been reported in a few cases.

Contra-indications

The drug has anticholinergic effect. Ginger and its products must not be administered with anticoagulants at the same time. Ginger may enhance absorption of sulphaguanidine.

Pregnancy and lactation

No data available. In accordance with general medical practice, ginger and its preparations should not be used internally during pregnancy and lactation without medical advice.

Curcumae xanthorrhizae rhizoma

Plant

Curcuma xanthorrhiza Roxb. – Turmeric, javanese (Zingiberaceae)

The plant is cultivated in Indonesia.

Drug

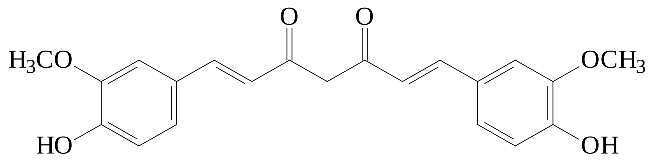
Curcumae xanthorrhizae rhizoma (Turmeric, javanese; Ph. Eur.)

Javanese turmeric consists of the dried rhizome, cut in slices, of *Curcuma xanthorrhiza* Roxb. (*C. xanthorrhiza* D. Dietrich). It contains not less than 50 ml/kg of essential oil and not less than 1.0% of dicinnamoyl methane derivatives expressed as curcumin, both calculated with reference to the anhydrous drug. Javanese turmeric has an aromatic odour.

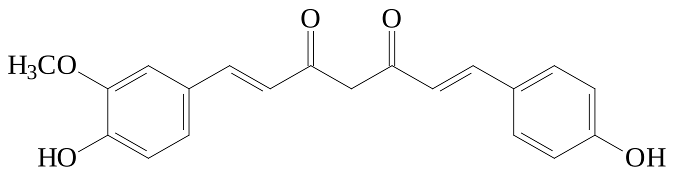
Figure 10.16
Curcumae xanthorrhizae rhizoma (Turmeric, javanese)

Constituents

The major characteristic constituents are curcuminoids (1-2%) – a mixture of dicinnamoylmethane derivatives such as curcumin (diferuloylmethane), monodemethoxycurcumin (*p*-coumaroylferuloyl-methane) and other phenolic and non-phenolic diarylheptanoids, and essential oil (3-12%) containing bisabolane sesquiterpenes such as *ar*-curcumene, xanthorrhizol, β-curcumene and germacrone. The presence of xanthorrhizol and absence of bisdemethoxycurcumin (di-*p*-coumaroylmethane) are species-specific, distinguishing Javanese turmeric from turmeric (Curcuma longa = *C. domestica*).



curcumin (diferuloylmethane)



monodemethoxycurcumin (*p*-coumaroylferuloyl-methane)

Figure 10.17-18
The structure of curcumin (diferuloylmethane) and monodemethoxycurcumin (*p*-coumaroylferuloyl-methane).

Uses

Therapeutic indications include the symptomatic treatment of mild digestive disturbances and minor biliary dysfunction.

Dosage

Adult and elderly average daily dose: 2 g of the drug or corresponding extracts.

Patients with cholelithiasis should take Javanese turmeric only after consulting a physician.

Contra-indications

The drug is not recommended in case of biliary obstruction.

Pregnancy and lactation

No human data available. In accordance with general medical practice, the drug and its preparations should not be used during pregnancy and lactation without medical advice.

Anisi fructus

Plant

Pimpinella anisum L. – Anise (Apiaceae)

This annual plant is widely cultivated in Europe (Spain, Germany, Italy, Hungary, Bulgaria), Egypt and in America (Chile, Mexico). Spain and Egypt are the principal producers of the anise essential oil.

Drug

Anisi fructus (Aniseed, Ph. Eur.). **Other Drug** *Anisi aetheroleum* (Anise oil, Ph. Eur.).

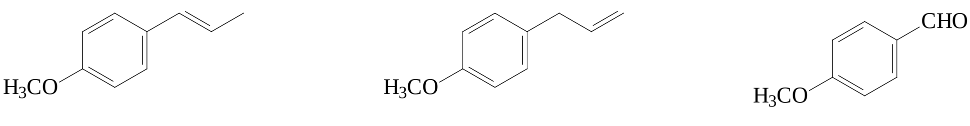
Aniseed consists of the whole dry cremocarp of *Pimpinella anisum* L. It contains not less than 20 ml/kg of essential oil. Aniseed has an odour reminiscent of anethole. The fruit is a cremocarp and generally entire; a small fragment of the thin, rigid, slightly curved pedicel is frequently attached.

Essential oil is obtained by steam distillation from the dry ripe fruits of *Pimpinella anisum* L. It is a clear, colourless or pale yellow liquid.

Figure 10.19
Anisi fructus (Aniseed)

Constituents

The active constituent of the drug is the essential oil (2-6%). The essential oil contains predominantly *trans*-anethole (80-95%) with smaller amounts of estragole (methyl-cavicol), anisaldehyde, *cis*-anethole; sesquiterpene and monoterpene hydrocarbons are also present. Other constituents include coumarins (umbelliferone, scopoletin), furocoumarins, flavonoids, phenolic acids and fixed oil.



trans-anethole methyl-cavicol (estragole) anisaldehyde

Figure 10.20-22
The structure of *trans*-anethole, estragole and anisaldehyde.

Uses

Therapeutic indications include dyspeptic complaints such as mild spasmodic gastrointestinal complaints, bloating, flatulence and catarrh of the upper respiratory tract. The drug has expectorant, carminative, stomachic, spasmolytic (in case of urinary and gastrointestinal tract) and antibacterial activities. Aniseed is used as a component of herbal teas for stimulation of breast milk (because of lactiferous effect). Aniseed is a spice, it is also used in the food and liqueur industries.

Dosage

Adult average daily dose: 3 g of crushed fruits as an infusion or similar preparations.

Children average daily dose: up to 1 year of age, 0.5 g of crushed fruits as an infusion; *1-4 years of age*, 1 g; *4-10 years of age*, 2 g; *10-16 years of age*, the adult dose (3 g).

The maximum daily dose of the essential oil is 0.3 g (greater doses are hepatotoxic and toxic for children).

Undesirable effect

Rare cases of contact dermatitis caused by anethole-containing toothpastes and cosmetic creams have been reported.

Contra-indications

Persons with known sensitivity to anethole should avoid aniseed.

Pregnancy and lactation

Aniseed may be used during pregnancy and lactation at the recommended dosage, as aqueous infusion only. It should be highlighted that preparations containing essential oil or alcoholic extracts should not be used during pregnancy and lactation. Mild oestrogenic activity and antifertility effects of anethole have been demonstrated in rats.

Anisi stellati fructus

Plant

Illicium verum Hook. – Star anise (Illiciaceae)

Star anise is an evergreen tree, indigenous to the south-west provinces of China. The fruits are collected and the oil is distilled locally in China and Vietnam.

Drug

Anisi stellati fructus (Star anise, Ph. Eur.). **Other Drug** *Anisi stellati aetheroleum* (Star anise oil, Ph. Eur.).

The drug consists of the dried composite fruit (aggregate of follicles) of *Illicium verum* Hook. It contains minimum 70 ml/kg of essential oil (anhydrous drug). The fruit carpels are brown and emit the odour of anethole.

Essential oil is obtained by steam distillation from the dry ripe fruits of *Illicium verum* Hook. It is a clear, colourless or pale yellow liquid.

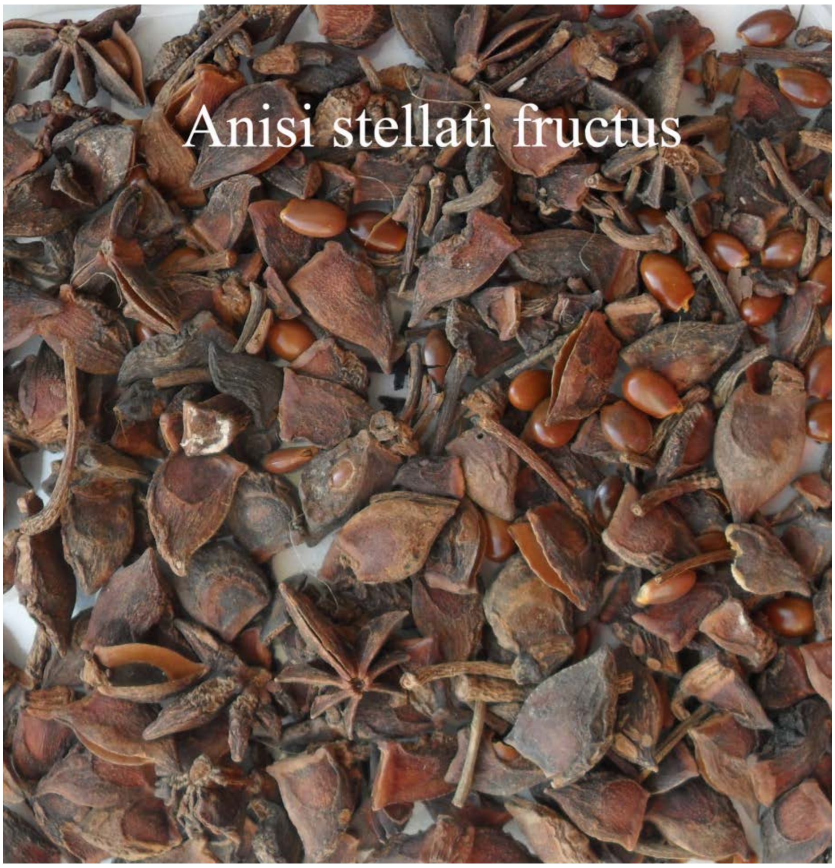


Figure 10.23
Anisi stellati fructus (Star anise)

Constituents

The active constituent of the drug is the essential oil (2-8%), with similar chemical composition as we have seen in aniseed (*Pimpinella anisum* L.). See above.

It should be noted that another *Illicium* species, *Illicium anisatum* (Japanese star anise), can not substitute Chinese star anise. Japanese star anise is a poisonous species (with bitter taste) containing anisatin, a sesquiterpene lactone!

Uses

Therapeutic indications and other uses are similar to those of aniseed (*Pimpinella anisum* L.). See above.

Dosage

It is similar to that of aniseed (*Pimpinella anisum* L.). See above.

Undesirable effect

It is similar to aniseed (*Pimpinella anisum* L.). See above.

Contra-indications

It is similar to aniseed (*Pimpinella anisum* L.). See above.

Pregnancy and lactation

It is similar to aniseed (*Pimpinella anisum* L.). See above.

Foeniculi dulcis fructus and Foeniculi amari fructus

Plants

Foeniculum vulgare Miller subsp. *vulgare* var. *dulce* – Sweet fennel (Apiaceae), *Foeniculum vulgare* Miller subsp. *vulgare* var. *vulgare* – Bitter fennel (Apiaceae)

Sweet fennel is mainly cultivated in Europe. Bitter fennel is also cultivated in many parts of Europe and substantial amounts are imported from India, China and Egypt.

Figure 10.24
Sweet fennel (*Foeniculum vulgare* Miller subsp. *vulgare* var. *dulce*)

Drugs

Foeniculi dulcis fructus (Sweet fennel, Ph. Eur.), *Foeniculi amari fructus* (Bitter fennel, Ph. Eur.). **Other Drug** *Foeniculi amari fructus aetheroleum* (Bitter fennel fruit oil, Ph. Eur.).

Sweet fennel consists of the dry cremocarps and mericarps of *Foeniculum vulgare* Miller sp. *vulgare* var. *dulce* (Miller) Thellung. It contains not less than 20 ml/kg of essential oil, calculated with reference to the anhydrous drug. The oil contains not less than 80.0 per cent of anethole. Sweet fennel is pale green or pale yellowish-brown.

Bitter fennel consists of the dry cremocarps and mericarps of *Foeniculum vulgare* Miller sp. *vulgare* var. *vulgare*. It contains not less than 40 ml/kg of essential oil, calculated with reference to the anhydrous drug. The oil contains not less than 60.0% of anethole and not less than 15.0% of fenchone. Bitter fennel is greenish-brown, brown or green.

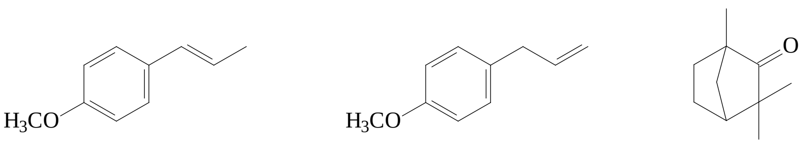
Bitter fennel fruit oil is obtained by steam distillation from the ripe fruits of *Foeniculum vulgare* Miller, ssp. *vulgare* var. *vulgare*. It contains fenchone (12.0% to 25.0%) and *trans*-anethole (55.0% to 75.0%). Appearance: clear, colourless or pale yellow liquid. It has a characteristic odour.

Figure 10.25
Foeniculi dulcis fructus (Sweet fennel)

Constituents

The active constituent of the drugs is the essential oil. The essential oil of sweet fennel contains predominantly *trans*-anethole with not more than 10% of estragole and not more than 7.5% of fenchone. Other components of the oil are α- and β-pinene, limonene and *p*-cymene. Bitter fennel fruit oil contains predominantly *trans*-anethole and fenchone with not more than 5% of estragole. The taste of the essential oil depends on the ratio of *trans*-anethole (sweet compound) and fenchone (bitter compound).

It also contains pinenes, *p*-cymene, sabinene, α-phellandrene and γ-terpinene. Other constituents of the fruits include water-soluble glycosides of monoterpenoid, alkyl and aromatic compounds, coumarins (scopoletin, bergapten) and flavonoids.



trans-anethole estragole fenchone

Figure 10.26-28
The structure of *trans*-anethole, estragole and fenchone.

Uses

Therapeutic indications include dyspeptic complaints such as mild, spasmodic gastrointestinal ailments, bloating and flatulence and catarrh of the upper respiratory tract. The drugs have antibacterial, antifungal, expectorant (in case of upper respiratory catarrh), spasmolytic (especially in biliary and renal colic) and galactogogue activities. Due to children's preference of sweet taste to bitter taste, sweet fennel fruit is predominantly used in paediatrics in case of gastrointestinal problems because of its carminative and stomachic effects, and in case of bronchitis as an expectorant and cough suppressant. It should be noted that the essential oil should not be recommended for children, because it may trigger epileptic seizures.

Dosage

Adult daily dose: 5-7 g of crushed fruits as an infusion or similar preparations.

Children average daily dose: up to 1 year of age, 1-2 g of crushed fruits as an infusion; *1-4 years of age*, 1.5-3 g; *4-10 years of age*, 3-5 g; *10-16 years of age*, the adult dose (5-7 g).

Undesirable effect

Rare cases of contact dermatitis caused by anethole-containing preparations have been reported.

Contra-indications

Persons with known sensitivity to anethole should avoid the use of fennel.

Pregnancy and lactation

Fennel may be used during pregnancy and lactation at the recommended dosage, as aqueous infusion only. It should be highlighted that preparations containing essential oil or alcoholic extracts should not be used during pregnancy and lactation. Mild oestrogenic activity and antifertility effects of anethole have been demonstrated in rats.

Calami rhizoma

Plant

Acorus calamus L. – Calamus or Sweet flag (Araceae)

This perennial plant is common on the banks of streams. Originating in Asia, it is now widely distributed in Asia, Europe and North America. In Hungary, it can only be collected with the permission of the Inspectorate of Environment and Nature Protection, e.g. along the Drava river. The plant has different varieties according to ploidy level; *Acorus calamus* var. *calamus* (European, 3*n*), *A. calamus* var. *americanus* (2*n*) and *A. calamus* var. *angustata* (East Asian, 4*n*).

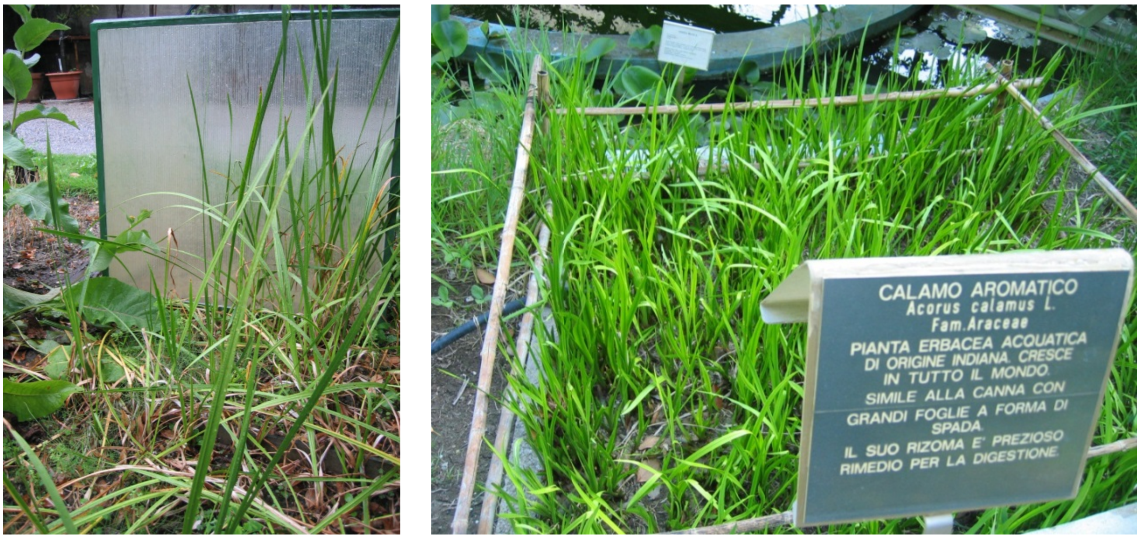


Figure 10.29
Calamus (*Acorus calamus* L.)

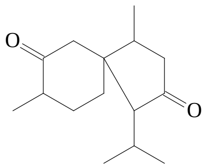
Drug

Calami rhizoma (Calamus, Ph. Helv.). **Other Drug** *Calami aetheroleum* (Calamus oil). The drug consists of the dried, cut rhizome of *Acorus calamus* L.

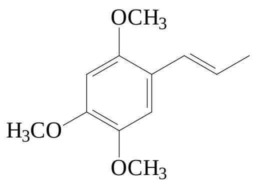
Figure 10.30
Calami rhizoma (Calamus)

Constituents

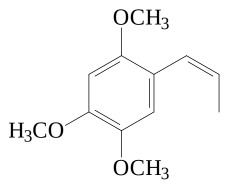
Calamus contains 1.7-9.3% of essential oil containing diketo-spirane mono- and sesquiterpenes (acorone, acorenone), which are responsible for the bitter taste. Another relevant component of the oil is asarone (phenylpropane derivative). The composition of the oil from 2*n*, 3*n* and 4*n* varieties differs and the *β*-asarone content increases with ploidy (in var. *americanus*: *β*-asarone (0-0.5%), var. *calamus*: *β*-asarone (3-13%), var. *angustata*: *β*-asarone (80%). The phenylpropane derivative cis-isoasarone (= *β*-asarone) is potentially carcinogenic. Therefore some researchers recommend the selection of races for pharmaceutical use. Other cinnamic acid derivatives of the drug are methyl eugenol and methyl isoeugenol. Other constituents include mucilages, starch and lignan derivatives.



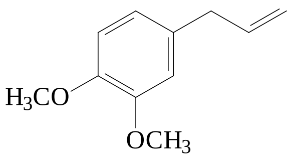
acorone



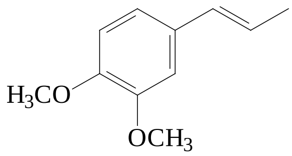
asarone



β-asarone



methyl eugenol



methyl isoeugenol

Figure 10.31-35

The structure of asarone, *β*-asarone, methyl eugenol, methyl isoeugenol and acorone.

Uses

Therapeutic indications include digestive disorders and loss of appetite. The drug and its product have stomachic, appetizer and carminative effects. Calamus is also used in liqueur industry. The prolonged used of calamus is not recommended (mostly 3*n* and 4*n* varieties)!

Today the drug is mainly used as a source of calamus oil, which is applied in perfumery industry.

Dosage

Adult daily dose: 1 g of crushed drug as an infusion (200 ml).

For children the drug and its products are not recommended.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Petroselini fructus

Plant

Petroselinum crispum (Mill.) Nym. var. *crispum* – Parsley (Apiaceae)

Parsley is a cultivated plant all over the world.

Figure 10.36
Parsley (*Petroselinum crispum* (Mill.) Nym. var. *crispum*)

Drug

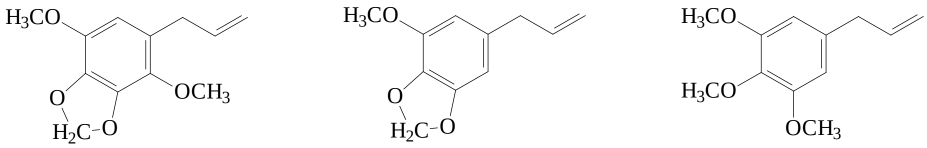
Petroselini fructus (Parsley fruit). **Other drugs:** *Petroselini radix* (Parsley root), *Petroselini aetheroleum* (Parsley oil).

The drug consists of the dried fruits of *Petroselinum crispum* (Mill.) Nym. var. *crispum*.

Figure 10.37
Petroselini fructus (Parsley fruit)

Constituents

Parsley fruits contain 2-6% of essential oil containing phenylpropane derivatives (apiol, myristicin, elemicin, allyl tetramethoxy benzene) and monoterpenes (α- and β-pinene, myrcene). Other constituents include furocoumarins (bergapten).



apiol myristicin elemicin

Figure 10.38-40
The structure of apiol, myristicin and elemicin.

Uses

The drug has spasmolytic and strong diuretic effects. The essential oil is abortive in higher doses! Patients with nephritis should not use the drug.

Dosage

Adult daily dose: 1 g of crushed drug as an infusion (200 ml).

For children the drug and its products are not recommended.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice. Because of the abortive property of the essential oil it should not be used during pregnancy.

Balsamum peruvianum

Plant

Myroxylon balsamum (L.) Harms. var. *pereirae* (Royle) Harms. – Peru balsam (Fabaceae)

The plant is cultivated in Sri Lanka and Sumatra. Peru balsam is produced in Central America (San Salvador, Honduras and Quatemala).

Drug

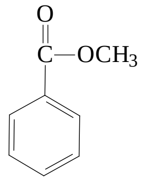
Balsamum peruvianum (Peru balsam, Ph. Eur.)

Peru balsam is the balsam obtained from the scorched and wounded trunk of *Myroxylon balsamum* (L.) Harms var. *pereirae* (Royle) Harms. It contains not less than 45.0% *m/m* and not more than 70.0% *m/m* of esters, mainly benzyl benzoate and benzyl cinnamate. A dark brown, viscous liquid which is transparent and yellowish-brown when viewed in a thin layer; the liquid is not sticky, it is non-drying and does not form threads; practically insoluble in water, freely soluble in ethanol, not miscible with fatty oils, except for castor oil.

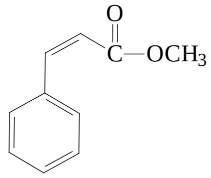
Figure 10.41
Balsamum peruvianum (Peru balsam)

Constituents

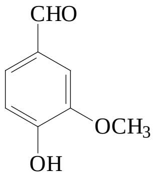
The balsam contains vanillin, benzoic acid benzyl ester, cinnamic acid benzyl ester, methyl benzoate and methyl cinnamate.



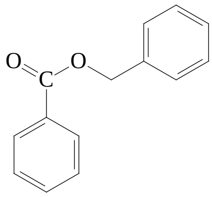
methyl benzoate



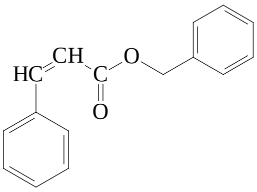
methyl cinnamate



vanillin



benzoic acid benzyl ester



cinnamic acid benzyl ester

Figure 10.42-46
The structure of benzoic acid benzyl ester, cinnamic acid benzyl ester, methyl benzoate, methyl cinnamate and vanillin.

Uses

Peru balsam is used as an antiseptic dressing for wounds, in case of freezing and ulcus cruris. Allergic skin reactions may occur.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Filipendulae ulmariae herba

Plant

Filipendula ulmaria (L.) Maxim. – Meadowsweet (Rosaceae)

The plant is native to Europe, and prefers wet habitats (e.g. meadows and slashes).

Figure 10.47
Meadowsweet [*Filipendula ulmaria* (L.) Maxim.]

Drug

Filipendulae ulmariae herba (Meadowsweet, Ph. Eur.)

The drug consists of the whole or cut, dried flowering tops of *Filipendula ulmaria* (L.) Maxim. (= *Spiraea ulmaria* L.). It contains minimum 1 ml/kg of steam-volatile substances, calculated with reference to the dried drug. It has aromatic odour of methyl salicylate, after crushing.

Figure 10.48
Filipendulae ulmariae herba (Meadowsweet)

Constituents

The drug contains glycosides of salicylaldehyde, of methyl salicylate (spiraein) and of salicyl alcohol. Steam distillation of the dried flowers yields a small amount (0.2%) of essential oil (arising from the phenolic glycosides during drying and storage), of which about 75% is salicylaldehyde. Other constituents are flavonoids (up to 6%) such as spiraeoside (quercetin-4'-glucoside), hyperoside and kaempferol-4'-glucoside. Ellagitannins (10-15%) are derived from galloyl-4,6-hexahydroxydiphenoyl-β-D-glucose units, the major one being the dimeric compound rugosin D.

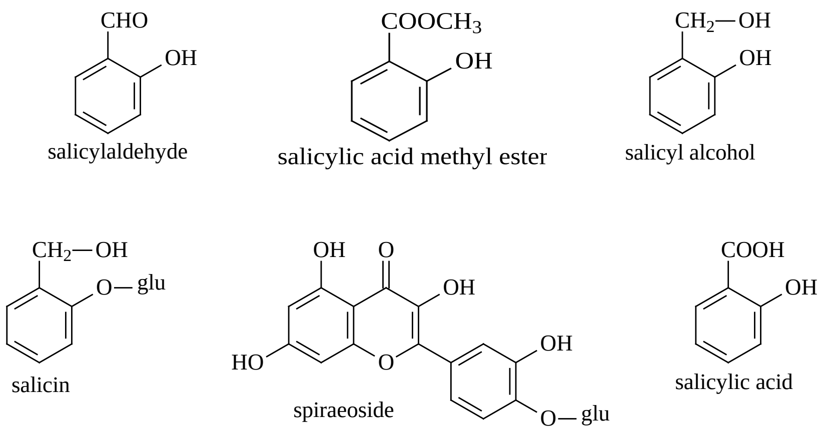


Figure 10.49-54
The structure of salicylaldehyde, salicyl alcohol, salicin, salicylic acid methyl ester and spiraeoside.

Uses

The drug is used in the supportive therapy for common cold. Meadowsweet is also used to enhance the renal elimination of water, but this indication is not supported by scientific evidence.

Dosage

The daily dose of the drug as a tea infusion:

Adults: 2-6 g, *children 1-4 years of age*: 1-2 g, *children 4-10 years of age*: 2-3 g, *children 10-16 years of age*: adult dose.

Liquid extract (1:2): 3-6 ml daily, tincture (1:5): 7-15 ml daily.

Contra-indications

The drug should not be used in cases of hypersensitivity to salicylates.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Salicis cortex

Plant

Salix alba L. or other *Salix* species – Willow (Salicaceae)

The plant is native to Europe, with a preference of wet habitats.

Figure 10.55
Willow (*Salix* sp.)

Drug

Salicis cortex (Willow bark, Ph. Eur.)

Willow bark consists of the whole or fragmented dried bark of young branches or whole dried pieces of current year twigs of various species of genus *Salix* including *S. purpurea* L., *S. daphnoides* Vill. and *S. fragilis* L. The drug contains not less than 1.5% of total salicylic derivatives, expressed as salicin, calculated with reference to the dried drug. Willow bark is markedly bitter.

Figure 10.56
Salicis cortex (Willow bark)

Constituents

The characteristic constituents are derivatives of salicin, mainly salicortin, 2'-O-acetylsalicortin and/or tremulacin. *Salix purpurea* contains 4-8% of total salicin. It also contains the chalcone isosalipurpuroside, the flavanone eriodictyol-7-glucoside and tannins.

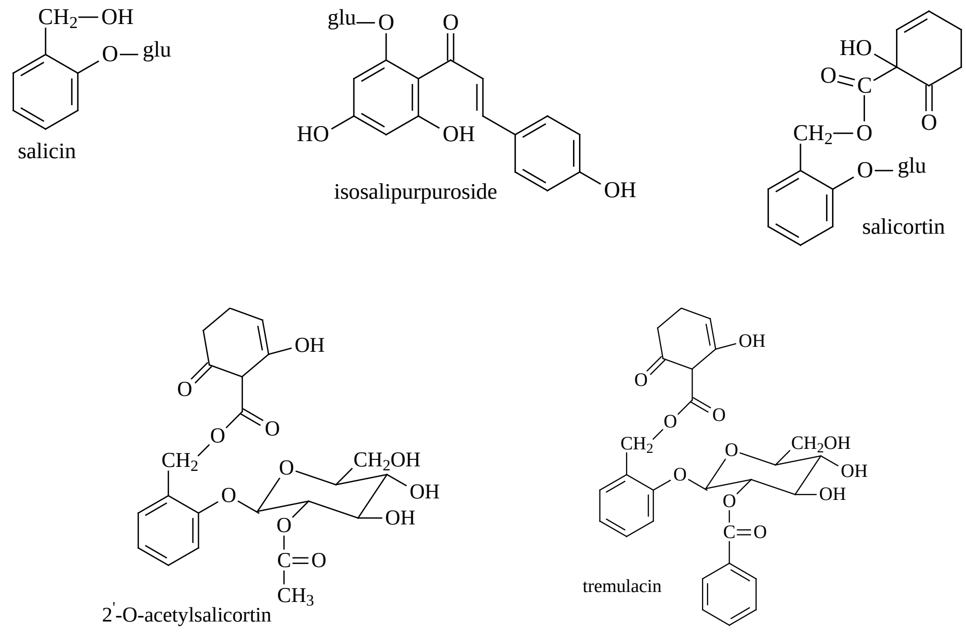


Figure 10.57-61
The structure of salicin, salicortin, 2’-O-acetylsalicortin, tremulacin and isosalipurpuroside.

Uses

Therapeutic indications of the drug include the relief of low back pain, symptomatic relief of mild osteoarthritic and rheumatic complaints.

Dosage

Adult daily dose: dried hydroalcoholic or aqueous extracts, tinctures or fluid extracts are recommended, equivalent to 120-240 mg of total salicin. The drug is not recommended for children.

Contra-indications

The drug should not be used in cases of hypersensitivity to salicylates.

Special warnings and praecautions

The treatment of children with willow bark extracts is not recommended because of the structural similarity of salicylic derivatives in willow bark to acetylsalicylic acid. The use of synthetic acetylsalicylic acid (aspirin) in children is still associated with the so-called Reye’s syndrome.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

10.2 Lignans

Lignans are dimeric compounds formed by the binding of two molecules of a phenylpropene derivative. About 300 lignans have been isolated and categorized into a number of groups according to their structural features (**Figure 10.62**). The lignans of

Podophyllum spp. are the most important pharmaceutical examples, which are formed from two molecules of coniferyl alcohol or the corresponding acid with subsequent modification. They are generally colourless, crystalline constituents. Neolignans are also derived from the same units as lignans but the C_6-C_3 moieties are linked head to tail or head to head and not through the β-β' carbons. They can be found in the heart-woods of trees of the Magnoliaceae, Lauraceae and Piperaceae. The most important biological effects of the lignans are antibacterial, antifungal, cytotoxic and antimitotic. Neolignans have antirheumatic and antiallergic actions.

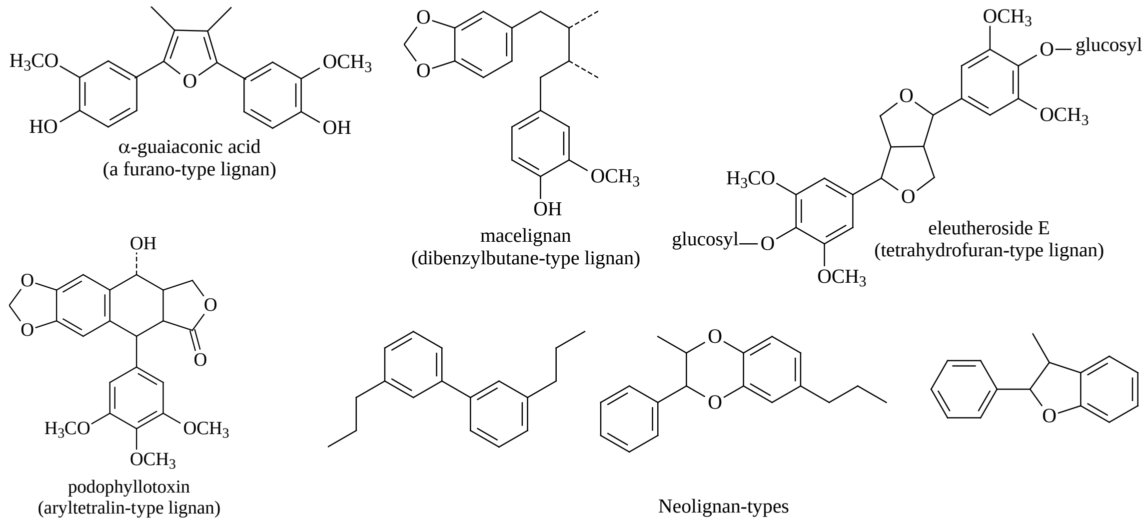


Figure 10.62
The most impotant types of lignans and neolignans in plants.

Drug

Podophylli rhizoma

Plant

Podophyllum peltatum L.– Podophyllum or May-apple (Berberidaceae)

The plant is native to North-America but it can be cultivated.

Figure 10.63
Podophyllum (*Podophyllum peltatum* L.)

Drug

Podophylli rhizoma (Podophyllum rhizome)

The drug consists of the whole or fragmented dried rhizomes of *Podophyllum peltatum* L. From the drug *Podophylli resina* is also prepared by an alcoholic extraction followed by a precipitation with diluted hydrochloric acid and drying process.

Figure 10.64
Podophylli rhizoma (Podophyllum rhizome)

Constituents

The characteristic constituents are 3-6% of resin containing lignans such as podophyllotoxin, α- and β-peltatin and other lignans. Podophyllotoxin is a highly toxic compound, therefore its semi-synthetic derivatives such as etoposide and teniposide are used in cancer therapy.

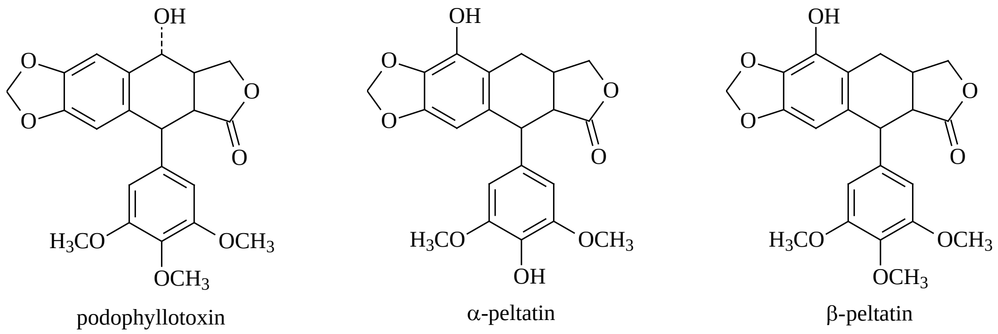


Figure 10.65-67
The structure of podophyllotoxin, α- and β-peltatin.

Uses

It was mentioned above that the semi-synthetic derivatives of podophyllotoxin are used in cancer therapy. Etoposide is currently available for the treatment of small-cell lung cancer and testicular cancer, and teniposide is used in paediatric cancers. Other podophyllotoxin-related analogues are also tested. Podophyllotoxin may be used topically, and is most effective in the treatment of venereal warts, condylomas. In these cases suspensions prepared with 25% of paraffin oil can be used.

Eleutherococci radix

Plant

Eleutherococcus senticosus (Rupr. et Maxim.) Maxim. – Eleutherococcus (Araliaceae)

This plant is native to China, East-Asia and Siberia.

Drug

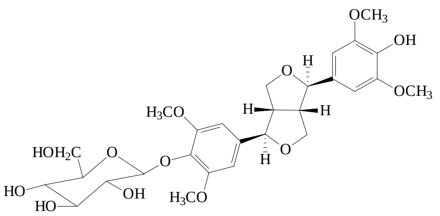
Eleutherococci radix (Eleutherococcus root, Ph. Eur.)

The drug consists of the dried, whole or cut underground organs of *Eleutherococcus senticosus* (Rupr. et Maxim.) Maxim. It contains minimum 0.08% for the sum of eleutheroside B and eleutheroside E.

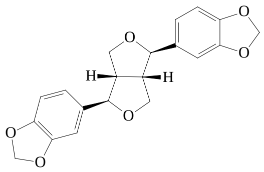
Figure 10.68
Fig. 5.99 *Eleutherococci radix* (Eleutherococcus root)

Constituents

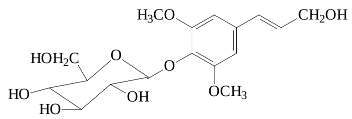
The main characteristic constituents are lignans, e.g. eleutheroside E (syringaresinol diglucoside, 0.1%) and eleutheroside B_4 (sesamin, 0.023%). Other constituents include phenylpropanoids, e.g. eleutheroside B (syringin, 0.5%), sinapyl alcohol, chlorogenic acid; coumarins, saponins (e.g. protoprimulagenin A), sterols (β-sitosterol) and polysaccharides such as glucans.



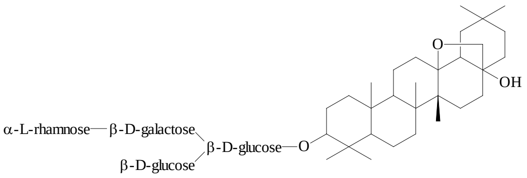
eleutheroside E_1



eleutheroside B_4



eleutheroside B



protoprimulagenin A

Figure 10.69-72
The structure of eleutheroside E, eleutheroside B_4, eleutheroside B and protoprimulagenin A.

Uses

Therapeutic indications of the drug include the treatment of decreased mental and physical capacities such as weakness, exhaustion, tiredness and loss of concentration, as well as during convalescence.

Dosage

Adults: 1-2 ml of fluid extract (1:1, ethanol 40% V/V), 1-3 times daily. 65-195 mg of dry extract (14-25:1, ethanol 40% V/V), daily. Other preparations corresponding to 2-3 g of dried root and rhizome daily.

Special warnings and precautions for use

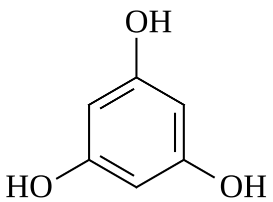
A few reports of blood pressure increase have been reported in hypertensive patients. A causal relationship to the use of the drug could not be established.

Pregnancy and lactation

No human data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

10.3 Phloroglucin derivatives

Phloroglucin derivatives rarely occur in higher plants, rather in ferns, (e.g. Polypodiaceae family). Their molecules are built up of one or more (2-4) phloroglucin „core”. They can be extracted with organic solvents (mainly ethyl ether). They have anthelminthic or sedative effect. Male fern, hop and St. John’s Wort belong to this group. The latter medicinal plant will be introduced in **Chapter 12**.



phloroglucinol

Figure 10.73
The structure of phloroglucinol.

Drugs

Filicis maris rhizoma

Plant

Dryopteris filix-mas (L.) Schott – Male fern (Dryopteridaceae)

The vermifuge properties of ferns were known to the ancients, their use being mentioned in the works of Dioskurides and Theophrastus. The plant is common all over the world. Hybridization readily occurs and the plant may be derived from *D. abbreviata* and other ferns of unknown source.

Figure 10.74
Male fern (*Dryopteris filix-mas* (L.) Schott)

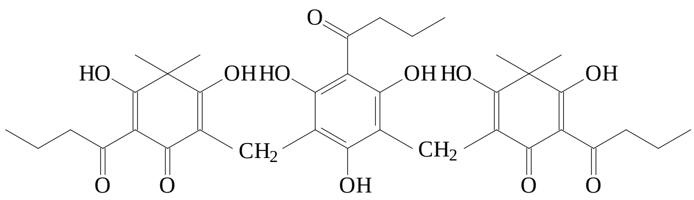
Drugs

Filicis maris rhizoma (Male fern rhizome), *Filicis maris herba* (Male fern aerial shoot)

The drug is the rhizome, the internal part of which is light green (yellowish-green). The rhizome should be dried quickly but carefully. On long-term storage the interior part becomes brown, and the amounts of active compounds decrease. The drug has slight odour and the taste is at first sweetish, afterwards becoming bitter and extremely nauseous.

Constituents

The active constituents of male fern are phloroglucinol derivatives which occur as mono-, bi-, tri- and tetracyclic compounds. Two or more molecules of the simple monocyclic derivatives such as aspidinol or filicinic acid may condense to give bicyclic compounds (e.g. albaspidin) and tricyclic ones such as filicic acid. In this compound the central phloroglucinol unit is apparently always a butyryl derivative but the other two units show great variability, and may not be identical even within a single molecule.



filicic acid

Figure 10.75
The structure of filicic acid.

Uses

Male fern, usually in the form of the oleoresin, is used as an anthelminthic drug. Its use requires care, as cases have occured in which it has been absorbed and caused blindness. Today safer drugs are available. The etheric extract of the plant may irritate the stomach and can cause nausea, therefore gelatin capsules can be used.

Dosage

Adults: approx. 6-8 g daily. Children under 4 years and elderly should not use the drug and its products.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Lupuli flos

Plant

Humulus lupulus L. – Hop (Cannabaceae)

The plant is cultivated, mostly in England, Germany, Belgium, France, Russia and California. In the Early Middle Ages the German monks started to use wild hops for brewing. Hop pillows were used to promote the onset of sleep. In Hungary the plant has been known since the 11th century.

Figure 10.76
Hop (*Humulus lupulus* L.)

Drug

Lupuli flos (Hop strobile, Ph. Eur.)

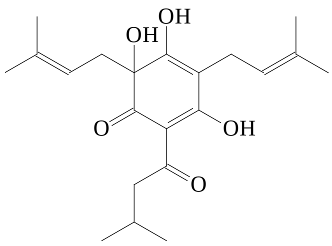
The plant is dioecious. The drug is the female inflorescence and the multiple fruit of the cultivated hop species. Female inflorescence = the flowers located in the axil of the bracts in pairs. The inside of the bracts is covered with small, glossy, light yellow glandular scales, which contain hop bitter (e.g. lupulin).

The drug consists of the dried, generally whole, female inflorescences of *Humulus lupulus* L. The aromatic scent can become unpleasant during long-term storage.

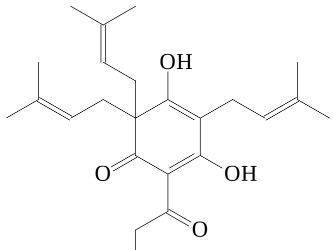
Figure 10.77
Lupuli flos (Hop strobile)

Constituents

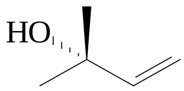
Bitter principles consisting mainly of prenylated phloroglucinol derivatives called α-acids or humulones (2-12% of dried strobile), principally humulone (35-70%), and β-acids or lupulones (1-10% of dried strobile), principally lupulone (30-55%). Other relevant constituent is essential oil (consisting mainly of myrcene, humulene and β-caryophyllene). Although only a trace of 2-methyl-3-buten-2-ol is found in the freshly-harvested drug, the amount is higher in stored material after 2 years due to degradation of humulones and lupulones. The most important flavonoids are quercetin and kaempferol glycosides, prenylated flavonoids, notably the chalcones xanthohumol (up to 1% of dried strobile and 80-90% of total flavonoids), and 8- and 6-prenylnaringenin.Other constituents include phenolic acids, tannins, polysaccharides and minerals.



humulone



lupulone



2-methyl-3-buten-2-ol

Figure 10.78-80
The structure of humulone, lupulone and 2-methyl-3-buten-2-ol.

Uses

The drug has sedative effect. The therapeutic indications include tenseness, restlessness and sleep disorders. It promotes the onset of sleep. Hop strobile is recommended by the Commission E for excitement, anxiety and sleep disorders. Because of the bitter taste the drug is an appetizer. The bactericid effect of phloroglucin derivatives has been demonstrated. The potent phyto-oestrogen of the drug is 8-prenylnaringenin. Its oestrogenic activity has also been verified.

Dosage

Internal use

Adults and children over 12 years of age: 0.5 g of the drug as an infusion, 2-4 times daily; 0.5-2 ml of liquid extract (1:1, 45% ethanol) or 1-2 ml of tincture (1:5, 60% ethanol), up to 3 times daily or other equivalent praparations. Combination with other herbal sedatives may be beneficial.

External use

Infants and young children: up to 500 g of dry hop strobile (previously stored for 1-2 years) in a hop pillow.

Side effects, Contra-indications, Interactions

The drug can increase the effects of other CNS depressants, e.g. alcohol, sedatives. In extremly high doses oestrogen-like effects may occur. Interaction may develop with hormone-containing medicines taken simultaneously.

Pregnancy and lactation

No data available. In accordance with general medical practice, hop strobile preparations should not be used internally during pregnancy and lactation without medical advice.

Chapter 11
Drugs containing coumarin derivatives

11.1 Coumarins, furanocoumarins and pyranocoumarins

Derivatives of benzo-α-pyron such as coumarin (the lactone of O-hydroxycinnamic acid), umbelliferone and scopoletin are common in plants both in the free state and as glycosides. First coumarin was isolated from tonco bean (*Dipteryx odorata*) by Vogel in 1820. In coumarins an O atom (e.g. in the form of OH or CH_3OH) links to the 7^{th} carbon atom (C-7) (**Figure 11.1**). Some 1100 natural coumarins have been isolated. Coumarin has been found in approx. 150 species belonging to over 30 different plant families. It occurs in the undamaged plant as *trans*-O-glucosyloxycinnamic acid, while in the damaged plant tissue an enzyme activity leads to a loss of glucose and *trans→cis* isomerization followed by ring closure. Coumarin emits a characteristic odour of new-mown hay. It occurs mostly in Fabaceae (e.g. sweet clover, melilot and tonco bean) family. In ammoniacal solution coumarins show blue fluorescence under UV-light.

- Furanocoumarins (e.g. marmesin, bergapten) and pyranocoumarins (e.g. visnadin) occur particularly in the Rutaceae and Apiaceae families. (**Figure 11.2**)

Coumarin derivatives can be classified as

- Non-condensed coumarins: substituted with OH or OCH_3 at positions C-6 and C-7, less commonly at C-5 and C-8. For example: umbelliferon (7-hydroxy-coumarin in Angelicae radix), scopoletin (6-methoxy-7-hydroxy-coumarin in Scopoliae radix), fraxin, izofraxidin and fraxetin in Fraxini cortex and herniarin (in Herniariae herba). C-prenylated coumarins: rutamarin (in Rutae herba), umbelliprenin (in Angelicae radix)
- Furanocoumarins: an additional furan ring is fused at C-6 and C-7 (psoralen-type) or C-7 and C-8 (angelicin-type). Some examples: imperatorin, bergapten, angelicin (in Angelicae, Imperatoriae, Pimpinellae radix), xanthotoxin (Ammi majoris fructus), psoralen (Rutae herba)
- Pyranocoumarins: an additional pyran ring is fused at C-7 and C-8 (seselin-type). For example: visnadin (Ammi majoris fructus)
- Dimeric coumarins, e.g. daphnoretin (Daphne mezerei cortex)

Coumarin and its derivatives have relevant pharmacological effects such as anticoagulant, spasmolytic, photoprotective or inducing photosensibility, antibacterial and/or antifungal and diuretic.

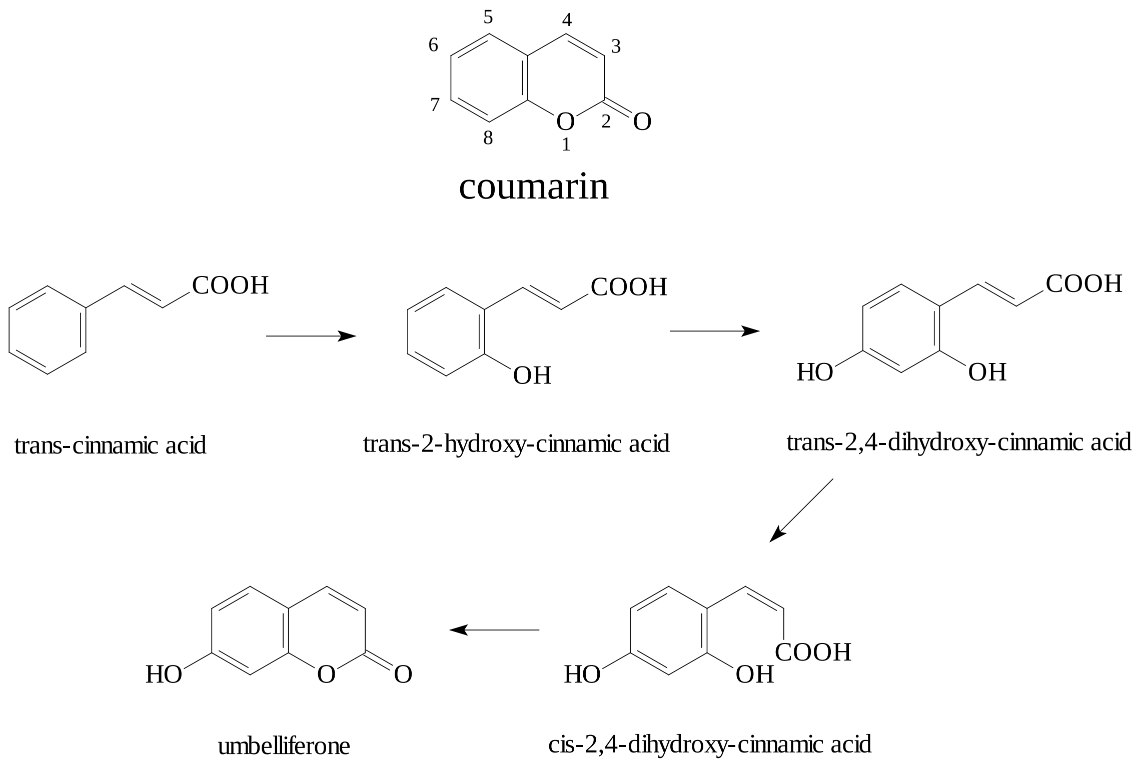


Figure 11.1
The structure of coumarin and the biosynthesis of umbelliferone from *trans*-cinnamic acid.

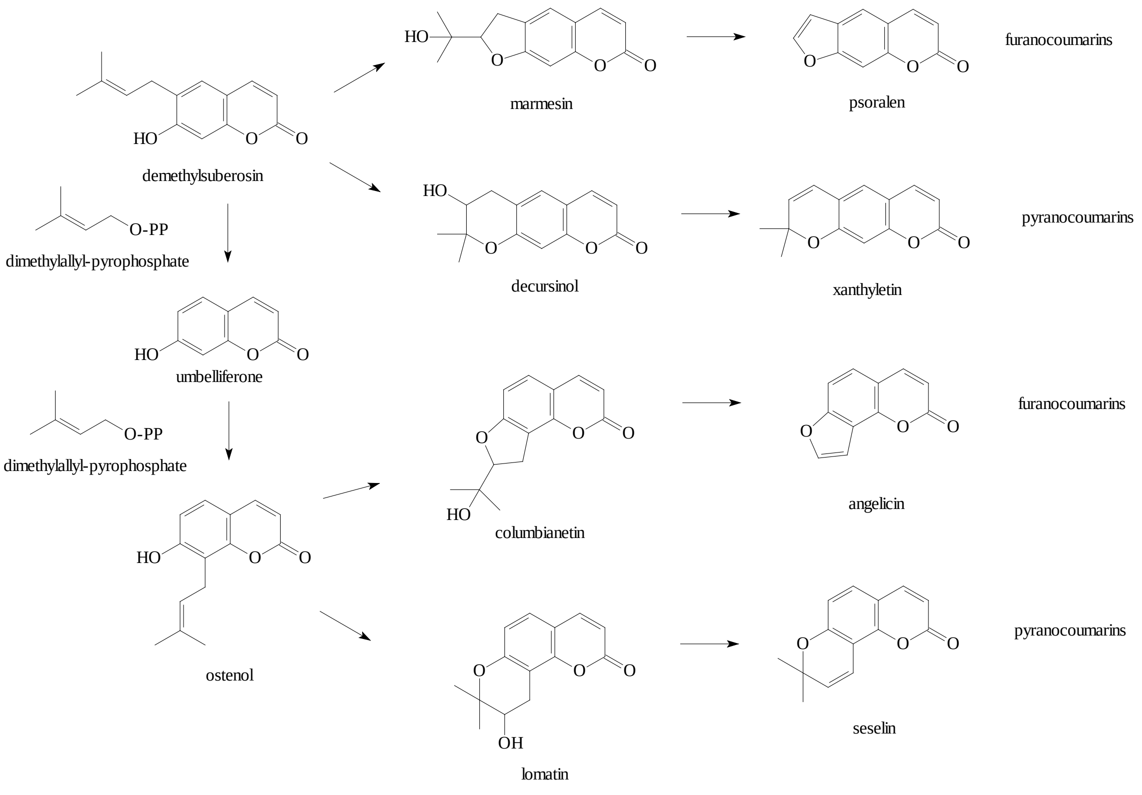


Figure 11.2
Some coumarin derivatives

Drugs

Meliloti herba

Plant

Melilotus officinalis (L.) Pall. – Melilot (Fabaceae)

The plant is native to Eurasia and introduced in North America, Africa and Australia. In Hungary it can be found at roadsides, railroads, abandoned fields and along rivers.

Figure 11.3
Melilot (*Melilotus officinalis* (L.) Pall.)

Drug

Meliloti herba (Melilot)

Melilot consists of the dried flowering tops of *Melilotus officinalis* (L.) Pall.

Figure 11.4
Meliloti herba (Melilot)

Constituents

The main characteristic constituents are coumarin, 3,4-dihydrocoumarin (melilotin), scopoletin and umbelliferone. Other constituents include flavonoids (mostly kaempferol and quercetin glycosides), triterpene saponins, phenolic acids (caffeic acid, melilotic acid = *o*-dihydrocoumaric acid) and essential oil.

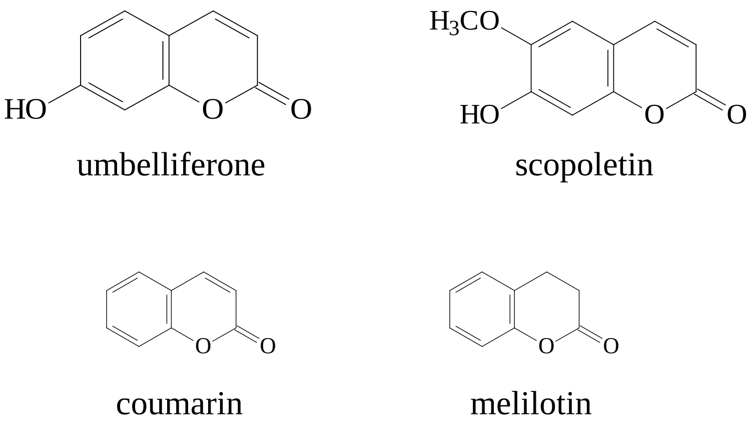


Figure 11.5-8
The structure of coumarin, 3,4-dihydrocoumarin (melilotin), scopoletin and umbelliferone.

Uses

The therapeutic indications include symptomatic treatment of problems related to varicose veins, such as painful and heavy legs, nocturnal cramps in the legs, itching and swelling. If the symptoms persist for more than 2 weeks, a doctor or a qualified health care practitioner should be consulted.

Dosage:

Internal use

Adults: Drug or preparation correcponding to 3-30 mg of coumarin daily.

External use

Extracts in semi-solid preparations.

Side effects, Contra-indications, Interactions

Hypersensitivity to the active substances may develop. If there is inflammation of the skin, thrombophlebitis, varicosis or subcutaneous induration, ulcers, sudden swelling of one or both legs, cardiac or renal insufficiency, a doctor should be consulted. Interactions between anticoagulants and Melilotus-containing medicinal products have been reported.

Pregnancy and lactation

No data available. In accordance with general medical practice, melilot and its preparations should not be used internally during pregnancy and lactation without medical advice.

Angelicae radix

Plant

Angelica archangelica L. – Angelica (Apiaceae)

Angelica archangelica grows wild in Europe (Finland, Sweden, Norway, Denmark, Hungary). It is cultivated in France, Germany and in Asia. Its appearance is similar to several poisonous species of Apiaceae (*Conium*, *Heracleum*), and should not be consumed unless it has been identified with absolute certainty.

Figure 11.9
Angelica (*Angelica archangelica* L.)

Drug

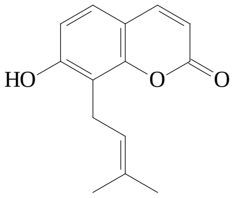
Angelicae radix (Angelica root, Ph. Eur.)

Whole or cut, carefully dried rhizome and root of *Angelica archangelica* L. (*Archangelica officinalis* Haffm.). It contains minimum 2.0 ml/kg of essential oil, calculated with reference to the dried drug. It has bitter taste.

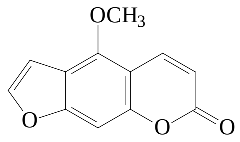
Figure 11.10
Angelicae radix (Angelica root)

Constituents

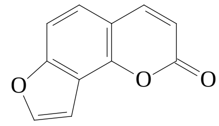
The characteristic constituents are coumarins, principally the prenylcoumarins osthenol and osthol, and further 20 furanocoumarins including bergapten, angelicin, imperatorin, isoimperatorin, xanthotoxin, psoralen and isopimpinellin. Other relevant constituents of the drug include essential oil (0.3-1.3%) containing mainly monoterpenes with small amount of sesquiterpenes; phenolic acids (caffeic and chlorogenic acids), angelic acid, fatty acids, tannins and starch.



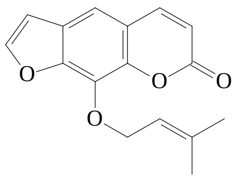
prenyl-coumarin (osthenol)



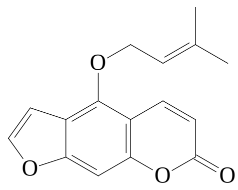
bergapten



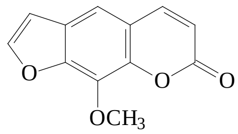
angelicin



imperatorin



isoimperatorin



xanthotoxin

Figure 11.11-16
The structure of osthenol, bergapten, angelicin, imperatorin, isoimperatorin and xanthotoxin.

Uses

The therapeutic indications include dyspeptic complaints such as mild gastrointestinal spasms, sluggish digestion, flatulence and feeling of fullness, lack of appetite, anorexia and bronchitis.

Dosage

Adult and elderly daily dose: 3-6 g of the drug, or as an infusion, 1-6 ml of liquid extract (1:1 in 25% ethanol), 1-6 ml of tincture (1:5 in 50% ethanol) divided into three doses.

Children over 4 years, average daily dose: 4-10 years of age, 2-3 g; 10-16 years of age, 3-4 g.

Special warnings and special precautions for use

Prolonged exposure to sunlight should be avoided during taking angelica root since skin photosensitization is possible due to the presence of furanocoumarins.

Pregnancy and lactation

No data available. In accordance with general medical practice, angelica and its preparations should not be used internally during pregnancy and lactation without medical advice.

Ammi visnagae fructus

Plant

Ammi visnaga (L.) Lam. – Bisnaga (Apiaceae)

The plant is native to the Mediterranean region, Asia, Argentina, Chile and Mexico.

Figure 11.17
Bisnaga (*Ammi visnaga* (L.) Lam.)

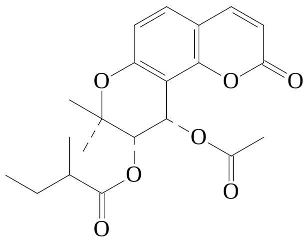
Drug

Ammi visnagae fructus (Bisnaga fruit)

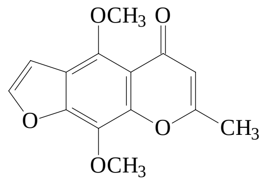
The drug consists of the ripe, dried seeds of *Ammi visnaga* (L.) Lam.

Constituents

The characteristic constituents are 2-4% of furanocoumarins (khellin), 0.2-0.5% of pyranocoumarins (visnadin). Other constituents include flavonoids, essential oil, fatty oil and proteins.



khellin



visnadin

Figure 11.18-19
The structure of khellin and visnadin.

Uses

Furano- and pyranocoumarins are used in the pharmaceutical industry as smooth muscle relaxant compounds. Visnadin is a coronary artery vasodilator. Khellin can be used in the treatment of asthma.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used internally during pregnancy and lactation without medical advice.

Ammi majoris fructus

Plant

Ammi majus L.– Ammi (Apiaceae)

The plant is native to the Mediterranean region, West Asia and Caucasus.

Drug

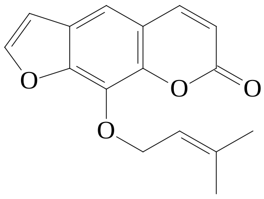
Ammi majoris fructus (Ammi fruit)

The drug consists of the ripe, dried seeds of *Ammi majus* L.

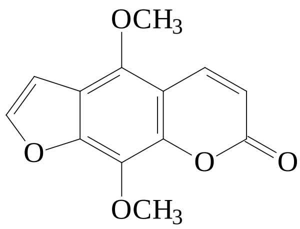
Figure 11.20
Ammi majoris fructus (Ammi fruit)

Constituents

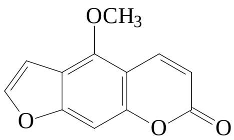
The characteristic constituents are furanocoumarins (xanthotoxin, imperatorin, bergapten and isopimpinellin). Other constituents include flavonoids, essential oil, fatty oil and proteins.



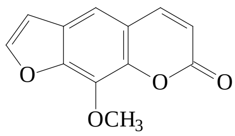
imperatorin



isopimpinellin



bergapten



xanthotoxin

Figure 11.21-24
The structure of xanthotoxin, imperatorin, bergapten and isopimpinellin.

Uses

Furanocoumarins are used as smooth muscle relaxant compounds. In dermatology xanthotoxin can be used for treatment of vitiligo (leucoderma), psoriasis (consultation with medical doctor is recommended).

Special warnings and special precautions for use

Prolonged exposure to sunlight should be avoided since skin photosensitization is possible due to the presence of furanocoumarins.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used internally during pregnancy and lactation without medical advice.

Levistici radix

Plant

Levisticum officinale Koch – Lovage (Apiaceae)

The plant is native to West Asia (Iran) and South Europe. In Hungary it can be cultivated.

Figure 11.25
Lovage (*Levisticum officinale* Koch)

Drug

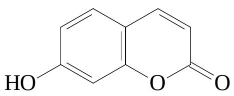
Levistici radix (Lovage root, Ph. Eur.)

The drug consists of the whole or cut, dried rhizome and root of *Levisticum officinale* Koch. It contains minimum 4.0 ml/kg of essential oil for the whole drug and minimum 3.0 ml/kg of essential oil for the cut drug (dried drug).

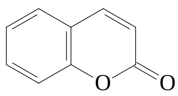
Figure 11.26
Levistici radix (Lovage root)

Constituents

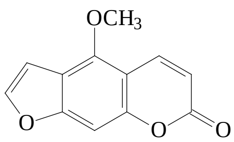
The characteristic constituents of the drug are coumarins (e.g. coumarin, umbelliferon) and furanocoumarins (bergapten and psoralen), and some essential oil (0.6-1%).



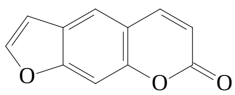
umbelliferon



coumarin



bergapten



psoralen

Figure 11.27-30
The structure of coumarin, umbelliferon, bergapten and psoralen.

Uses

Traditional herbal medicinal product used to increase the amount of urine to achieve flushing of the urinary tract as an adjuvant in minor urinary complaints. The drug has diuretic effect.

Dosage

Adults and elderly

As a herbal tea

Single dose: 2-3 g of comminuted herbal substance in 150 ml of boiling water as a herbal infusion, twice daily. Average daily dose: 4-6 g.

The use in children and adolescents under 18 years of age is not recommended. Duration of use: not to be used for more than 2-4 weeks.

If the symptoms persist during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.

Contra-indication

Hypersensitivity to the active substance and to other plants of the Apiaceae family or to *trans*-anethole may develop.

Special warnings and special precautions for use

The use in children and adolescents under 18 years of age is not recommended because of concerns requiring medical advice. If complaints or symptoms such as fever, dysuria, spams, or blood in urine occur during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted. Prolonged exposure to sunlight should be avoided since skin photosensitization is possible due to the presence of furanocoumarins.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

Apii fructus

Plant

Apium graveolens L. – Celery (Apiaceae)

The plant is cultivated all over the world.

Figure 11.31
Celery (*Apium graveolens* L.)

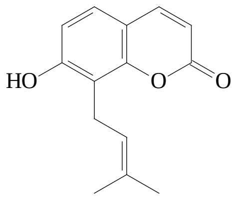
Drug

Apii fructus (Celery fruit)

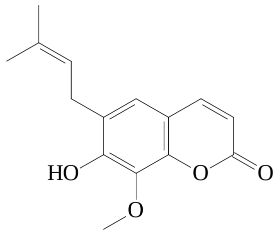
The drug consists of the whole and ripe fruits of *Apium graveolens* L.

Constituents

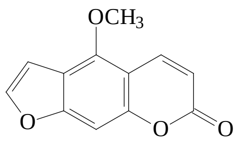
The characteristic constituents of the drug are coumarins, furanocoumarins (e.g. bergapten, isopimpinellin) and prenyl-coumarins (e.g. ostenol, apigravin). Other constituents include essential oil (2-3%) and fatty oil.



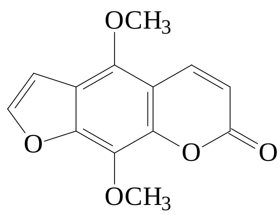
ostenol



apigravin



bergapten



isopimpinellin

Figure 11.32-35
The structure of bergapten, isopimpinellin, ostenol and apigravin.

Uses

Traditional herbal medicinal product used to increase the amount of urine to achieve flushing of the urinary tract as an adjuvant in minor urinary complaints. The drug has diuretic effect. The drug has long-standing use in the treatment of rheumatic diseases.

Dosage

Adults and elderly

As a herbal tea

Single dose: 2-3 g of comminuted herbal substance in 150 ml of boiling water as a herbal infusion, twice daily. Average daily dose: 4-6 g.

The use in children and adolescents under 18 years of age is not recommended. Duration of use: not to be used for more than 2-4 weeks.

If the symptoms persist during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.

Contra-indication

Hypersensitivity to the active substance and to other plants of the Apiaceae family. Patients with nephritis must not use the drug and its preparations.

Special warnings and special precautions for use

The use in children and adolescents under 18 years of age is not recommended because of concerns requiring medical advice. If complaints or symptoms such as fever, dysuria, spams, or blood in urine occur during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted. Prolonged exposure to sunlight should be avoided since skin photosensitization is possible due to the presence of furanocoumarins.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

Chapter 12
Drugs containing anthraquinone and naphthoquinone derivatives

In this chapter quinone, naphthoquinone, anthraquinone, dianthrone and naphthodianthrone derivatives will be introduced.

Quinones are a class of organic compounds that are formally derived from aromatic compounds (such as benzene or naphthalene) by conversion of an even number of –CH= groups into –C(=O)– groups with any necessary rearrangement of double bonds, resulting in a fully conjugated cyclic dione structure. The class includes some heterocyclic compounds. The typical member of the class is 1,4-benzoquinone, often simply called quinone. Other important examples are 1,4-naphthoquinone and 9,10-anthraquinone (**Figure 12.1**). Quinones are oxidized derivatives of aromatic compounds and are often readily made from reactive aromatic compounds with electron-donating substituents such as phenols and catechols, which increase the nucleophilicity of the ring and contribute to the large redox potential needed to break aromaticity. (Quinones are conjugated but not aromatic). Quinones are electrophilic Michael acceptors stabilised by conjugation. Depending on the quinone and the site of reduction, reduction can either rearomatise the compound or break the conjugation. Conjugate addition nearly always breaks the conjugation.

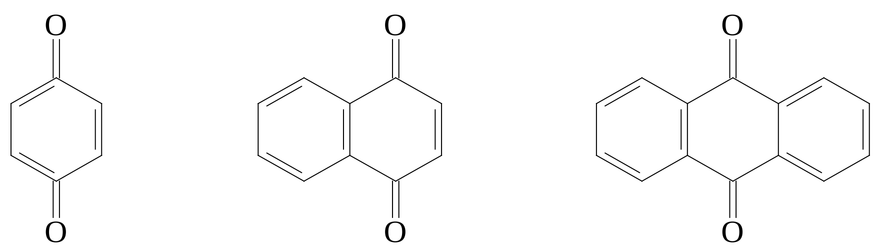


Figure 12.1
The structure of quinone, 1,4-naphthoquinone and 9,10-anthraquinone.

12.1 Quinone derivatives

Drugs

Uvae ursi folium

Plant

Arctostaphylos uva-ursi (L.) Spreng. – Bearberry (Ericaceae)

The plant is a small evergreen shrub found in central and northern Europe and in North America.

Figure 12.2
Bearberry (*Arctostaphylos uva-ursi* (L.) Spreng.)

Drug

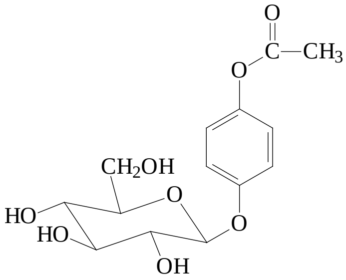
Uvae ursi folium (Bearberry leaf, Ph. Eur.)

Bearberry leaf consists of the whole or cut, dried leaf of *Arctostaphylos uva-ursi* (L.) Spreng. It contains minimum 7.0% of anhydrous arbutin calculated with reference to the dried drug.

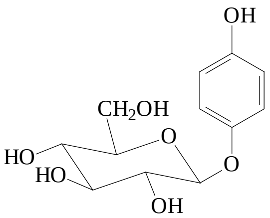
Figure 12.3
Uvae ursi folium (Bearberry leaf)

Constituents

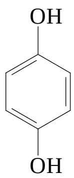
The main characteristic constituents of the drug are arbutin (5-15%), methylarbutin (up to 4%), piceosid, small amounts of the free aglycones hydroquinone and methylhydroquinone. Other constituents include gallic acid and gallotannins (up to 20%), flavonoids and triterpenes (mainly ursolic acid and uvaol).



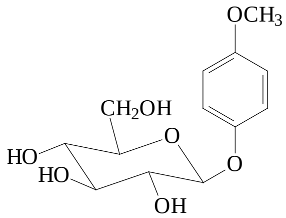
piceosid



arbutin



hydroquinone



methylarbutin

Figure 12.4-7
The structure of arbutin, methylarbutin, piceosid and hydroquinone.

Uses

Therapeutic indications include the uncomplicated infections of the lower urinary tract such as cystitis, when antibiotic treatment is not considered essential.

Dosage

Adults and elderly: cold water maceration of the dried leaves corresponding to 400-800 mg of arbutin daily, divided into 2-3 doses or equivalent preparations. The daily dose of the drug is 3 g daily.

Patients should be advised to consume plenty of liquid during the treatment. Alkalinization of the urine may be beneficial. Treatment should be continued until complete disappearance of symptoms (up to a max. of 2 weeks). If the symptoms worsen during the first week of treatment medical advice should be sought.

Not recommended for children.

Contra-indication

Patients with kidney disorders must not use the drug and its preparations.

Special warnings and special precautions for use

The amount of free hydroquinone in bearberry leaf preparations should be controlled. Hydroquinone is a topical irritant and a hepatotoxin, oral ingestion of 5-12 g has been fatal. Long term external application of creams containing up to 10% of hydroquinone has caused skin colloid degeneration (ochronosis).

Undesirable effects

Nausea and vomiting may occur due to stomach irritation from the high tannin content of the drug.

Interaction

Concomitant acidification of the urine (by other remedies) may result in a reduction of efficacy.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

Vitis idaeae folium

Plant

Vaccinium vitis-idaea L. – Cowberry/Lingonberry (Ericaceae)

The plant is a short shrub and native to boreal forests and the Arctic tundra throughout the Northern Hemisphere from Eurasia to North America.

Figure 12.8
Cowberry (*Vaccinium vitis-idaea* L.)

Drug

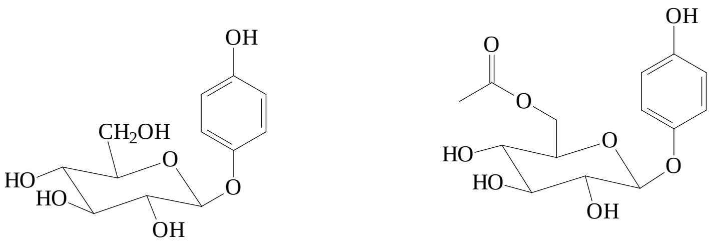
Vitis idaeae folium (Cowberry leaf)

Cowberry leaf consists of the whole or cut, dried leaf of *Vaccinium vitis-idaea* L.

Figure 12.9
Vitis idaeae folium (Cowberry leaf)

Constituents

The main characteristic constituents of the drug are arbutin (3-8%), 6'-O-acetyl-arbutin, and small amounts of the free aglycone hydroquinone. Other constituents include tannins (catechins) and flavonoids.



arbutin 6'-O-acetyl-arbutin

Figure 12.10-11
The structure of arbutin and 6'-O-acetyl-arbutin.

Uses

Therapeutic indications include the uncomplicated infections of the lower urinary tract such as cystitis, when antibiotic treatment is not considered essential.

Dosage

Adults and elderly: cold water maceration of the dried leaves corresponding to 400-800 mg of arbutin daily, divided into 2-3 doses or equivalent preparations.

Patients should be advised to consume plenty of liquid during the treatment.

This drug is safer than bearberry leaf because of lower amount of tannins.

Contra-indication

Patients with kidney disorders must not use the drug and its preparations.

Special warnings and special precautions for use

The amount of free hydroquinone in the leaf preparations should be controlled. Hydroquinone is a topical irritant and a hepatotoxin, oral ingestion of 5-12 g has been fatal.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

12.2 Naphthoquinone derivatives

Naphthoquinones are a class of organic compounds derived from naphthalene. Several isomeric naphthoquinones are known [1,2-naphthoquinone, 1,4-naphthoquinone (= para-naphthoquinone)]. 1,4-naphthoquinone forms volatile yellow triclinic crystals and has a sharp odor reminiscent of benzoquinone. It is almost insoluble in cold water, slightly soluble in petroleum ether, and more soluble in polar organic solvents. In alkaline solutions it produces a reddish-brown color. Vitamin K is a derivative of 1,4-naphthoquinone. Naphthoquinones are produced by higher plants, fungi and Actinomycetes bacteria and have significant biological actions including antibacterial, fungicidal, insecticidal, cytostatic and anticarcinogenic. They have been shown to be biosynthesized via a variety of pathways including acetate and malonate (e.g. plumbagin), shikimate/succinyl CoA combined pathway (e.g. lawsone) and shikimate/mevalonate combined pathway (e.g. alkannin) (**Figure 12.12**). In plants they occur in reduced or glycosidic form. Juglone (5-hydroxy-1,4-naphthalenedione) is one of the most relevant constituents in the group of naphthoquinones. It occurs naturally in the leaves, roots, husks, and bark of plants in the Juglandaceae family, particularly the black walnut (*Juglans nigra*), and is toxic or growth-stunting to many types of plants. It is sometimes used as a herbicide, as a dye for cloth and inks, and as a coloring agent in foods and cosmetics. Juglone is an example of allelopathic compounds, a substance that is synthesized by one type of plant and affects the growth of another.

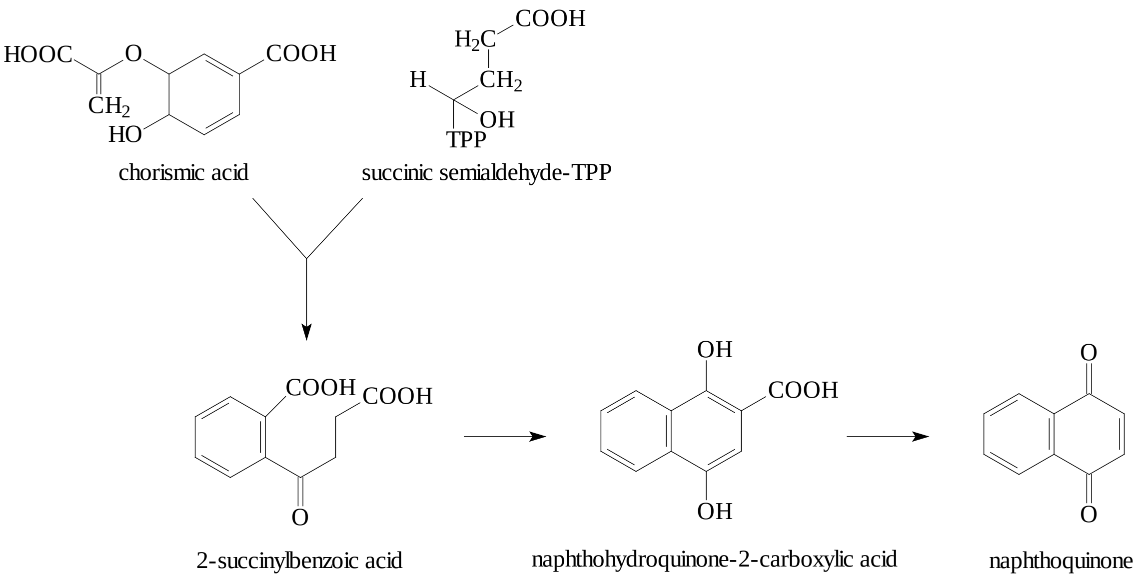


Figure 12.12
Biosynthesis of naphthoquinone.

Drugs

Juglandis folium

Plant

Juglans regia L. – Common walnut (Juglandaceae)

The plant is native to the region stretching from the Balkans eastward to the Himalayas and southwest China. *Juglans regia* is a large, deciduous tree attaining heights of 25–35 m, and a trunk up to 2 m diameter.

Figure 12.13
Common walnut (*Juglans regia* L.)

Drug

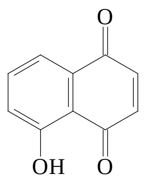
Juglandis folium (Walnut leaf)

Walnut leaf consists of the whole or cut, dried leaf of *Juglans regia* L. When the leaves become dark it means that the drug cannot be used for making preparations.

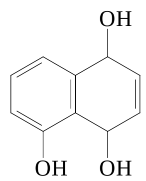
Figure 12.14
Juglandis folium (Walnut leaf)

Constituents

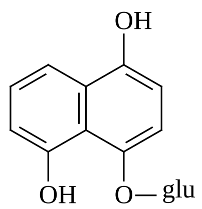
The main characteristic constituents of the drug are the naphthoquinone derivatives juglone**,** hydrojuglone and hydrojuglone glycoside. Other constituents include 10% of tannins, mainly ellagitannins, flavonoids (hiperoside, quercetine and kaempferol glycosides), phenolcarboxylic acids (e.g. caffeic acid) and 0.01-0.03% of essential oil (with β-caryophyllene, germacrene D, ocimene).



juglone



hydrojuglone



hydrojuglone glucoside

Figure 12.15-17
The structure of juglone, hydrojuglone and hydrojuglone glycoside.

Uses

Its products are traditional herbal medicinal products for use in the specified indications exclusively based upon long-standing use. Therapeutic indications of walnut leaf include the relief of minor inflammatory conditions of the skin and its medicinal products are used in excessive perspiration of hands and feet.

Dosage

Relief of minor inflammatory conditions of the skin

Adults and elderly: 4-6 g of the comminuted herbal substance in 200 ml of boiling water as a decoction. Apply as an impregnated dressing to the affected areas of the skin 2 -4 times daily.

In the case of excessive perspiration of hands and feet

Adults and elderly: 4-6 g of the comminuted herbal substance in 200 ml of boiling water as a decoction. Apply as an impregnated dressing to the affected areas of the skin up to 30 minutes twice daily. The use in children and adolescents under 18 years of age is not recommended because of lack of adequate data.

Duration of use: not to be used for more than 1 week.

Contra-indication

Hypersensitivity to the active substance may occur. Patients with open wounds and large skin injuries must not use the drug and its preparations.

Pregnancy and lactation

Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

Alkannae radix

Plant

Alkanna tinctoria (L.) Tausch. – Alkanet (Boraginaceae)

The plant is found in Hungary, southern Europe and Turkey. It can be found on calciferous ground and sandy soil. In Hungary it is a protected plant. The leaves have whitish, bristly hairs.

Figure 12.18
Alkanet (*Alkanna tinctoria* (L.) Tausch.)

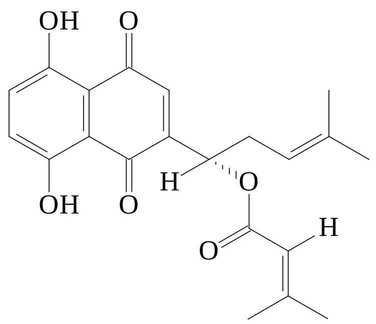
Drug

Alkannae radix (Alkanet root)

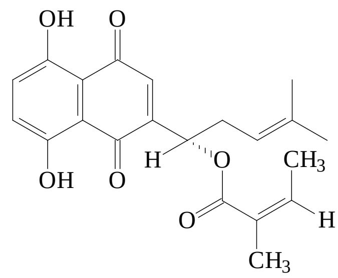
It consists of reddish-purple roots about 10-15 cm long and 1-2 cm diameter. The surface is deeply fissured and readily exfoliates.

Constituents

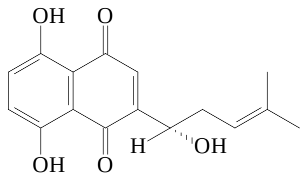
The main characteristic constituents of the drug are naphthoquinone derivatives, 5-6% of alkannin (a natural red dye) and alkannin esters. Other constituents include pyrrolizidine alkaloids.



alkannin-β,β-dimethylacrylate



alkannin isovalerate



alkannin

Figure 12.19-21

The structure of alkannin, alkannin-*β,β*-dimethylacrylate and alkannin isovalerate.

Uses

Alkannin and its derivatives have antibacterial and antifungal effects. Therapeutic indications include the relief of inflammatory conditions of the skin, e.g. ulcus cruris. Cosmetic industry uses the drug as a natural dye in colouring oils and eye-shadow. In the form of a tincture it is used for the microscopical detection of oils and fats. Because of its pyrrolizidine alkaloid content the drug and its preparations can only be applied externally.

Dosage

Adults and elderly: 4-5 g of the comminuted herbal substance in 150 ml of boiling water as an infusion. Apply as an impregnated dressing to the affected areas of the skin 2-4 times daily. In ointment: 5-10 g of aqueous or ethanolic extract of the drug in 100 g.

Contra-indication

Hypersensitivity to the active substance may occur. Patients with open wounds and large skin injuries must not use the drug and its preparations.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

Droserae herba

Plants

Drosera rotundifolia L., *D. ramentacea* Burch. ex. Harv. et Sond, *Drosera* sp. – Drosera, Sundews (Droseraceae)

Drosera, commonly known as the sundews, comprise one of the largest genera of carnivorous plants, with at least 194 species. These members of the family Droseraceae attract, capture, and digest insects using stalked mucilaginous glands covering their leaf surfaces. The insects are used to supplement the poor mineral nutrition of the soil in which they grow. Various species, which vary greatly in size and form, can be found growing natively on every continent except Antarctica. Sundews generally grow in seasonally moist or more rarely constantly wet habitats with acidic soils and high levels of sunlight. Common habitats include bogs, fens, swamps and marshes. Many species grow in association with sphagnum moss, which absorbs much of the soil's nutrient supply and also acidifies the soil, making nutrients less available to other plants. The plant is found in Hungary, but it is strictly protected. It can also be cultivated (e.g. in Finland).

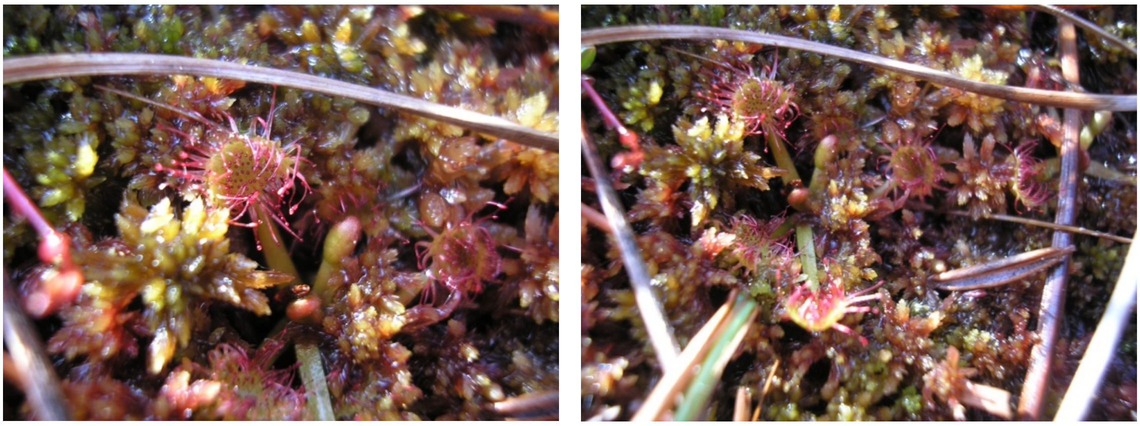


Figure 12.22
Sundew (*Drosera rotundifolia* L.)

Drug

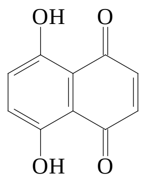
Droserae herba (Sundew herb)

Sundew consists of the dried above- and below-ground parts of *Drosera rotundifolia* L., *D. ramentacea* Burch. ex. Harv. et Sond, *D. longifolia* L., *D. intermedia* Hayne and other *Drosera* species. The herb contains 0.1-0.2% of naphthoquinone derivatives calculated as juglone in respect to the dry mass of the herb.

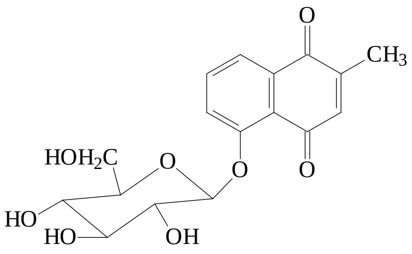
Figure 12.23
Droserae herba (Sundew herb)

Constituents

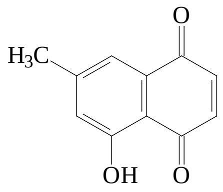
The main characteristic constituents of the drug are naphthoquinone derivatives such as plumbagin, plumbagin-5-O-glucoside, ramenton, ramentaceon and rossoliside (7-methyl-hydrojuglone-4-O-β-D-glucoside). Other constituents include flavonoids, mucilage and proteolytic enzymes.



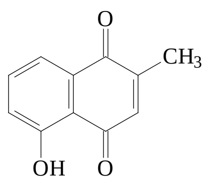
ramenton



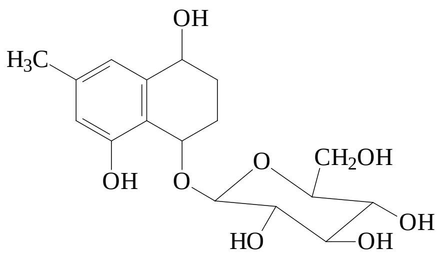
plumbagin-5-O-glucoside



ramentaceon



plumbagin



rossoliside (7-methyl-hydrojuglone-4-O-β-D-glucoside)

Figure 12.24-28

The structure of plumbagin, plumbagin-5-O-glucoside, ramenton, ramentaceon and rossoliside (7-methyl-hydrojuglone-4-O-β-D-glucoside).

Uses

The drug and its preparations have antibacterial, bronchoantispasmodic and antitussive activities. Therapeutic indications include the relief of inflammatory conditions of the respiratory tract, e.g. bronchitis, pharyngitis and laryngitis.

Dosage

Adults and elderly: 1 g of the comminuted herb in 200 ml of boiling water as an infusion, 2-3 times daily. 3 g is the daily dose.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

Lawsoniae folium

Plant

Lawsonia inermis L. – Henna (Lythraceae)

Henna is a tall shrub or small tree, 2.6 m high. The henna plant is native to tropical and subtropical regions of Africa, southern Asia, and northern Australasia in semi-arid zones.

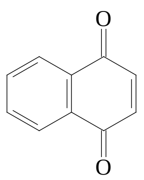
Drug

Lawsoniae folium (Henna leaf)

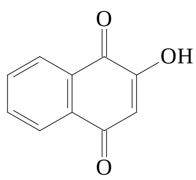
Henna consists of the dried leaves of *Lawsonia inermis* L. The leaves are greenish-brown to brown and about 2.5-5 cm long.

Constituents

The main characteristic constituents of the drug are naphthoquinone derivatives such as 1,4-naphthoquinone and 2-hydroxy-1,4-naphthoquinone (lawsone). Other constituents include phenolic glycosides, coumarins, xanthones, flavonoids (mainly luteolin and its 7-O-glucoside) and tannins.



1,4-naphthoquinone



2-hydroxy-1,4-naphthoquinone (lawsone)

Figure 12.29-30
The structure of 1,4-naphthoquinone and 2-hydroxy-1,4-naphthoquinone (lawsone).

Uses

Henna is commonly used as a dye for the hair, and wool washed in a dilute solution of ammonia and boiled in a decoction of the drug should be dyed Titian red. Because of tannin content, the drug can be used for treating burns, wounds and fungal infections of the skin.

The adstringent stem-bark of L. *inermis* is traditionally used in India for the treatment of jaundice, enlargement of the liver and spleen, and for various skin diseases.

Dosage

Adults and elderly: 1 g of the comminuted herb in 200 ml of boiling water as an infusion, 2-3 times daily. For External use 3 g of the drug, daily. Prolonged use of the drug is not recommended for internal purposes.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice.

12.3 Anthraquinone derivatives

Substances of the anthraquinone type may occur both in free state and as glycosides. Natural compounds also contain reduced derivatives of the anthraquinones (oxanthrones, anthranols and anthrones) and compounds formed by the union of two anthrone molecules (**Figure 12.31**).

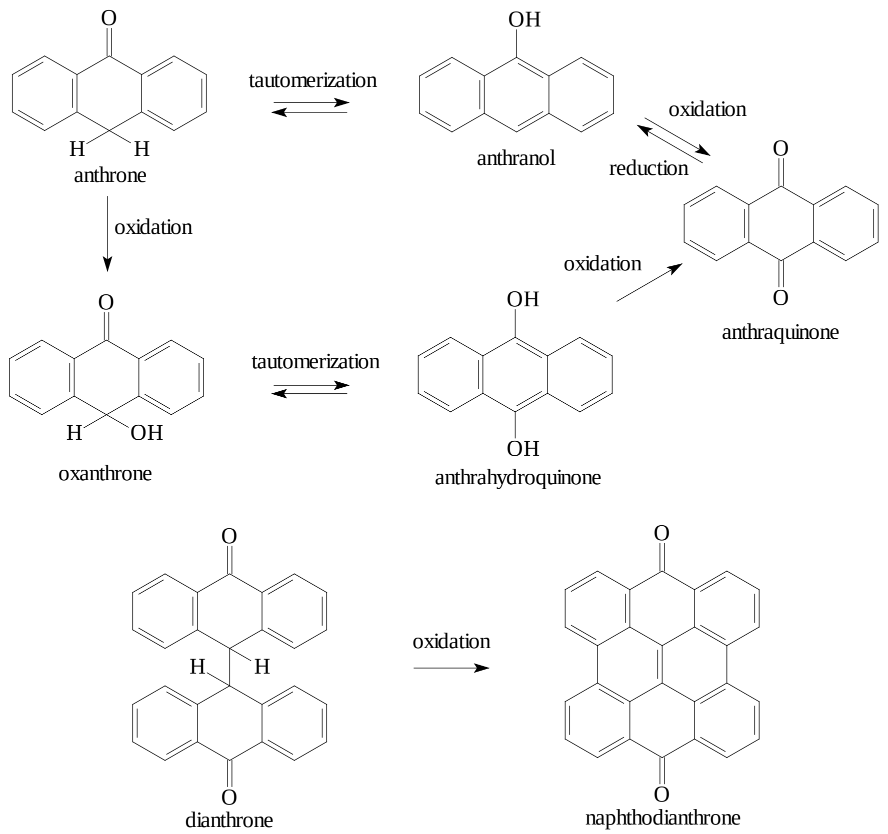


Figure 12.31
Interrelationship of anthraquinone derivatives.

Anthraquinone glycosides are often easily hydrolysed. The following aglycones have long been established: chrysophanol (from rhubarb and cascara), aloe-emodin (from rhubarb and senna), rhein (from rhubarb and senna), emodin (from frangula and cascara) and physcion (from frangula and cascara) (**Figure 12.32**).

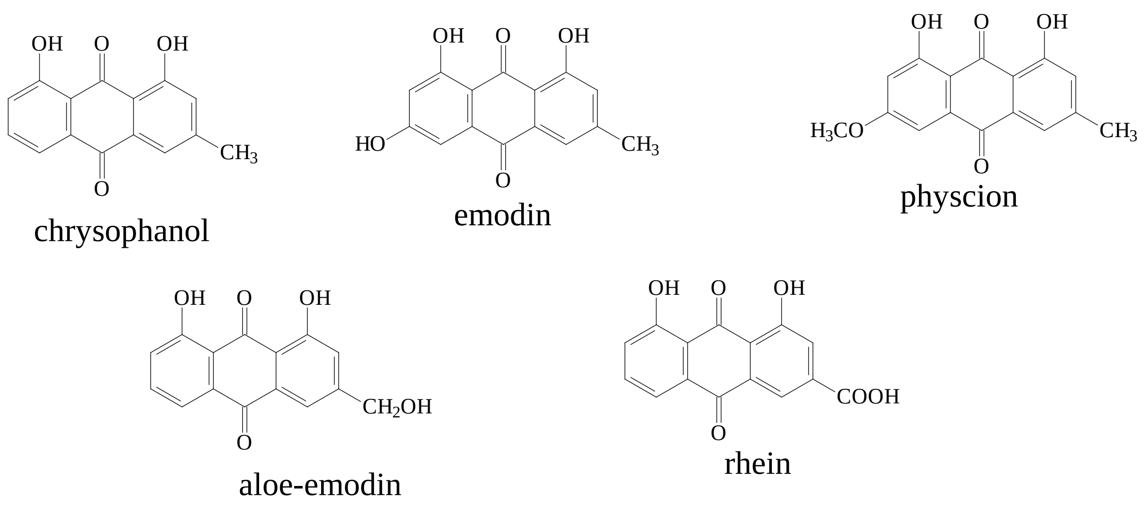


Figure 12.32
The main anthraquinone aglycones.

In monocotyledons, anthraquinone derivatives are found only in the Liliaceae, in the form of C-glycosides (e.g. barbaloin). Among dicotyledons they occur in the Rubiaceae, Polygonaceae, Rhamnaceae, Ericaceae, Euphorbiaceae and Scrophulariaceae. Anthraquinones are either synthetized via the acetate-mevanolate pathway or they are derived from shikimate and mevalonate. The medicinally important purgative anthraquinones are formed by this way and all have 1,8-dihydroxy substitution. In their structure there is a –OH group at a C-6 position, and its oxydated forms (-CH_2OH, -COOH) are at C-3 position.

Anthraquinone derivatives are often orange-red compounds. They are usually soluble in hot water or dilute alcohol. Bornträger's test is often used for their detection (the free anthraquinone-derivatives (aglycones = 1,8-dihydroxy-anthraquinone derivatives) can be extracted with chloroform and separated with aqueous-base (ammonia) solution. The aqueous layer becomes reddish). Anthranol and anthrone derivatives are isomeric and one may be partially converted to the other in solution. Anthrone is a pale yellow, nonfluorescent substance, which is insoluble in alkali. Its isomer, anthranol, is a brownish-yellow compound and forms a strongly fluorescent solution in alkali. Anthranol derivatives, for example aloin, show green fluorescence in borax or other alkaline solutions (Schouteten reaction). Anthraquinones can be found in a variety of forms in plants. It depends on the plant species, the part of the plant (the drug), the developmental stage of the plant, the method of drying and storage.

Anthraquinone derivatives have laxative activity. Anthrones and dianthrones are the most effective substances. The action of the compounds is restricted to the large bowel (hence their effect is delayed up to 6 h or longer). It has been suggested that anthraquinone derivatives influence the ion transport across colon cells by inhibition of Cl^- channels.

Drugs

Frangulae cortex

Plant

Rhamnus frangula L. – Frangula (Alder buckthorn) (Rhamnaceae)

The plant is a tall deciduous shrub. It is native to Europe, northernmost Africa, and western Asia, from Ireland and Great Britain north to Scandinavia, east to central Siberia and in western China, and south to northern Morocco, Turkey, and in the Caucasus Mountains. It is also introduced in eastern North America. Its ripe, black fruits and fresh bark are poisonous.

Drug

Frangulae cortex (Frangula bark, Ph. Eur.). **Other Drug** *Frangulae corticis extractum siccum normatum* (Frangula bark dry extract, standardised, Ph. Eur.)

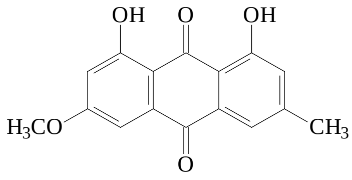
Frangula bark consists of the dried, whole or fragmented bark of the stems and branches of *Rhamnus frangula* L. (*Frangula alnus* Miller). It contains not less than 7.0% of glucofrangulins, expressed as glucofrangulin A and calculated with reference to the dried drug. Bark for medicinal use is dried and stored for a year before use, as fresh bark is violently purgative and its high amounts of anthrones and anthranoles are responsible for spasms in the bowel.

Standardised frangula bark dry extract is produced from *Frangula bark*. It contains not less than 15.0% and not more than 30.0% of glucofrangulins, expressed as glucofrangulin A and calculated with reference to the dried extract. The measured content should not deviate from that stated on the label by more than ± 10%. The extract is produced from the drug and ethanol (50 to 80 per cent *V/V*) by an appropriate procedure. It's a yellowish-brown, fine powder.

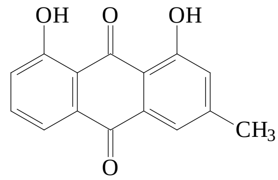
Figure 12.33
Frangulae cortex (Frangula bark)

Constituents

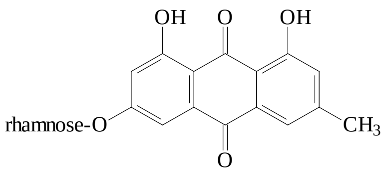
The main characteristic constituents of the dried bark are glucofrangulin A and B (emodin-6-O-α-L-rhamnosyl-8-O-β-D-glucoside and emodin-6-O-β-D-apiosyl-8-O-β-D-glucoside respectively), frangulin A, B and C (emodin-6-O-α-L-rhamnoside, emodin-6-O- β-D-apioside and emodin-6-O-β-D-xyloside) and emodin-8-O-β-D-glucoside, together with small amounts of other anthraquinone glycosides, dianthrones and aglycones (chrysophanol, physcion). Tannins can be found in frangula bark, as well.



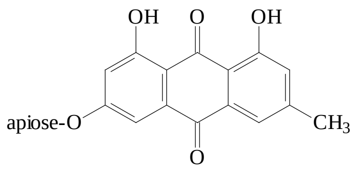
physcion



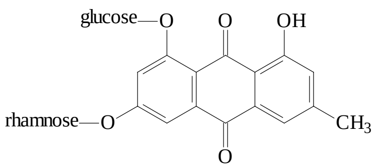
chrysophanol



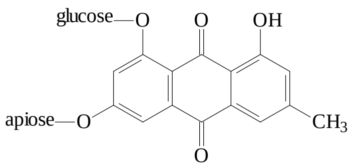
frangulin A



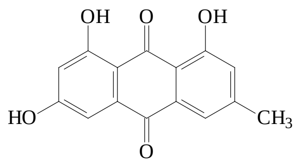
frangulin B



glucofrangulin A



glucofrangulin B



frangulaemodin

Figure 12.34-40
The structure of glucofrangulin A and B, frangulin A and B, frangulaemodin, chrysophanol and physcion.

Uses

Therapeutic indications include the short term treatment of occasional constipation.

Dosage

The correct individual dose is the smallest required to produce a confortable soft-formed motion.

Adults, *elderly and children over 10 years*: preparations equivalent to 20-30 mg of glucofrangulins daily, calculated as glucofrangulin A. The drug and its preparations are not recommended for children under 10 years of age.

Overdose

The major symptoms are griping and severe diarrhoea with consequent loss of fluid and electrolytes, which should be replaced. Treatment should be supportive with generous amounts of fluid. Electrolytes, particularly potassium, should be monitored, this is especially important in the elderly and the young.

Contra-indication

The drug and its preparations should not be used in the following cases: intestinal obstruction and stenosis, atony, inflammatory colon diseases (e.g. ulcerative colitis, Crohn’s disease), appendicitis, abdominal pain of unkown origin, severe dehydration states with water and electrolyte depletion.

Special warnings and special precautions for use

As for all laxatives, frangula bark should not be given when any undiagnosed acute or persistent abdominal symptoms are present. If laxatives are needed every day the cause of the constipation should be investigated. Long term use of laxatives should be avoided. Use for more than 2 weeks requires medical supervision. Chronic use may cause pigmentation of the colon (pseudomelanosis coli) which is harmless and reversible after drug discontinuation. Abuse with diarrhoea and consequent fluid and electrolyte losses may cause: dependence with possible need for increased dosages, disturbance of the water and electrolyte (mainly hypokalaemia) balance, an atonic colon with impaired function. Intake of anthranoid-containing laxatives for more than a short period of time may result in aggravation of constipation. Hypokalaemia can result in cardiac and neuromuscular dysfunction, especially if cardiac glycosides, diuretics or corticosteroids are taken. Chronic use may result in albuminuria and haematuria. In chronic constipation stimulant laxatives are not an acceptable alternative to a changed diet.

Interactions with other medicaments and other forms of interactions

Hypokalaemia potentiates the action of cardiac glycosides and interacts with antiarrhythmic drugs or with drugs which induce reversion to sinus rhythm (e.g. quinidine). Concomitant use with other drugs inducing hypokalaemia (e.g. thiazide diuretics, adrenocorticosteroids and liquorice root) may aggravate electrolyte imbalance.

Undesirable effects

Abdominal spasm and pain and yellow or red-brown (pH dependent) discolouration of urine by metabolites, which is not clinically significant, may develop.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice. Excretion of active principles in breast milk has not been investigated. However, small amounts of active metabolites (e.g. rhein) from other anthranoids are known to be excreted in breast milk.

Rhamni purshianae cortex

Plant

Rhamnus purshiana DC. – Cascara buckthorn (Rhamnaceae)

Cascara is a large shrub or small tree and it is native to western North America from southern British Columbia south to central California, and eastward to northwestern Montana.

Drug

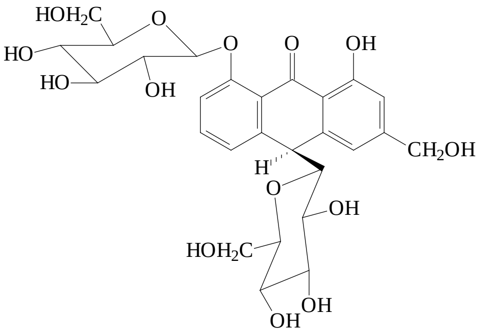
Rhamni purshianae cortex (Cascara, Ph. Eur.)

Cascara consists of the dried, whole or fragmented bark of *Rhamnus purshianus* D.C. (*Frangula purshiana* (D.C.) A. Gray ex J. C. Cooper). It contains not less than 8.0% of hydroxyanthracene glycosides of which not less than 60% consists of cascarosides, both expressed as cascaroside A and calculated with reference to the dried drug.

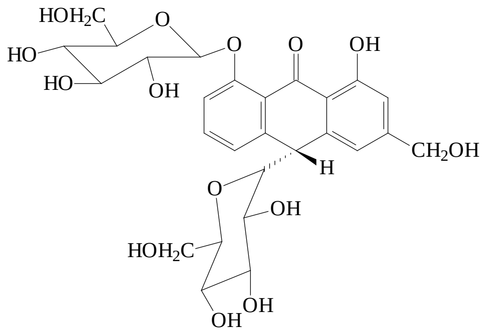
Figure 12.41
Rhamni purshianae cortex (Cascara)

Constituents

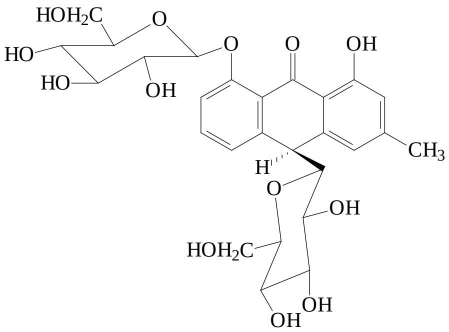
The main active constituents of the dried bark are cascarosides A, B, C, D, E and F. Cascarosides A and B are mixed anthrone-C and O-glycosides, being the 8-O-β-D-glucosides of 10-(S)-deoxyglucosyl aloe-emodin anthrone and of 10-(R)-deoxyglucosyl aloe-emodin anthrone (aloins A and B) respectively. Cascarosides C and D are the 8-O-β-D-glucosides of 10-(R)(S)-deoxyglucosyl chrysophanol anthrone (chrysaloins A and B). Cascarosides E and F are 8-O-β-D-glucosides of 10-deoxyglucosyl emodin. The cascarosides comprise between 60-70% of the total hydroxyanthracene complex. Aloins A and B together with chrysaloins A and B account for 10-30% of the total hydroxyanthracene complex. The remaining 10-20% consists of a mixture of hydroxyanthracene O-glycosides including monoglycosides of chrysophanol, aloe-emodin, emodin and physcion together with the corresponding aglycones.



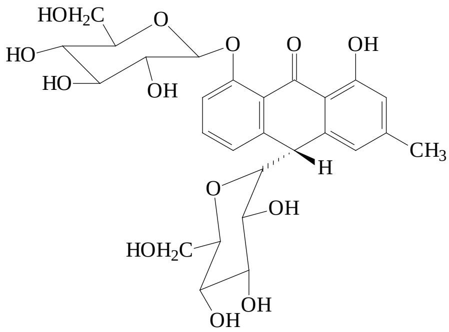
cascaroside A



cascaroside B



cascaroside C



cascaroside D

Figure 12.42-47
The structure of cascarosides A, B, C, D, E and F.

Uses

Therapeutic indications include the short term treatment of occasional constipation.

Dosage

The correct individual dose is the smallest required to produce a confortable soft-formed motion.

Adults, elderly and children over 10 years: dried bark: 0.3-1 g in a single daily dose. Infusion: 1.5-2 g of dried bark in 150 ml of hot water. Preparations equivalent to 20-30 mg of hydroxyanthracene derivatives daily, calculated as cascaroside A. The drug and its preparations are not recommended for children under 10 years of age.

Overdose

The major symptoms are griping and severe diarrhoea with consequent loss of fluid and electrolytes, which should be replaced. Treatment should be supportive with generous amounts of fluid. Electrolytes, particularly potassium, should be monitored, this is especially important in the elderly and the young.

Contra-indication

The drug and its preparations should not be used in the following cases: intestinal obstruction and stenosis, atony, inflammatory colon diseases (e.g. ulcerative colitis, Crohn’s disease), appendicitis, abdominal pain of unkown origin, severe dehydration states with water and electrolyte depletion.

Special warnings and special precautions for use

As for all laxatives, cascara bark should not be given when any undiagnosed acute or persistent abdominal symptoms are present. If laxatives are needed every day the cause of the constipation should be investigated. Long term use of laxatives should be avoided. Use for more than 2 weeks requires medical supervision. Chronic use may cause pigmentation of the colon (pseudomelanosis coli) which is harmless and reversible after drug discontinuation. Abuse with diarrhoea and consequent fluid and electrolyte losses may cause: dependence with possible need for increased dosages, disturbance of the water and electrolyte (mainly hypokalaemia) balance, an atonic colon with impaired function. Intake of anthranoid-containing laxatives for more than a short period of time may result in aggravation of constipation. Hypokalaemia can result in cardiac and neuromuscular dysfunction, especially if cardiac glycosides, diuretics or corticosteroids are taken. Chronic use may result in albuminuria and haematuria. In chronic constipation stimulant laxatives are not an acceptable alternative to a changed diet.

Interactions with other medicaments and other forms of interactions

Hypokalaemia potentiates the action of cardiac glycosides and interacts with antiarrhythmic drugs or with drugs which induce reversion to sinus rhythm (e.g. quinidine). Concomitant use with other drugs inducing hypokalaemia (e.g. thiazide diuretics, adrenocorticosteroids and liquorice root) may aggravate electrolyte imbalance.

Undesirable effects

Abdominal spasm and pain and yellow or red-brown (pH dependent) discolouration of urine by metabolites, which is not clinically significant, may develop.

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug should not be used during pregnancy and lactation without medical advice. Excretion of active principles in breast milk has not been investigated. However, small amounts of active metabolites (e.g. rhein) from other anthranoids are known to be excreted in breast milk.

Rhei radix

Plants

Rheum palmatum L. – Chinese rhubarb or *R. officinale* Baill. – Rhubarb (Polygonaceae)

Chinese rhubarb is native to North and Northwest China, and *R. officinale* can be found in South China and Indochina. It can be cultivated in Hungary. The 8-10-year-old plants are used.

Figure 12.48
Rhubarb (*Rheum palmatum* L.)

Drug

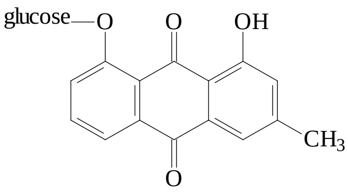
Rhei radix (Rhubarb, Ph. Eur.)

Rhubarb consists of the whole or cut, dried underground parts of *Rheum palmatum* L. or of *Rheum officinale* Baillon or of hybrids of these two species or of a mixture. The underground parts are often divided; the stem and most of the bark with the rootlets are removed. It contains not less than 2.2% of hydroxyanthracene derivatives, expressed as rhein, calculated with reference to the dried drug. Rhubarb has a characteristic, aromatic odour.

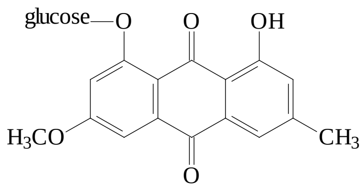
Figure 12.49
Rhei radix (Rhubarb)

Constituents

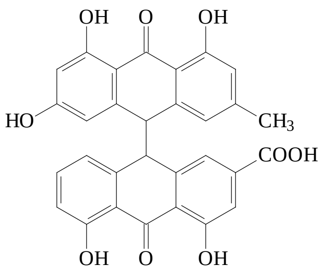
The main active constituents of the drug are hydroxyanthracene derivatives (3-12%) consisting mainly (60-80%) of mono- and diglucosides of rhein, chrysophanol, aloe-emodin, physcion and emodin, and only small amounts of the respective aglycones. Dianthrone glycosides (sennosides) are also present and small amounts of anthrone glycosides depending on the time of harvesting and the conditions of drying. Other constituents include gallotannins, pectin, flavonoids and oxalic acid.



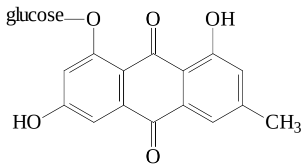
chrysophanol-8-O-glucoside



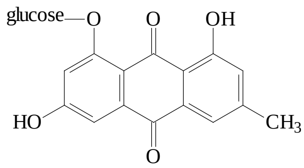
physcion-8-O-glucoside



rheumemodin-rhein-dianthrone



rheumemodin-8-O-glucoside



rhein-8-O-glucoside

Figure 12.50-54

The structure of chrysophanol-8-O-glucoside, rheumemodin-8-O-glucoside, physcion-8-O-glucoside, rhein-8-O-glucoside and rheumemodin-rhein-dianthrone.

Uses

Therapeutic indications include the short term treatment of occasional constipation.

Dosage

The correct individual dose is the smallest required to produce a confortable soft-formed motion.

Adults, *elderly and children over 10 years*: dried bark: drug or its preparations are equivalent to 15-50 mg of hydroxyanthracene derivatives daily (calculated as rhein), preferably taken in one dose at night. The drug and its preparations are not recommended for children under 10 years of age. Because of its tannin content the drug can be used also against diarrhoea. With this indication, the recommended dose of the drug is 0.1-0.3 g daily.

Overdose

It is similar to the Frangula or Cascara drugs (see above these drugs).

Contra-indication

It is similar to the Frangula or Cascara drugs (see above these drugs). The drug is not recommended for long-term use. Due to oxalic acid content renal stones may develop.

Special warnings and special precautions for use

It is similar to the Frangula or Cascara drugs (see above these drugs).

Interactions with other medicaments and other forms of interactions

It is similar to the Frangula or Cascara drugs (see above).

Undesirable effects

It is similar to the Frangula or Cascara drugs (see above).

Pregnancy and lactation

It is similar to the Frangula or Cascara drugs (see above).

Aloe capensis

Plant

Aloë ferox Mill. – Cape aloes (Liliaceae)

Aloë ferox is native to South and East Africa and Macaronesia. Its powder is extremly bitter. The plant can be cultivated. *Aloë ferox* prefers dry-tropical climates, open areas, sandy-loamy soils, full sun, and moderate watering with a good drainage system.

Figure 12.55
Cape aloes (*Aloë ferox* Mill.)

Drug

Aloe capensis (Cape aloes, Ph. Eur.). **Other Drug** *Aloes extractum siccum normatum* (Aloes dry extract, standardised, Ph. Eur.).

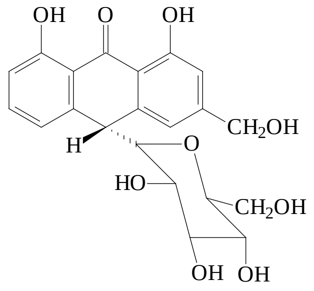
Cape aloes consists of the concentrated and dried juice of the leaves of various species of *Aloe*, mainly *Aloe ferox* Miller and its hybrids. It contains not less than 18.0% of hydroxyanthracene derivatives, expressed as barbaloin and calculated with reference to the dried drug. The drug comprises dark brown masses tinged with green and having a shiny conchoidal fracture, or a greenish-brown powder, soluble in hot alcohol, partly soluble in boiling water.

Standardised aloes dry extract is prepared from Barbados aloes or Cape aloes, or a mixture of the two, by treatment with boiling water. It is adjusted, if necessary, to contain not less than 19.0% and not more than 21.0% of hydroxyanthracene derivatives, expressed as barbaloin and calculated with reference to the dried extract. A brown or yellowish-brown powder, sparingly soluble in boiling water.

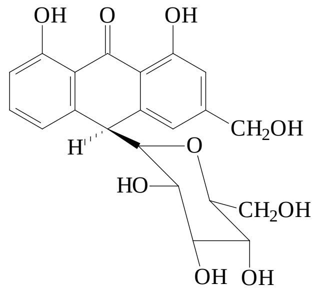
Figure 12.56
Aloe capensis (Cape aloes)

Constituents

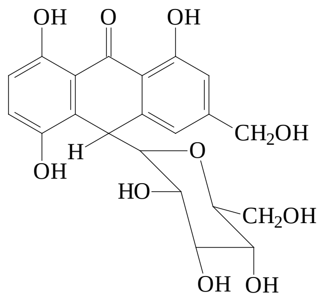
The main active constituents are aloin A and B (barbaloin) and 5-hydroxyaloin A, which are aloe-emodin anthrone-C-glycosides. Aloinosides A and B, which are anthrone-C and O-glycosides, are also considered as active constituents. Other compounds are 2-acetonyl-5-methyl-chromones (aloeresins) and small quantities of 1,8-dihydroxy-anthraquinones (e.g. aloe-emodin).



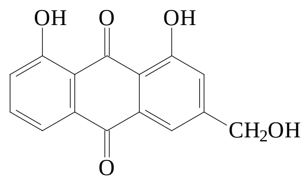
aloin B



aloin A



5-hydroxyaloin



aloe-emodin

Figure 12.57-60
The structure of aloin A and B, 5-hydroxyaloin and aloe-emodin.

Uses

Therapeutic indications include the short term treatment of occasional constipation. It should be highlighted that aloes are the most violent laxatives among drugs containing anthranoids.

Dosage

The correct individual dose is the smallest required to produce a confortable soft-formed motion.

Adults, elderly and children over 10 years: preparations are equivalent to 10-30 mg of hydroxyanthracene derivatives, calculated as barbaloin, to be taken in one dose daily at night. The drug and its preparations are not recommended for children under 10 years of age.

Overdose

It is similar to the Frangula, Cascara and Rhubarb drugs (see above).

Contra-indication

It is similar to the Frangula, Cascara and Rhubarb drugs (see above).

Special warnings and special precautions for use

It is similar to the Frangula, Cascara and Rhubarb drugs (see above).

Interactions with other medicaments and other forms of interactions

It is similar to the Frangula, Cascara and Rhubarb drugs (see above).

Undesirable effects

It is similar to the Frangula, Cascara and Rhubarb drugs (see above).

Pregnancy and lactation

It is similar to the Frangula, Cascara and Rhubarb drugs (see above).

Aloe barbadensis

Plant

Aloë barbadensis Mill. – Barbados aloes (syn.: *Aloë vera* (L.) Burm.) (Liliaceae)

Aloë vera is a succulent plant species that probably originated in northern Africa. It is widely cultivated throughout the world.

Figure 12.61
Barbados aloes (*Aloë barbadensis* Mill.)

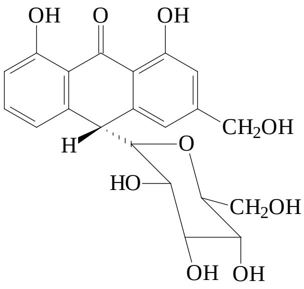
Drug

Aloe barbadensis (Barbados aloes, Ph. Eur.)

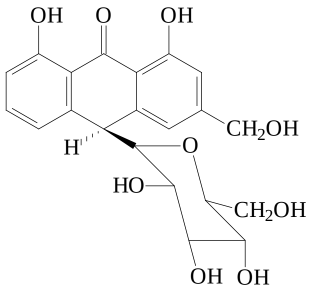
Barbados aloes consists of the concentrated and dried juice of the leaves of *Aloe barbadensis* Miller. It contains not less than 28.0% of hydroxyanthracene derivatives, expressed as barbaloin and calculated with reference to the dried drug. The drug comprises dark brown masses, slightly shiny or opaque with a conchoidal fracture, or a brown powder, soluble in hot alcohol, partly soluble in boiling water.

Constituents

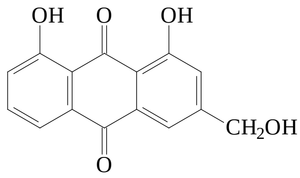
The main active constituents are 25-40% of barbaloin (mixture of aloin A and B), and their respective 6-O-*p*-coumaroyl esters, 3-4% of 7-hydroxyaloin A and B and their 6-O-*p*-coumaroyl esters (characteristic for Barbados aloes). All these compounds are aloe-emodin anthrone-C-glycosides. Small amounts of the aglycones aloe-emodin and chrysophanol are also present. Other constituents are 5-methylchromone glycosides, mainly the 8-glucosyl derivative aloeresin B with smaller amounts of its coumaroyl and cinnamoyl esters.



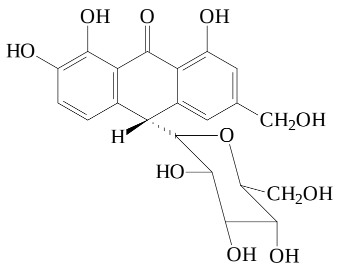
aloin B



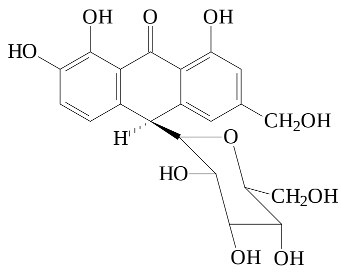
aloin A



aloe-emodin



7-hydroxyaloin B



7-hydroxyaloin A

Figure 12.62-66
The structure of aloin A and B, 7-hydroxyaloin A and B and aloe-emodin.

Uses

Therapeutic indications include the short term treatment of occasional constipation. It should be highlighted that aloes are the most powerful laxatives among drugs containing anthranoids. Aloe gel is frequently used in dermatology. This is a liquid containing mucilage and obtained by mechanical pressure from the epidermic cells of *A. barbadensis*.

Dosage

The correct individual dose is the smallest required to produce a confortable soft-formed motion.

Adults, elderly and children over 10 years: preparations are equivalent to 10-30 mg of hydroxyanthracene derivatives, calculated as barbaloin, to be taken in one dose daily at night. The drug and its preparations are not recommended for children under 10 years of age.

Overdose

It is similar to the other laxative drugs (see above).

Contra-indication

It is similar to the other laxative drugs (see above).

Special warnings and special precautions for use

It is similar to the other laxative drugs (see above).

Interactions with other medicaments and other forms of interactions

It is similar to the other laxative drugs (see above).

Undesirable effects

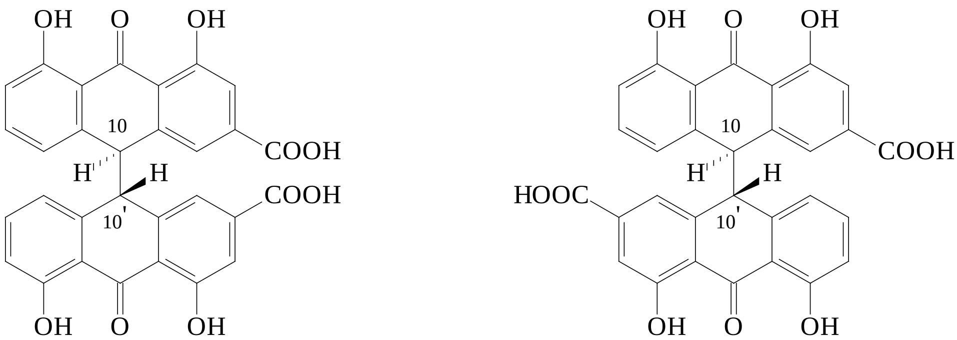
It is similar to the other laxative drugs (see above).

Pregnancy and lactation

It is similar to the other laxative drugs (see above).

12.4 Dianthrone derivatives

These are compounds derived from two anthrone molecules. They readily form as a result of mild oxidation of anthrone or mixed anthrones. They can be found in species of *Cassia*, *Rheum* and *Rhamnus*. In this group the sennidins, aglycones of the sennosides, are among the best-known compounds. It should be noted that two chiral centres (at C-10 and C-10’) are present in the dianthrones, and for a compound having two identical anthrone moieties, e.g. sennidin A, two forms (the 10*S*, 10’*S* and 10*R*, 10’*R*) are possible together with the meso form (sennidin B) (**Fig. 12.67-12.68**).



sennidin A sennidin B

Figure 12.67-68
The structure of sennidin A and B.

Drugs

Sennae folium

Plants

Cassia angustifolia Vahl. - Tinnevelly senna and/or *C. acutifolia* Delile - Alexandrian senna (Caesalpiniaceae)

The senna plants are small shrubs. *C. acutifolia* is indigenous to tropical Africa and is cultivated in Sudan. *C. angustifolia* is native to Somaliland, Arabia and is cultivated in South India (Tinnevelly).

Drug

Sennae folium (Senna leaf, Ph. Eur.). **Other Drug** *Sennae folii extractum siccum normatum* (Senna leaf dry extract, standardised, Ph. Eur.).

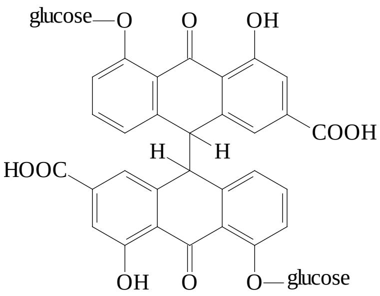
Senna leaf consists of the dried leaflets of *Cassia senna* L. (*C. acutifolia* Delile), known as Alexandrian or Khartoum senna, or *Cassia angustifolia* Vahl, known as Tinnevelly senna, or a mixture of the two species. It contains not less than 2.5% of hydroxyanthracene glycosides, calculated as sennoside B with reference to the dried drug. Senna leaf has a slight characteristic odour.

Standardised senna leaf dry extract is produced from Senna leaf. It contains not less than 5.5% and not more than 8.0% of hydroxyanthracene glycosides, calculated as sennoside B with reference to the dried extract. The measured content does not deviate from the value stated on the label by more than ± 10%. The extract is produced from the drug and ethanol 50 to 80% *V/V* with an appropriate procedure. Brownish or brown powder.

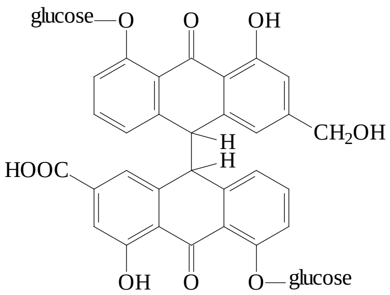
Figure 12.69
Sennae folium (Senna leaf)

Constituents

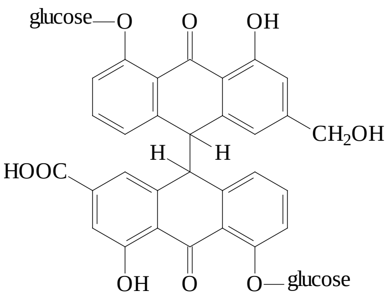
The main active constituents are sennoside A and B (3%), which are rhein-dianthrone diglucosides. Smaller amounts of other dianthrone diglucosides, monoanthraquinone glucosides and aglycones are also present.



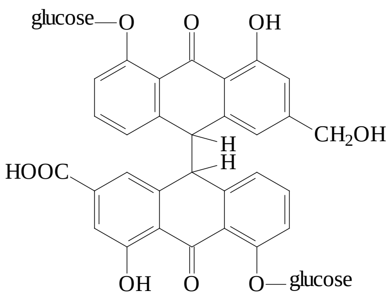
sennoside A



sennoside B



sennoside C



sennoside D

Figure 12.70-73
The structure of sennoside A, B, C and D.

Uses

Therapeutic indications include the short term treatment of occasional constipation.

Dosage

The correct individual dose is the smallest required to produce a confortable soft-formed motion.

Adults, elderly and children over 10 years: preparations are equivalent to 15-30 mg of hydroxyanthracene derivatives, calculated as sennoside B, to be taken once daily at night. The drug and its preparations are not recommended for children under 10 years of age.

Overdose

It is similar to the other laxative drugs (see above).

Contra-indication

It is similar to the other laxative drugs (see above).

Special warnings and special precautions for use

It is similar to the other laxative drugs (see above).

Interactions with other medicaments and other forms of interactions

It is similar to the other laxative drugs (see above).

Undesirable effects

It is similar to the other laxative drugs (see above).

Pregnancy and lactation

It is similar to the other laxative drugs (see above).

Sennae fructus acutifoliae

Plant

Cassia acutifolia Delile – Alexandrian senna (Caesalpiniaceae)

Drug

Sennae fructus acutifoliae (Senna pods, Alexandrian, Ph. Eur.).

Alexandrian senna pods consist of the dried fruits of *Cassia senna* L. (*C. acutifolia* Delile). They contain not less than 3.4% of hydroxyanthracene glycosides, calculated as sennoside B with reference to the dried drug. Alexandrian senna pods have a slight odour.

Figure 12.74
Sennae fructus (Senna pods)

Constituents

The main active constituents are sennoside A and B (ca. 4%), which are rhein-dianthrone diglucosides. Smaller amounts of other dianthrone diglucosides, monoanthraquinone glucosides and aglycones are also present.

Uses

Therapeutic indications include the short term treatment of occasional constipation.

Dosage

The correct individual dose is the smallest required to produce a confortable soft-formed motion.

Adults, elderly and children over 10 years: preparations are equivalent to 15-30 mg of hydroxyanthracene derivatives, calculated as sennoside B, to be taken once daily at night. The drug and its preparations are not recommended for children under 10 years of age.

Overdose

It is similar to the other laxative drugs (see above).

Contra-indication

It is similar to the other laxative drugs (see above).

Special warnings and special precautions for use

It is similar to the other laxative drugs (see above).

Interactions with other medicaments and other forms of interactions

It is similar to the other laxative drugs (see above).

Undesirable effects

It is similar to the other laxative drugs (see above).

Pregnancy and lactation

It is similar to the other laxative drugs (see above).

Sennae fructus angustifoliae

Plant

Cassia angustifolia Vahl. - Tinnevelly senna (Caesalpiniaceae)

Drug

Sennae fructus angustifoliae (Senna pods, Tinnevelly, Ph. Eur.).

Tinnevelly senna pods consist of the dried fruits of *Cassia angustifolia* Vahl. They contain not less than 2.2% of hydroxyanthracene glycosides, calculated as sennoside B with reference to the dried drug. Tinnevelly senna pods have a slight odour.

Constituents

The main active constituents are sennoside A and B (ca. 3%), which are rhein-dianthrone diglucosides. Smaller amounts of other dianthrone diglucosides, monoanthraquinone glucosides and aglycones are also present.

Uses

Therapeutic indications include the short term treatment of occasional constipation.

Dosage

The correct individual dose is the smallest required to produce a confortable soft-formed motion.

Adults, elderly and children over 10 years: preparations are equivalent to 15-30 mg of hydroxyanthracene derivatives, calculated as sennoside B, to be taken once daily at night. The drug and its preparations are not recommended for children under 10 years of age.

Overdose

It is similar to the other laxative drugs (see above).

Contra-indication

It is similar to the other laxative drugs (see above).

Special warnings and special precautions for use

It is similar to the other laxative drugs (see above).

Interactions with other medicaments and other forms of interactions

It is similar to the other laxative drugs (see above).

Undesirable effects

It is similar to the other laxative drugs (see above).

Pregnancy and lactation

It is similar to the other laxative drugs (see above).

12.5 Naphthodianthrone derivatives

Hypericin is the most well-known example of naphthodianthrone derivatives. The large chromophore system in the molecule means that it can cause photosensitivity when ingested beyond threshold amounts. Photosensitivity is often seen in animals that have been allowed to graze on St. John's Wort. Because hypericin accumulates preferentially in cancerous tissues, it is also used as an indicator of cancerous cells. In addition, hypericin is under research as an agent in photodynamic therapy, whereby a biochemical is absorbed by an organism to be later activated with spectrum-specific light from specialized lamps or laser sources, for therapeutic purposes. The antibacterial and antiviral effects of hypericin are also believed to arise from its ability for photo-oxidation of cells and viral particles.

Drugs

Hyperici herba

Plant

Hypericum perforatum L. – St. John’s Wort (Hypericaceae)

The plant is abundant throughout Europe in grasslands, woodlands and hedges, extending to the Himalayas and Asia. It is an herbaceous perennial with bright yellow flowers.

Figure 12.75
St. John's Wort (*Hypericum perforatum* L.)

Drug

Hyperici herba (St. John's Wort, Ph. Eur.). **Other Drug** *Hypericum perforatum ad praeparationes homeopathicas* (Hypericum for homoeopathic preparations, Ph. Eur.).

St. John's Wort consists of the whole or cut, dried flowering tops of *Hypericum perforatum* L., harvested during flowering. It contains not less than 0.08% of total flavonoids, expressed as hypericin and calculated with reference to the dried drug.

Figure 12.76
Hyperici herba (St. John's Wort)

Constituents

The main active constituents are naphthodianthrones, phloroglucinols and flavonoids. Naphthodianthrones (0.05-0.3%), consisting mainly of hypericin and pseudohypericin, accumulate primarily in the flowers and buds. Protohypericin and protopseudohypericin are transformed into hypericin and pseudohypericin respectively on exposure to light. The principal phloroglucinols are hyperforin (2-4%) and adhyperforin. Both compounds have limited stability and their oxidated derivatives are also present. The main flavonoids (2-4%) include hyperoside, quercitrin, isoquercitrin and rutin (quercetin glycosides). Biflavonoids (e.g. amentoflavone) occur mainly in the flowers. Other constituents include chlorogenic acid, tannins and essential oil (0.1%) containing monoterpenes.

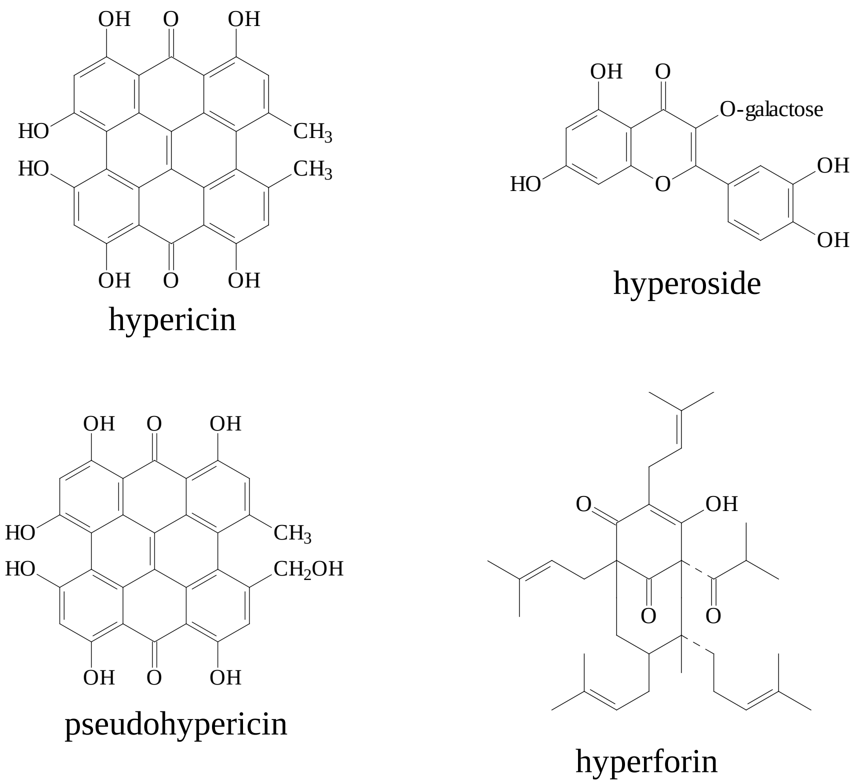


Figure 12.77-80
The structure of hypericin, pseudohypericin, hyperforin and hyperoside.

Uses

Therapeutic indications include the treatment of mild or mild to moderate depressive episodes. Traditional herbal medicinal products of the drug are used for the symptomatic treatment of minor inflammations of the skin (such as sunburn) and as an aid in healing of minor wounds.

Dosage

Preparations based on hydroalcoholic extracts (50-60% ethanol):

Adults, elderly and children over 12 years: 450-1050 mg of hydroalcoholic dry extracts with drug-to-extract ratios of 2.5-5:1, 4-7:1, 5-7:1, daily.

Herbal tinctures and teas:

3-4.5 ml of tincture (1:5, ethanol 60% V/V), daily and 2-4 g of the drug as an infusion, daily.

Children from 6 to 12 years under medical supervision only: half the adult dose.

Overdose

Serious phototoxic reactions may occur at much higher dosages than used therapeutically (3600 mg of hydroalcoholic extract containing 11.25 mg of hypericin). Typical phototoxic symptoms include rash, pruritus and erythema. During treatment exposure to direct sunlight should be avoided.

Contra-indication

Hypersensitivity to the active substance may occur. Hypericum extracts must not be used concomitantly with cyclosporine, tacrolimus, digoxin, amprenavir, indinavir and other protease-inhibitors, irinotecan and other cytostatic agents.

Special warnings and special precautions for use

As with all antidepressant treatments, full manifestation of the therapeutic effect may take 3-4 weeks. There is a risk of suicide, particularly at the begining of treatment, due to the delay between treatment and clinical improvement. If a significant treatment response in depressive disorders is not apparent after 4 weeks, the medication should be discontinued.

Interactions with other medicaments and other forms of interactions

A number of interactions with preparations of St. John’s wort have been reported. Induction of several subtypes of the enzyme cytochrome P450 has been discussed as a potential mechanism of the interactions, but increased expression of the P-glycoprotein drug transporter has also been reported. Documented and hypothetical interactions of St. John’s wort are introduced in the following table.

Table 12.1 Documented and hypothetical interactions of St. John’s Wort

Drug	Mechanism	Result
HIV protease inhibitors	1,2	Insufficient therapy
HIV reverse transcriptase inhibitors	1	Insufficient therapy
Warfarin	1	Reduced anticoagulant effect
Cyclosporine	1,2	Rejection of transplanted organs
Combined oral contraceptives	1	Spotting between periods, unwanted pregnancy
Antiepileptics	1	Increased risk of epileptic seizure
Digoxin	2	Heart failure, heart rhythm problems
Theophylline	1	Insufficient asthma therapy
Triptans	3	Serotonin syndrome
SSRIs	3	Serotonin syndrome

Mechanism: 1 Hepatic enzyme induction; **2** Induction of the permeability glycoprotein; **3** Synergistic effects with serotonin reuptake inhibitors

Undesirable effects

Gastrointestinal disorders, allergic reactions of the skin, fatigue and restlessness may occur. The frequency is not known. Fair-skinned individuals may react with intensified sunburn-like symptoms under intense sunlight.

Pregnancy and lactation

In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

Chapter 13
Drugs containing flavonoids

Flavonoids are the largest group of naturally occuring phenols. Today more than 3000 of these compounds are known. Chemically they are diphenyl-propanes (C_6-C_3-C_6). Flavonoids are formed from three acetate units and a phenylpropane unit (**Figure 13.1**) They can be classified according to the binding site of C_6 part: flavonoids: α-binding site; isoflavonoids: β-binding site and neoflavonoids: γ-binding site (**Figure 13.1**). They are also classified according to the state of oxygenation of the C_3 unit (**Figure 13.2**). Dimeric compounds with e.g. 5'-8-carbon-carbon linkage are also known (isoflavonoids, e.g. amentoflavone, see **Figure 13.3**).

Most flavonoids have yellow colour, and they are more common in higher plants, where they are localised in the cell sap. Flavonoids are used as chemotaxonomic markers. They occur both in the free state and as glycosides (mostly in *O*-glycoside form, but a considerable number of *C*-glycosides are known). Flavonoid-glycosides are soluble in water and alcohol, but insoluble in organic solvents. In alkaline solution (NH_3 steam or NaOH) flavonoids produce intensive yellow colour (in the case of flavanon, isoflavon types this colour is pale; in the case of chalcones this colour is orange). With $FeCl_3$, flavonoids produce blue or green colour, if they have free -OH (hydroxyl) group on the fifth carbon atom. Flavonoids form a chelate complex (which shows orange fuorescence) with basic lead-(II)-acetate. 5-hydroxy-flavons and flavonols form yellow fluorescent chelate complex with zirconium oxychloride ($ZrOCl_3$). 5-hydroxy-flavons and flavonols form yellow chelate complex with aluminium-salts ($AlCl_3$) (**Figure 13.4**). This complex shows yellowish-green fluorescence under UV-light. This complex dissolves after treatment with hydrochloric acid. 5-hydroxy-flavons and flavonols form borine-complex with oxalic-boric acid solution, which shows yellow fluorescence under UV-light.

Flavonoids have many important physiological roles in plants:

- Attract insects – they provide the yellow colour of flowers (pollination)
- Repellents, insecticide materials

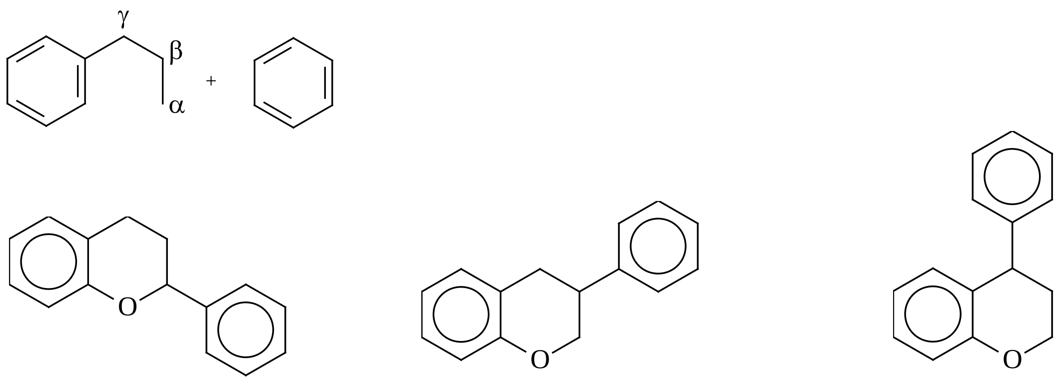
▪ e.g. rotenoids (**Figure 13.5**) (*Derris* sp., *Tephrosia* sp., *Amorpha* sp.)

- Phytoalexins – they protect plants from infections caused by fungi or bacteria (phytoalexins = „plant antibodies")

▪ e.g. pterocarpans (Figure 13.5) (Fabaceae)

- Enzyme inhibitors, take part in oxidation-reduction processes (antioxidant, radical scavengers)
- Influence plant growth
- Colouring matters (e.g. haematoxilin in Hematoxylon sp.)

Plants containing flavonoids are used in medicine and phytotherapy for different purposes. They have different properties. Some flavonoids decrease the permeability of capillary vessels and increase the resistance of capillaries [e.g. Vitamin P (citrin = hesperidin + eriodictin) and rutin]. They have anti-inflammatory activity and prevent oedema formation, therefore they can be used for treating varicose veins [e.g. the product Rutascorbin, hydroxyethylrutoside (in the product Venoruton]. Procyanidins are coronary artery dilators and cardiac tonics (e.g. *Crataegus* sp., *Ginkgo* sp.). They have diuretic activity (e.g. *Betula*, *Solidago*, *Viola*, *Orthosiphon*, *Ononidis* sp.). *Citrus* flavonoids (e.g. nobiletin, tangeretin) showed anti-allergic effect. Other effects include diaphoretic (e.g. *Tilia*, *Sambucus*, *Filipendula*), spasmolytic (apigenin in chamomile), isoliquiritigenin in liquorice root), anti-hepatotoxic and choleretic (*Silybum*, *Helichrysum*) and phytooestrogen (isoflavonoids in soy bean). Phytooestrogens, which are chemically isoflavonoids, are similar both functionally and structurally to oestradiol and related sex hormones and exert weak oestrogenic effects. Phytooestrogens may have positive effects in the prevention of cancer, heart diseases and postmenopausal symptoms.



flavonoids (2-phenyl-chromone) | isoflavonoids (3-phenyl-chromone) | neoflavonoids (4-phenyl-chromone)

Figure 13.1
The building units and main groups of flavonoids.

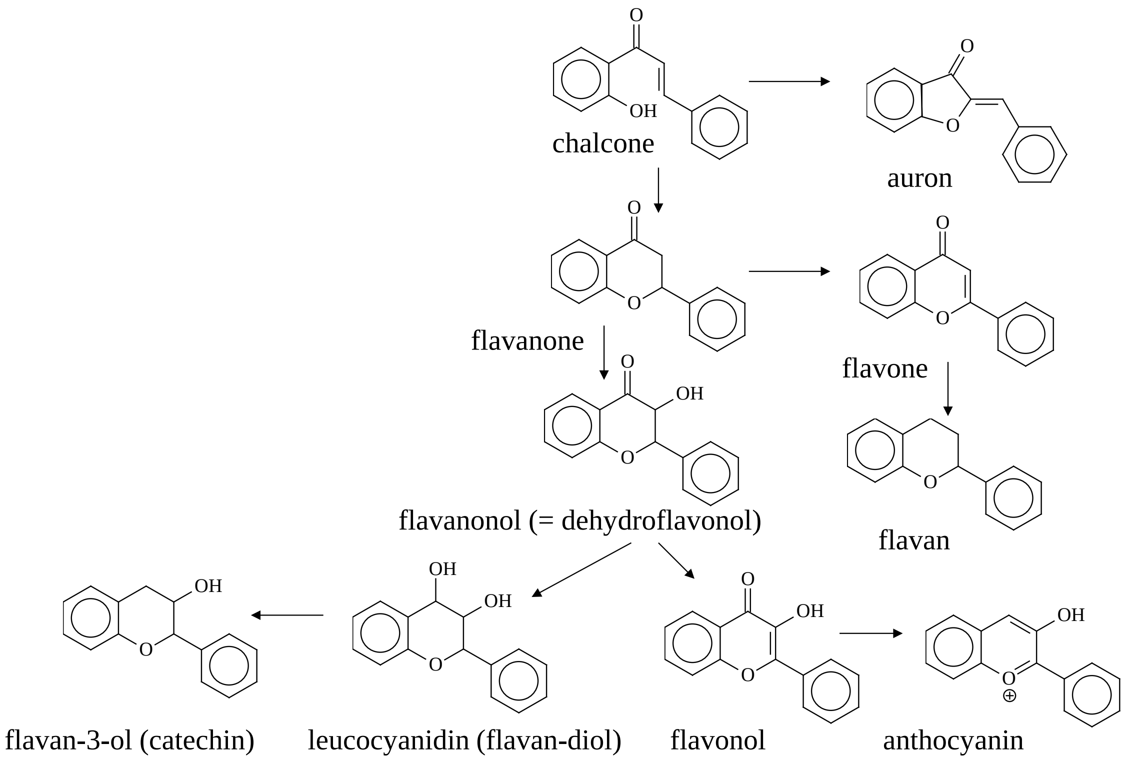


Figure 13.2
Structural types of flavonoids.

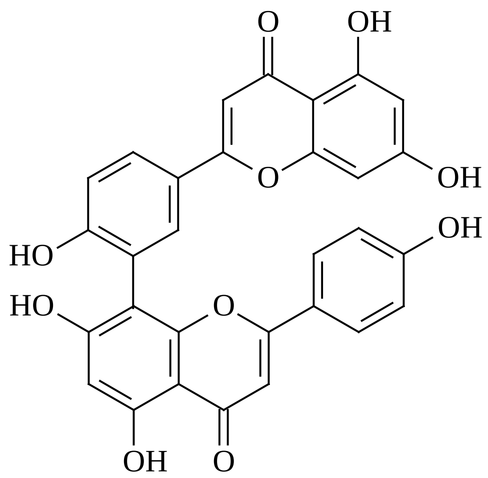


Figure 13.3
The structure of amentoflavone.

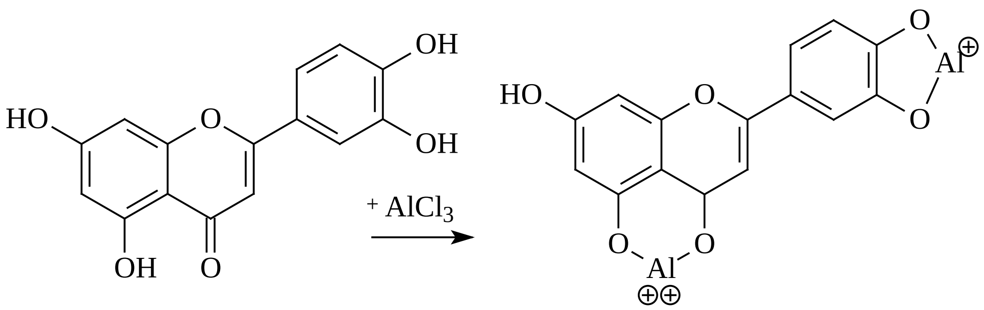
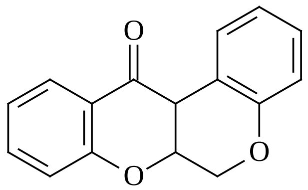
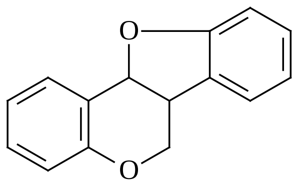


Figure 13.4
Formation of flavonoid complex with aluminium-salts ($AlCl_3$).



rotenoid



pterocarpan

Figure 13.5
The structure of rotenoid and pterocarpan.

Drugs

Tiliae flos

Plants

Tilia cordata Mill. (Small-leaved lime), *T. platyphyllos* Scop. (Large-leaved lime), *Tilia* x *vulgaris* Heyne (Lime) - (Tiliaceae)

Tilia is a genus of about 30 species of trees native throughout most of the temperate Northern Hemisphere. The genus occurs in Europe and eastern North America, but the greatest species diversity is found in Asia.

Figure 13.6
Small-leaved lime (*Tilia cordata* Mill.)

Figure 13.7
Large-leaved lime (*T. platyphyllos* Scop.)

Drug

Tiliae flos (Lime flower, Ph. Eur.)

Lime flower consists of the whole, dried inflorescence of *Tilia cordata* Miller, of *Tilia platyphyllos* Scop., of *Tilia* × *vulgaris* Heyne or a mixture of these. Lime flower has a faint aromatic odour and a faint, sweet and mucilaginous taste. The drug has to be checked for the presence of *T. argentea* (silver lime)! This plant contains stellate hairs on the abaxial surfaces of the leaves. Its drug has narcotic smell and unpleasant taste.

Figure 13.8
Silver lime (*Tilia argentea* L.)

Figure 13.9
Tiliae argenteae flos (Silver lime flower)

Figure 13.10
Tiliae flos (Lime flower)

Constituents

Lime flower contains 1% of flavonoids. The most characteristic flavonoids include astragalin (kaempferol-3-O-glycoside), isoquercitrin (quercetin-3-O-glycoside), quercitrin (quercetin-3-O-rhamnoside), tiliroside [kaempferol-3-(6”-*p*-coumaroil-glucoside)] and hyperoside (quercetin-3-O-galactoside). The drug contains 0.01-0.02% of essential oil, which is responsible for the faint odour of the dried drug. Other constituents include phenolic acids (e.g. caffeic acid, chlorogenic acid and *p*-coumaric acid), proanthocyanidins, tannins and 10% of mucilage (galactomannans).

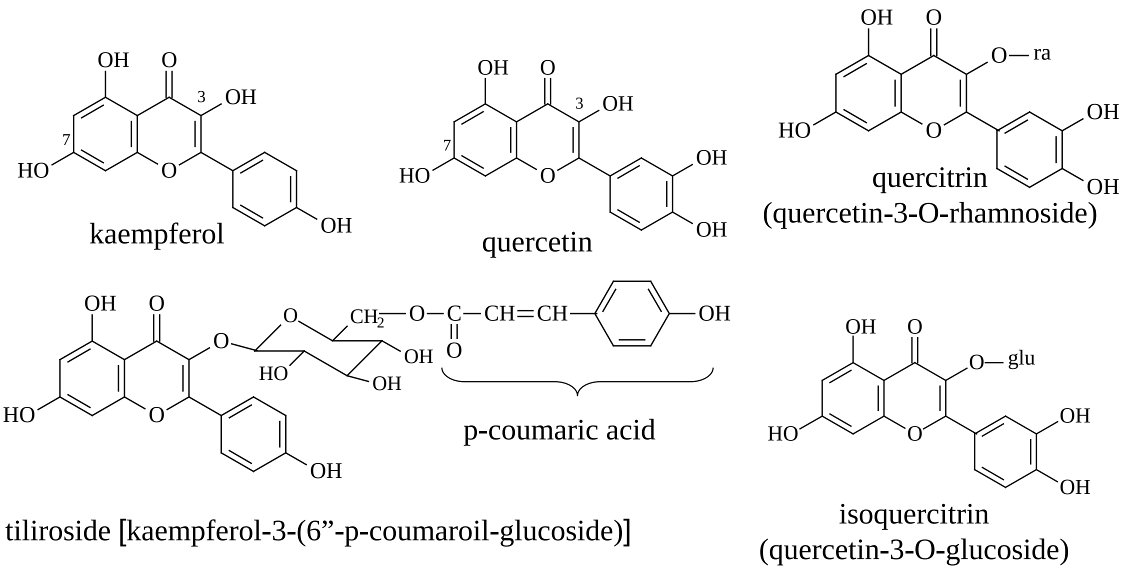


Figure 13.11-15
The structure of tiliroside [kaempferol-3-(6”-*p*-coumaroil-glucoside)], quercitrin (quercetin-3-O-rhamnoside), isoquercitrin (quercetin-3-O-glycoside), kaempferol and quercetin.

Uses

Lime flower has multiple applications. Therapeutic indications include the treatment of common cold, unproductive cough and sore throat. It has antimicrobial, expectorant and diaphoretic effect. Traditional use of the drug includes the relief of mild symptoms of mental stress.

Dosage

Relief of symptoms of common cold and mild symptoms of mental stress:

Adult and elderly daily dose: Herbal tea: 1.5 g of the comminuted herbal substance in 150 ml of boiling water as an herbal infusion 2-4 times daily. Daily dose: 3-6 g. In liquid extract: single dose is 2 ml, 1-2 times daily. Daily dose: 2-4 ml. In tincture: single dose is 1 ml, 1-2 times daily. Daily dose: 1-2 ml.

Children between 4 and 12 years of age: Herbal tea: 1 g of the comminuted herbal substance in 150 ml of boiling water as an herbal infusion 2-4 times daily. Daily dose: 2-4 g. In case of mild symptoms of mental stress: the use in children under 12 years of age is not recommended.

Contra-indications

Hypersensitivity to the active substance may occur.

Pregnancy and lactation

Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

Sambuci flos

Plant

Sambucus nigra L. – Elder (Caprifoliaceae)

This shrub or small tree is native throughout Europe and Western and Central Asia. This plant should be distinguished from *Sambucus ebulus* (danewort/dwarf elder) (**Figure 13.17**). It has unpleasant odour, purple anthers in the flowers, erected fruits. The fruits and seeds contain cyanogenetic glycosides. The consumption of few seeds can cause severe nausea and vomiting at children. The root of danewort (Ebuli radix) is used as a diuretic.

Figure 13.16
Elder (*Sambucus nigra* L.)

Figure 13.17
Danewort/Dwarf elder (*Sambucus ebulus* L.)

Drug

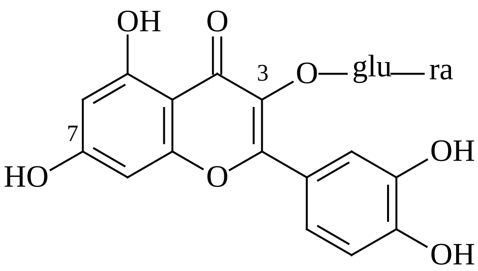
Sambuci flos (Elder flower, Ph. Eur.).

Elder flower consists of the dried flowers of *Sambucus nigra* L. It contains not less than 0.80% of flavonoids, calculated as isoquercitroside with reference to the dried drug.

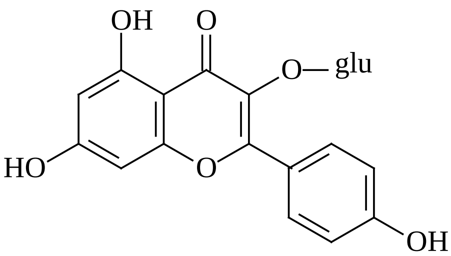
Figure 13.18
Sambuci flos (Elder flower)

Constituents

Elder flower contains approx. 3% of flavonoids (astragalin, isoquercitrin, quercetin, kaempferol, rutin and hyperoside). Other constituents include triterpenes (e.g. ursolic acid and oleanolic acid), sterols (e.g. β-sitosterol and stigmasterol), approx. 3% of phenolic acids (e.g. chlorogenic acid, p-coumaric acid and ferulic acid), 0.15% of essential oil and mucilage.



rutin
(quercetin-3-O-rutinoside)



astragalin
(kaempferol-3-O-glucoside)

Figure 13.19-20
The structure of astragalin (kaempferol-3-O-glucoside) and
rutin (quercetin-3-O-rutinoside).

Uses

Elder flower is administered mainly as an herbal tea for the treatment of feverish diseases and the common cold. It acts as a diaphoretic but the mechanism is unclear. The drug also has diuretic properties. In ethnomedicine the fruits of *S. nigra* (*Sambuci fructus*) are also used because of their mild laxative effect.

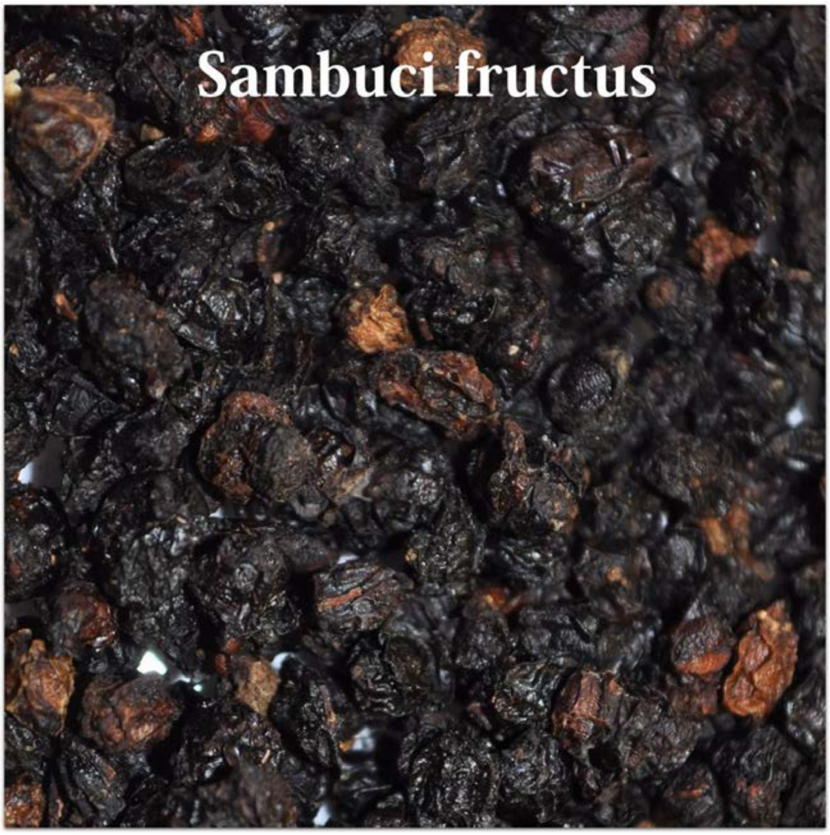


Figure 13.21
Sambuci fructus (Elder fruit)

Dosage

Adolescents over 12 years of age, adults, elderly: 2-5 g of dried drug or as an infusion, 3 times daily. Liquid extract (1:1, 25% V/V ethanol): 3-5 ml, 3 times daily. Tincture (1:5, 25% V/V ethanol): 10-25 ml, 3 times daily. The use is not recommended in children under 12 years of age.

Contraindications

Hypersensitivity to the active substance may occur. Patients with cardiac problems should not use diaphoretic drugs (e.g. *Tiliae* and *Sambuci flos*).

Pregnancy and lactation

No data available. In accordance with general medical practice, the drug and its preparations should not be used during pregnancy and lactation without medical advice.

Equiseti herba

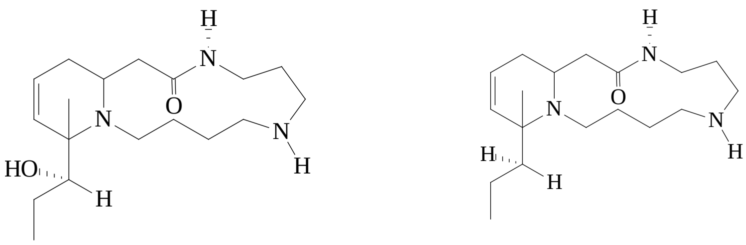
Plant

Equisetum arvense L. – Field horsetail (Equisetaceae)

Equisetum arvense is a herbaceous perennial plant, native throughout the arctic and temperate regions of the northern hemisphere. It has separate sterile, photosynthesizing and fertile spore-bearing stems, growing from a perennial underground rhizomatous stem system. The fertile stems are produced in early spring and are non-photosynthetic, while the green sterile stems start to grow after the fertile stems have wilted, and persist through the summer until the first autumn frosts. Sterile, green stems are collected as the drug. The presence of other *Equisetum* species should be excluded, mainly *E. palustre* (marsh horsetail) (**Figure 13.23**), because this plant contains toxic palustrine and deoxypalustrine (**Figure 13.24-25**). The shoots of *E. palustre* are shorter and its sporangia appear on the sterile shoot in June.

Figure 13.22
Field horsetail (*Equisetum arvense* L.)

Figure 13.23
Marsh horsetail (*Equisetum palustre* L.)



palustrine deoxypalustrine

Figure 13.24-25
The structure of palustrine and deoxypalustrine.

Drug

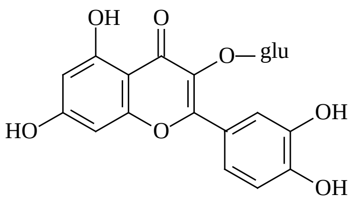
Equiseti herba (Equisetum stem, Ph. Eur.)

The drug is the whole or cut, dried sterile aerial parts of *Equisetum arvense* L. It contains minimum 0.3% of total flavonoids expressed as isoquercitroside calculated with reference to the dried drug.

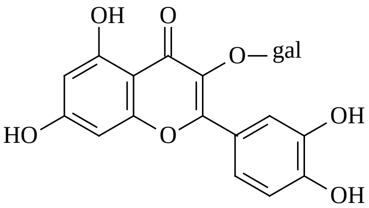
Figure 13.26
Equiseti herba (Equisetum stem)

Constituents

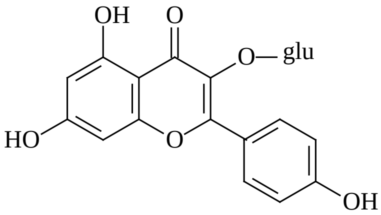
The drug contains approx. 8-10% of silicic acid and 1% of flavonoids. The most characteristic flavonoids are astragalin (kaempferol-3-O-glucoside), isoquercitrin (quercetin-3-O-glucoside) and hyperoside (quercetin-3-O-galactoside). Other constituents include approx. 1% of phenolic acids (e.g. chlorogenic and caffeic acid).



isoquercitrin
(quercetin-3-O-glucoside)



hyperoside
(quercetin-3-O-galactoside)



astragalin
(kaempferol-3-O-glucoside)

Figure 13.27-29
The structure of astragalin (kaempferol-3-O-glucoside),
isoquercitrin (quercetin-3-O-glucoside) and hyperoside (quercetin-3-O-galactoside).

Uses

The drug and its traditional herbal medicinal products can be used to increase the amount of urine to achieve flushing of the urinary tract as an adjuvant in minor urinary complaints. It has diuretic, antibacterial and anti-inflammatory activities.

Dosage

Adults and children over 12 years of age: 2-3 g of the powdered drug into 250 ml boiling water, prepared as tea infusion, 3 times daily.

Special warnings and precautions

The use is not recommended in children under 12 years of age because of the lack of available experience. If complaints or symptoms such as fever, dysuria, spasm or blood in urine occur during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.

Contra-indications

Conditions where a reduced fluid intake is recommended (e.g. severe cardiac or renal diseases).

Pregnancy and lactation

No data available. In accordance with general medical practice, horsetail and its preparations should not be used during pregnancy and lactation without medical advice.

Crataegi folium cum flore

Plants

Crataegus monogyna Jacq., *C. laevigata* DC. (syn. C. oxyacantha L.) – Common and Midland Hawthorn (Rosaceae)

Crataegus monogyna is a species of hawthorn native to Europe, northwest Africa and western Asia. It has been introduced to many other parts of the world where it is an invasive weed. *C. laevigata* is native to western and central Europe. In the flowers of *C. monogyna* there are yellow anthers and only one stigma can be found, while the flowers of *C. laevigata* contain deep purple anthers and two stigmas. *Crataegus* species have berry-like false fruits, but structurally they are pome fruits.

Figure 13.30
Common hawthorn (*Crataegus monogyna* Jacq.)

Figure 13.31
Midland hawthorn (*Crataegus laevigata* DC.)

Drug

Crataegi folium cum flore (Hawthorn leaf and flower; Ph. Eur.). **Other Drug** *Crataegi folii cum flore extractum siccum* (Hawthorn leaf and flower dry extract; Ph. Eur.)

The drug consists of the whole or cut, dried flower-bearing branches of *Crataegus monogyna* Jacq. (Lindm.), *C. laevigata* (Poiret) D.C. (*C. oxyacanthoides* Thuill.) or their hybrids or, more rarely, other European *Crataegus* species including *C. pentagyna* Waldst. et Kit. exWilld., *C. nigra* Waldst. et Kit., *C. azarolus* L. It contains minimum 1.5% of flavonoids expressed as hyperoside and calculated with reference to the dried drug.

Crataegi folii cum flore extractum siccum: The extract is produced from *Hawthorn leaf and flower*.

Content:

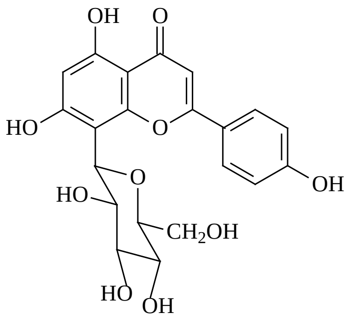
- for aqueous extracts: minimum 2.5% of flavonoids, expressed as hyperoside (dried extract);
- for hydroalcoholic extracts: minimum 6.0% of flavonoids, expressed as hyperoside (dried extract).

The extract is produced from the drug by a suitable procedure using either water or a hydroalcoholic solvent equivalent in strength to a minimum of 45% *V/V* ethanol. It is a light brown or greenish-brown powder.

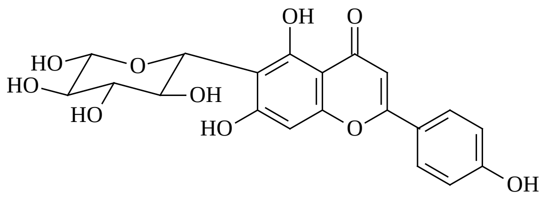
Figure 13.32
Crataegi folium cum flore (Hawthorn leaf and flower)

Constituents

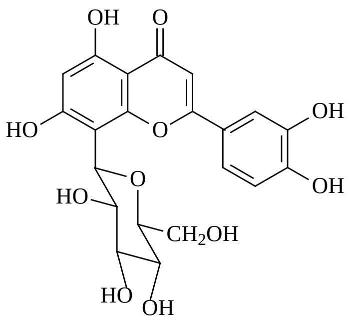
The major characteristic constituents are flavonoids (approx. 2%) such as vitexin (apigenin-8-C-glucoside), isovitexin (apigenin-6-C-glucoside), orientin (luteolin-8-C-glucoside), isoorientin (luteolin-6-C-glucoside), hyperoside (quercetin-3-O-galactoside) and rutin (quercetin-3-O-rutinoside). The drug contains 2.5-3% of procyanidins. They are based on the condensation of catechin and/or epicatechin with varying degrees of polymerisation. The most relevant are oligomeric procyanidins containing 2 to 8 monomeric units. Other constituents include tannins, triterpenes and phenolic acids (e.g. chlorogenic and caffeic acids).



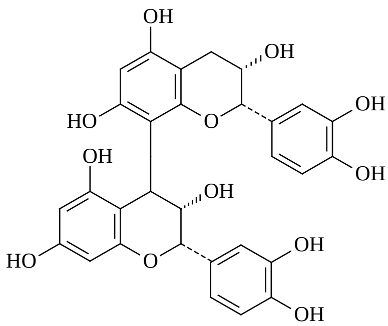
vitexin (apigenin-8-C-glucoside)



isovitexin (apigenin-6-C-glucoside)



orientin (luteolin-8-C-glucoside)



dimer-procyanidin (4β→8)

Figure 13.33-36

The structure of vitexin (apigenin-8-C-glucoside), isovitexin (apigenin-6-C-glucoside), orientin (luteolin-8-C-glucoside) and dimer-procyanidin (4β→8).

Uses

Therapeutic indications include nervous heart complaints. The drug preparations support the cardiac and circulatory functions. Hydroalcoholic extracts of the drug can be used in the case of declining cardiac performance corresponding to Functional Capacity Class II as defined by the New York Heart Association (NYHA).

Classification of Functional Capacity by the New York Heart Association:

Class II.: Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea or anginal pain.

Dosage

Adult and elderly

Preparations based on hydroalcoholic extracts: these extracts (drug to extract ratio 4-7:1) with defined oligomeric procyanidin or flavonoid content, 160-900 mg daily

Herbal teas and other preparations: 1-1.5 g of comminuted drug as an infusion, 3-4 times daily. Tincture: 20 drops 2-3 times daily.

Special warnings and precautions for use

A doctor must be consulted in cases where symptoms continue unchanged for longer than 6 weeks, or when fluid accumulates in the legs. Medical intervention is absolutely necessary when pain occurs in the region of the heart, spreading out to the arms, upper abdomen or the area around the neck or in cases of respiratory distress (dyspnoea).

Pregnancy and lactation

No human data available. In accordance with general medical practice, the drug and its preparations should not be used during pregnancy and lactation without medical advice.

Crataegi fructus

Plants

Crataegus monogyna Jacq. , *C. laevigata* DC. (syn. C. oxyacantha L.) – Common and Midland Hawthorn (Rosaceae)

Drug

Crataegi fructus (Hawthorn berries, Ph. Eur.).

Hawthorn berries consist of the dried false fruits of *Crataegus monogyna* Jacq. (Lindm.), or *Crataegus laevigata* (Poir.) D.C. (synonym: *Crataegus oxyacantha* L.) or their hybrids or a mixture of these false fruits. They contain not less than 1.0% of procyanidins, calculated as cyanidin chloride with reference to the dried drug. The false fruit has a sweet mucilaginous taste.

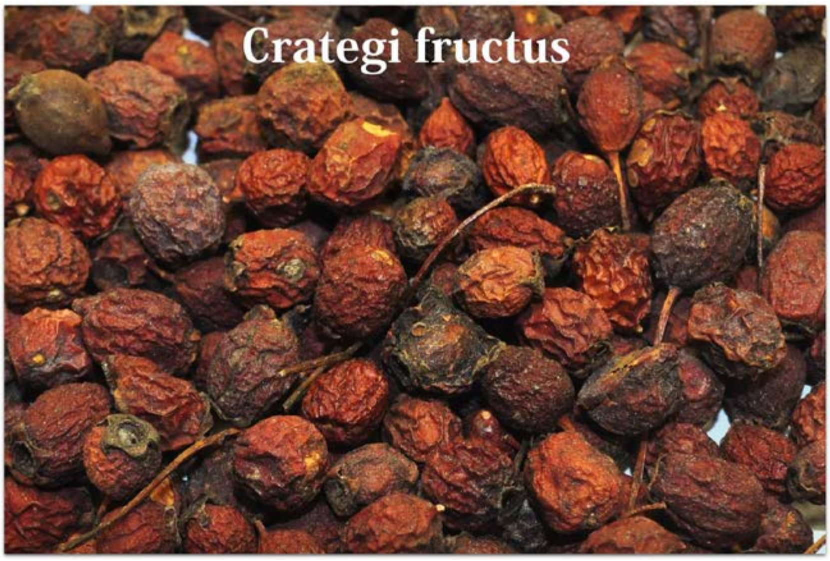


Figure 13.37
Crataegi fructus (Hawthorn berries)

Constituents

The active constituents of the drug are similar to those of the leaf and flower: procyanidins, flavonoids, triterpenes, phenolic acids, and ascorbic acids.

Uses

Therapeutic indications include cardiac complaints. The drug and its preparations support the cardiac and circulatory functions.

Dosage

Adults: hydroalcoholic extracts (1:1.3-3), 2-2.5 ml daily. Powdered hawthorn berries, 0.3-1 g three times daily or as an infusion; liquid extract (1:1 in 25% ethanol), 0.5-1 ml three times daily; tincture (1:5 in 45% ethanol), 1-2 ml three times daily.

Special warnings and precautions for use

A doctor must be consulted in cases where symptoms continue unchanged for longer than 6 weeks, or when fluid accumulates in the legs. Medical intervention is absolutely necessary when pain occurs in the region of the heart, spreading out to the arms, upper abdomen or the area around the neck or in cases of respiratory distress (dyspnoea).

Pregnancy and lactation

No human data available. In accordance with general medical practice, the drug and its preparations should not be used during pregnancy and lactation without medical advice.

Violae herba cum flore

Plants

Viola tricolor L. - Wild pansy, *V. arvensis* Murray - Field pansy (Violaceae)

Viola tricolor is a common European plant, *V. arvensis* is native to Europe, western Asia and North Africa.

Figure 13.38
Wild pansy (*Viola tricolor* L.)

Figure 13.39
Field pansy (*Viola arvensis* Murray)

Drug

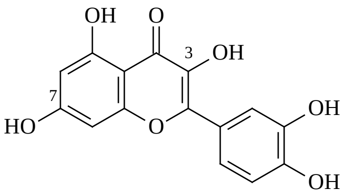
Violae herba cum flore (Wild pansy flowering aerial parts, Ph. Eur.)

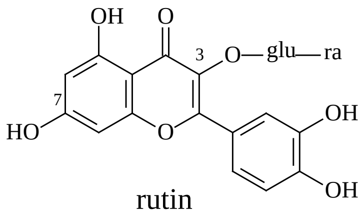
The drug consists of the dried flowering aerial parts of *Viola arvensis* Murray and/or *Viola tricolor* L. It contains minimum 1.5% of flavonoids, expressed as violanthin and calculated with reference to the dried drug.

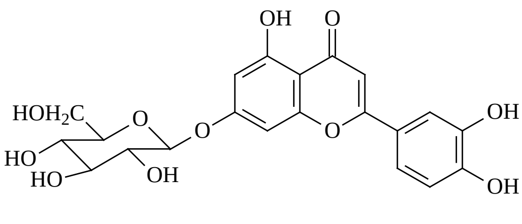
Figure 13.40
Violae herba cum flore (Wild pansy flowering aerial parts)

Constituents

The most important constituents of the drug are flavonoids (up to 3%) such as rutin (quercetin-3-O-rutinoside), quercetin (flavonol type), violanthin (flavon-C-glycoside) and luteolin-7-O-glucoside (flavone type). The flowers also contain anthocyanidins such as violanin [delphinidin-3-(6-*p*-coumaroyl-rhamnosylglucoside)-5-glucoside]. The drug contains approx. 0.1-0.3% of phenolic acid derivatives [e.g. salicylic acid, methyl salicylate, violutin (methyl salicylate arabinosylglucoside)]. Other important constituents are the carotenoids (e.g. violaxanthin, lutein and 15-*cis*-violaxanthin). Other constituents include 10% of mucilage, 2.5% tannins, ascorbic acid and minerals (mainly potassium salts). Saponins were not detected either in *V. tricolor* or in *V. arvensis,* contrary to an earlier report of about 5% saponins in *V. tricolor*.


quercetin


rutin
(quercetin-3-O-rutinoside)


luteolin-7-O-glucoside

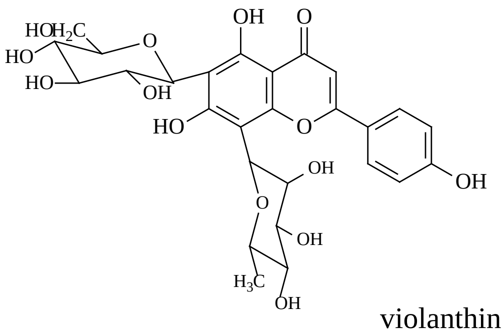

violanthin
(flavon-C-glycoside)

Figure 13.41-44
The structure of quercetin, rutin (quercetin-3-O-rutinoside), luteolin-7-O-glucoside and violanthin.

Uses

Therapeutic indications include skin disorders, such as eczema, seborrhoea, impetigo and acne, as well as cradle cap and nappy rash of infants. Efficacy in these indications is plausible on the basis of human experience and long-standing use.

Dosage

Internal use

Adults: 1.5-4 g of the drug as an infusion three times daily; fluid extract (1:1, ethanol 25%) 2-4 ml three times daily; dry extract (6:1) 2-4 g daily

Children: proportion of adult daily dose according to age or body weight

External use

3-4 g of the drug in 150 ml of hot water as a compress or poultice, several times daily

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Gingko folium

Plant

Ginkgo biloba L. – Ginkgo (Ginkgoaceae)

Ginkgo has no close living relatives. This plant is a living fossil and it is native to China, but the tree is widely cultivated.

Figure 13.45
Ginkgo (*Ginkgo biloba* L.)

Drug

Ginkgo folium (Gingko leaf, Ph. Eur.).

The drug consists of the whole or fragmented, dried leaf of *Ginkgo biloba* L. It contains not less than 0.5% of flavonoids, expressed as flavone glycosides and calculated with reference to the dried drug. Ginkgo leaf is greyish or yellowish-green or yellowish-brown.

Standardised Ginkgo dry extract: It consists of an extract produced from ginkgo leaf. It contains 22.0 to 27.0% of flavonoids, expressed as flavone glycosides, and 5.0 to 7.0% of terpene lactones including 2.8 to 3.4 % of ginkgolides A, B and C, and 2.6 to 3.2% of bilobalide.

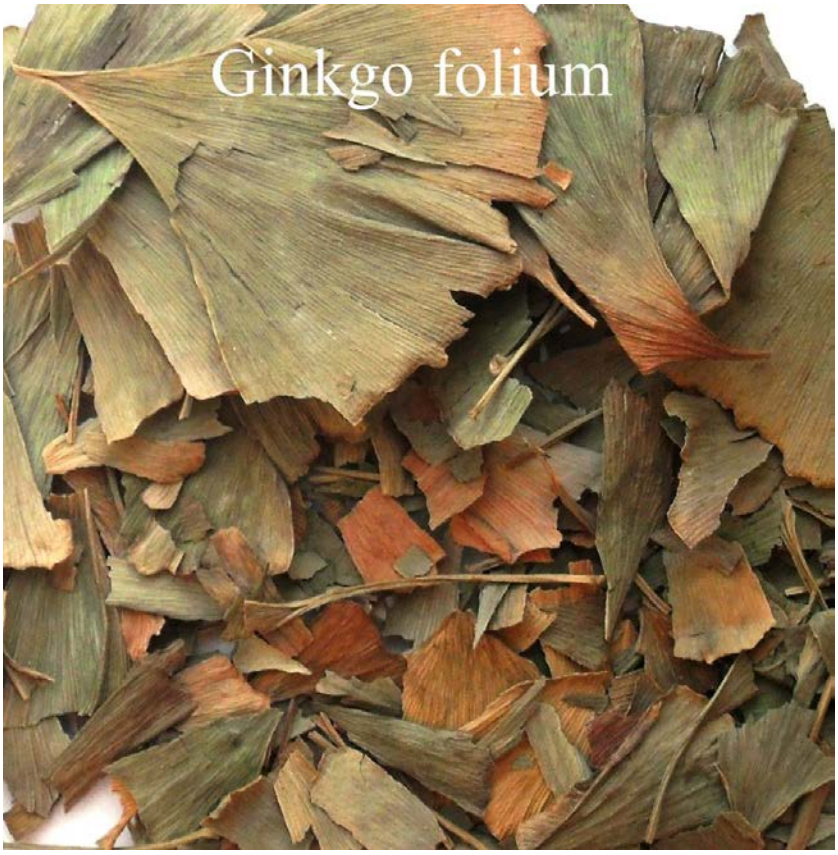
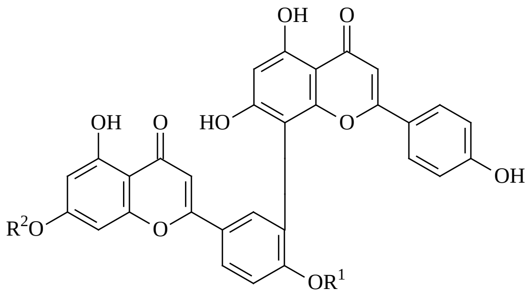


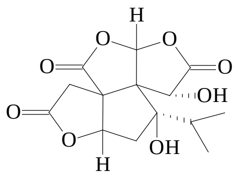
Figure 13.46
Ginkgo folium (Ginkgo leaf)

Constituents

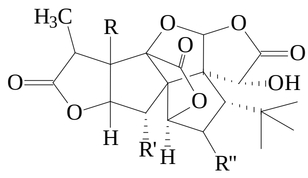
The active constituents of the drug are flavonoids and terpenes. The main flavonoids are mono-, di- and triglycosides of the flavonols quercetin, kaempferol and isorhamnetin. Diglycosides esterified with *p*-coumaric acid are also present. Other flavonoids include biflavones (e.g. bilobetin, amentoflavone, ginkgetin), monomeric flavan-3-ols such as (+)-catechin, (-)-epicatechin, (-)-epigallocatechin and (+)-gallocatechin, and oligomeric and polymeric procyanidins. The principal terpenes are diterpene trilactones called ginkgolides (A, B and C), which differ in the number and position of their hydroxyl groups, and the sesquiterpene trilactone bilobalide. The dried leaf of pharmacopoeial quality should contain not less than 0.1% of terpene lactones, calculated as the sum of bilobalide and gingkolide A, B and C. Long chain alkylphenolic acids (ginkgolic acid), organic acids and phytosterols are also present.



R^1	R^2	
-H	-H	amentoflavone
-CH^3	-H	bilobetin
-CH^3	-CH^3	ginkgetin



bilobalide



R	R'	R"	
-OH	-H	-H	Ginkgolide A
-OH	-OH	-H	Ginkgolide B
-OH	-OH	-OH	Ginkgolide C
-OH	-H	-OH	Ginkgolide D

gingkolide A, B, C and D

Figure 13.47-49
The structure of biflavones (bilobetin, amentoflavone, ginkgetin),
diterpene lactones (ginkgolide A, B, C and D) and sesquiterpene lactone (bilobalide).

Uses

Therapeutic indications include the symptomatic treatment of mild to moderate dementia syndromes including primary degenerative dementia, vascular dementia and mixed forms; celebral insufficiency; neurosensory disturbances such as dizziness/vertigo and tinnitus; enhancement of cognitive performance; and symptomatic treatment of peripheral arterial occlusive disease (intermittent claudication).

Dosage

Adult and elderly daily dose: 120-240 mg of standardized ginkgo dry extract divided into 2-3 doses and equivalent preparations. No data available for children.

In cases of dementia, treatment should be maintained for at least 12 weeks. After this period an evaluation should be carried out to determine whether the patient is a responder or a non-responder. The treatment should be continued only in the case of a responder.

Undesirable effects

In rare cases, mild gastrointestinal disorders, headache or allergic skin reactions have been reported.

Overdose

No significant adverse reactions have been reported in patients ingesting up to 600 mg of dry extract in single doses.

Contra-indications

Hypersensibility or intolerance to ginkgo leaf preparations may develop.

Interaction with other medicaments and other form of interaction

An interaction with substances that inhibit blood coagulation cannot be excluded.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Hyperici herba

Plant

Hypericum perforatum L. – St. John's Wort (Hypericaceae)

The description of this plant can be found in **Chapter 12**.

Ribis nigri folium

Plant

Ribes nigrum L. - Blackcurrant (Grossulariaceae)

This shrub is native to temperate parts of central and northern Europe and northern Asia where it prefers damp fertile soils and is widely cultivated both commercially and domestically.

Figure 13.50
Blackcurrant (*Ribes nigrum* L.)

Drug

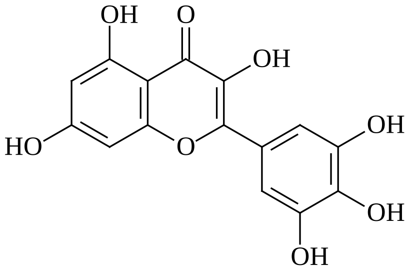
Ribis nigri folium (Blackcurrant leaf). **Other Drug** *Ribis nigri fructus* (Blackcurrant fruit)

The drug consists of the dried leaves of *Ribes nigrum* L. It contains not less than 1.5% of flavonoids, expressed as rutin and calculated with reference to the dried drug. In phytotherapy the fruits can also be used.

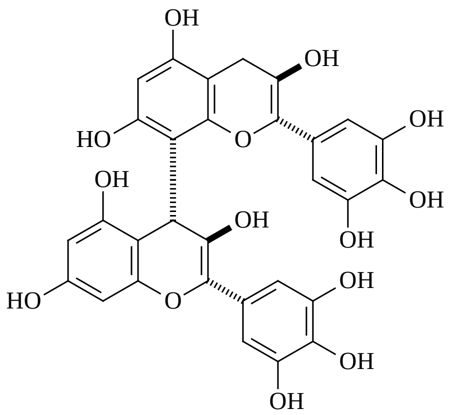
Figure 13.51
Ribis nigri folium (Blackcurrant leaf)

Constituents

The characteristic constituents of the leaf are approx. 0.5% of flavonoids (mono- and diglycosides of quercetin and kaempferol mainly isoquercitrin and rutin, myricetin), proanthocyanidins (e.g. dimeric prodelphinidin) and hydroxycinnamic acid derivatives including caffeic, chlorogenic and *p*-coumaric acids. The leaf contains traces of essential oil. In the fruit the following constituents are present: 10% of sugar, organic acids, flavonol glycosides and anthocyanidins (cyanidin-, delphinidin-glucoside).



myricetin



dimeric prodelphinidin

Figure 13.52-53
The structure of myricetin and dimeric prodelphinidin.

Uses

The preparations of the leaves can be used as an adjuvant in the treatment of rheumatic conditions. The preparations of the fruits have a mild antihypertensive, antioxidant and antifungal activities. The fresh products (e.g. fruit juice, wine and jam) play a role in the prevention of atherosclerosis and the treatment of anaemia.

Dosage (of the leaves)

Adults: Dried leaf as an infusion (20-50 g/L, infused for 15 minutes), 250-500 ml daily. Fluid extract (1:1), 5 ml twice daily, taken before meals.

Interaction with other medicaments and other form of interaction

The leaf has a diuretic action, therefore it should not be taken simultaneously with diuretics indicated for cardiac or renal insufficiency except on medical advice.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Stoechados flos (= Helichrysi flos)

Plant

Helichrysum arenarium (L.) Moench. – Dwarf everlast (Asteraceae)

This perennial plant is found in Eastern France to Denmark as well as in the mountains of Uzbekistan on sandy grasslands, and heathland. It is also widely spread on the Dalmatian Coast in Croatia. The flower heads are arranged in a loose panicle.

Drug

Stoechados flos (Dwarf everlast flowers, Ph. Helv.)

The drug consists of the dried flowers of *Helichrysum arenarium* (L.) Moench.

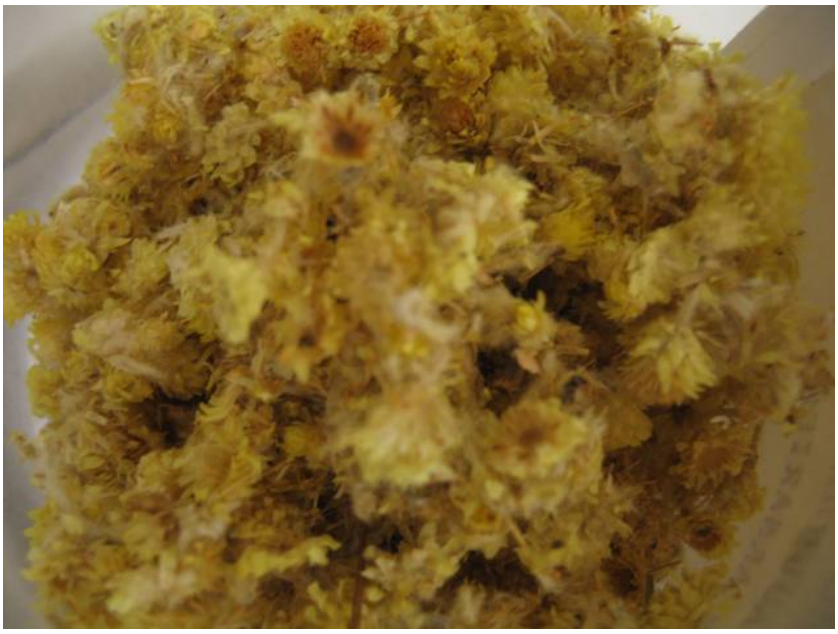
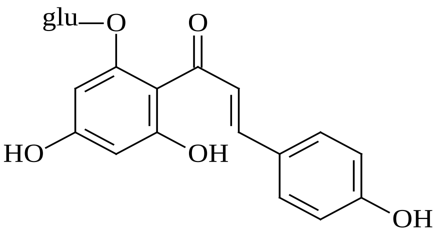


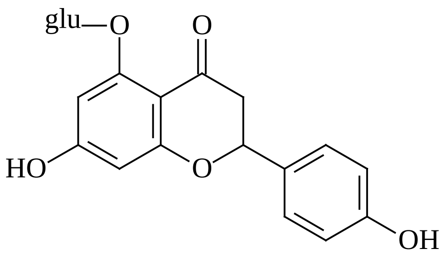
Figure 13.54
Stoechados flos (Dwarf everlast flowers)

Constituents

The main characteristic constituents of the drug are flavonoids (up to 0.4%) mainly the chalcon isosalipurpuroside, helicrysin (naringenin-5-O-glucoside) and the flavon-type apigenin, luteolin and their glucosides. Other constituents include coumarins (e.g. umbelliferone, scopoletin), sesquiterpene lactones and 0.05% essential oil.



isosalipurpuroside



helicrysin
(naringenin-5-O-glucoside)

Figure 13.55-56
The structure of isosalipurpuroside and helicrysin (naringenin-5-O-glucoside).

Uses

The drug has choleretic and spasmolytic effects. The therapeutic indications include the treatment of chronic gallbladder inflammation and the spasmodic pains of gallbladder. Efficacy in these indications is plausible on the basis of long-standing use.

Dosage

Adults: 3 g of the drug as an infusion, daily.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Populi gemma

Plant

Populus nigra L. – Black poplar (Salicaceae)

This tree is native to Europe, southwest and central Asia, and northwest Africa.

Drug

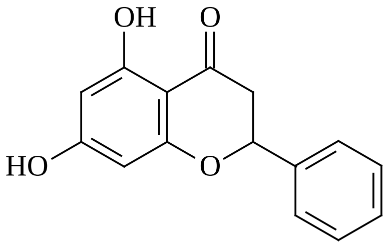
Populi gemma (Black poplar buds or balm of Gilead buds)

The drug consists of the dried, unopened leaf buds of *Populus nigra* L.

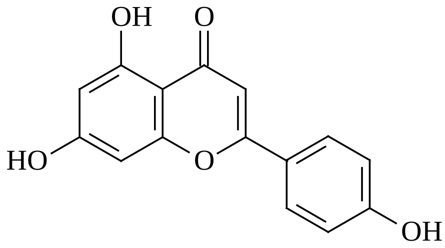
Figure 13.57
Populi gemma (Black poplar buds or balm of Gilead buds)

Constituents

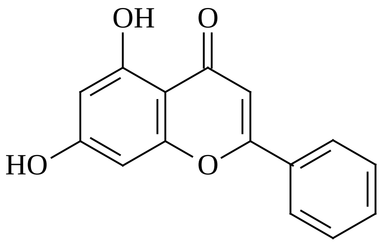
The main characteristic constituents of the drug are different types of flavonoids (e.g. crysin, apigenin, pinocembrin) and phenol glycosides (salicin, populin). Other constituents include 0.5% of essential oil (containing mainly sesquiterpenes) and wax.



pinocembrin (flavanon)



apigenin (flavon)



crysin (flavon)

Figure 13.58-60
The structure of pinocembrin (flavanon type), crysin (flavon type) and apigenin (flavon type).

Uses

The drug has anti-inflammatory, antibacterial, diuretic and expectorant activities. Its preparations stimulate wound healing. Therapeutic uses include superficial skin injuries, external hemorrhoids, frostbite and sunburn. Cosmetic industry also uses the drug in different products, e.g. creams, hair tonic.

Dosage

Semi-solid preparations equivalent to 20-30% of the drug.

Contra-indications

Sensitivity to poplar buds, propolis or salycilate.

Side effects

Occasional allergic skin reaction.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Propolis

Source

Apis mellifica L. – Honey bee (Apidae)

Drug

Propolis (Propolis or bee glue)

Propolis is the special material with which the honey bee seals cracks and crevices, and varnishes surfaces within the hive. Like honey, its composition varies according to botanical and geographical source. In temperate regions of Europe the resinous coating of poplar buds (*Populus nigra* and other *Populus* sp.) forms a major collection source for the bees.

Constituents

The main characteristic constituents of the drug are flavonoids (up to 6%), cinnamic acid derivatives (e.g. *p*-coumaric acid, caffeic acid, ferulic acid, vanillin, eugenol), mono- and sesquiterpenes, lipids, wax and microelements (e.g. Mn, Cu, Zn).

Uses

Propolis can be used in apitherapy. It has been shown to exhibit antiseptic, anti-inflammatory, antibacterial, antiviral and local anaesthetic properties. The drug and its preparations can be used in the case of different inflammations: gum, sore throat, ulceration of the leg.

Dosage

Tincture (90-96% ethanol), 20 drops, three times daily

Contra-indications

Sensitivity to poplar buds, propolis or salycilate. Allergy may occur.

Side effects

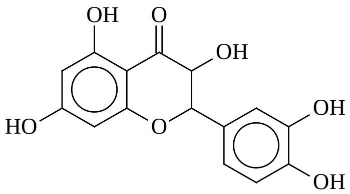
Occasional allergic skin reaction.

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

13.2 Flavonolignans

Flavonolignans are natural phenols composed of a flavonoid part and a lignan part. A number of flavonolignans arise from oxidative coupling of the 3-hydroxyflavanone taxifolin with coniferyl alcohol. The most important flavonolignans, e.g. silybin and silymarin, are produced by *Silybum marianum* (L.) Gärtn. These constituents have anti-hepatotoxic properties. Three flavonolignans derived from the flavone tricin have been isolated from the herb *Avena sativa*. Rhodiolin, the product of the oxidative coupling of coniferyl alcohol with the 7,8-dihydroxy grouping of the flavonol herbacetin, can be found in the rhizome of *Rhodiola rosea*.


taxifolin

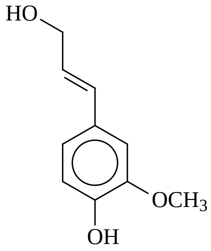

coniferyl alcohol

Figure 13.61-62
The structure of taxifolin and coniferyl alcohol.

Drugs

Silybi mariani fructus

Plant

Silybum marianum (L.) Gärtn. - Milk thistle (Marian thistle) (Asteraceae)

The plant is native to the Mediterranean region, from Southern Europe to Asia, it is now found throughout the world. As a cultivated plant it is grown as an annual or biennial ornamental for its attractive foliage.

Figure 13.63
Marian thistle (*Silybum marianum* (L.) Gärtn.)

Drug

Silybi mariani fructus (Milk thistle fruit, Ph. Eur.). **Other Drug** *Silybi mariani extractum siccum raffinatum et normatum* (Milk thistle refined and standardised dry extract, Ph. Eur.)

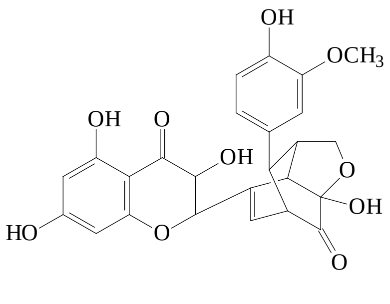
The drug consists of the mature fruit, devoid of the pappus, of *Silybum marianum* L. Gaertner. It contains minimum 1.5% of silymarin expressed as silibinin and calculated with reference to the dried drug.

Milk thistle dry extract consists of a refined and standardized dry extract produced from milk thistle fruit. It contains 90% of the nominal content of silymarin, expressed as silibinin, stated on the label. The nominal content of silymarin is within the range 30-65% m/m, calculated with reference to the dried extract.

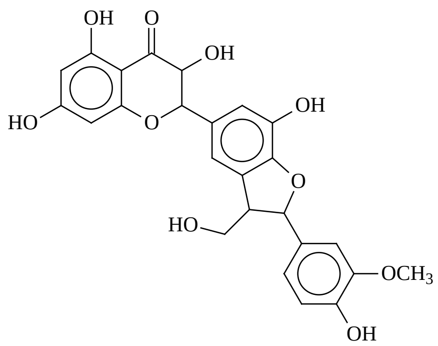
Figure 13.64
Silybi mariani fructus (Milk thistle fruit)

Constituents

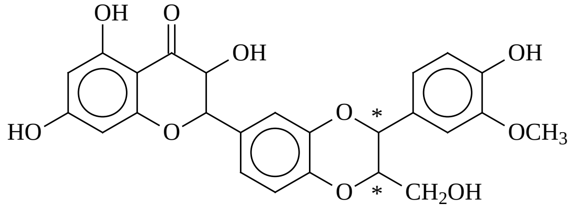
The active constituents of the drug are flavonolignans, collectively known as silymarin (1.5-3% by HPLC). Silymarin consists of silibinin, isosilibinin, silicristin and silidianin. Other constituents include the flavonoids taxifolin, quercetin, kaempferol, apigenin and eriodictyol; fatty oil (20-30%); phytosterols; the dimer dehydrodiconiferylalcohol, 5,7-dihydroxychromone and essential oil.



silidianin



silicristin



silibinin A, B (diastereoisomers)

Figure 13.65-67
The structure of silibinin A and B, silicristin and silidianin.

Uses

Therapeutic indications of the drug include toxic liver damage, supportive treatment in patients with chronic inflammatory liver conditions and hepatic cirrhosis.

Dosage

Adult daily dose: Solid or liquid extract equivalent to 154-324 mg of silymarin (HPLC method of the European Pharmacopoeia) or 200-420 mg of silymarin (UV spectroscopic method), taken in 2-3 divided doses. Silymarin can be dissolved poorly in water, therefore preparation of an infusion from the drug is not recommended.

Interaction with other medicaments and other form of interaction

It can moderately dicrease the plasma level of indinavir (used in AIDS therapy).

Pregnancy and lactation

No data available. In accordance with general medical practice, the product should not be used during pregnancy or lactation without medical advice.

Chapter 14
Drugs containing polyphenols

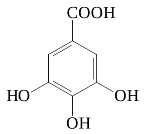
14.1 Tannins

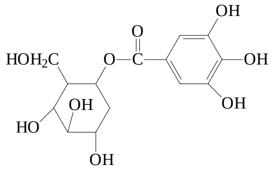
Tannins are polyphenolic secondary metabolites of higher plants. They comprise either galloyl esters and their derivatives (gallotannins, ellagitannins and complex tannins) or they are oligomeric and polymeric proanthocyanidins and can possess different interflavanyl coupling and substitution patterns (condensed tannins).

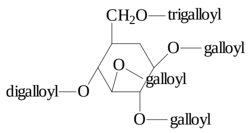
The hydrolysable tannins are gallotannins and elagitannins (**Figure 14.1-6**). They are polyesters of glucose and can be hydrolysed by acids or enzymes such as tannase. They release sugar upon hydrolysis. Gallotannins are the simplest hydrolysable tannins, containing a polyphenolic and a polyol residue (mostly derived from D-glucose). Tannic acid is a polymer of about eight monomers of gallic acid and glucose. Ellagitannins are formed from the gallotannins by the oxidative coupling of at least two galloyl units, yielding an axially chiral hexahydroxydiphenoyl (HHDP) unit. Ellagitannins are unstable and hydrolysed over time with formation of free ellagic acid and decrease of their solubility. Condensed tannins (**Figure 14.7-11**) are not very stable; they can be oxidized into soluble phlobaphens, which have no tanning properties anymore. Condensed and hydrolysable tannins can be distinguished with ferric chloride reaction but this reaction is not specific, every compound containing phenolic OH-groups gives this reaction. The structure of the complex can be seen in **Figure 14.12.** The color of the complex depends on the number and the position of the phenolic OH-groups. The hydrolysable-type tannins (they contain gallic and ellagic acids) produce blue color with ferric-(III)-chloride and the condensed-type tannins (catechins) green (greenish-blue), respectively. This reaction is accomplished in neutral or mildly acidic medium. The Fe^{3+}-ions can produce chelate complexes with phenolic, electron donor OH-groups located in ortho positions.

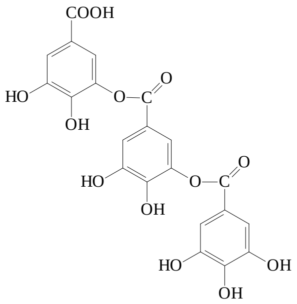
Tannins can be distinguished from other phenolic compounds based on their chemical reactivities and biological activities. Tannins were traditionally used for “tanning”, converting animal hides to leather. This refers to one of their leading properties, the ability to interact with proteins and precipitate them. Tannin-containing drugs have been used traditionally as styptics. Internally they can be used for the protection of inflamed surfaces of mouth and throat. They have antidiarroeal effect, and they have been applied as antidotes in heavy metal and alkaloid poisoning.

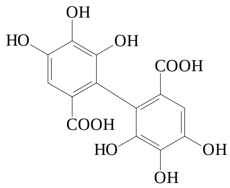
The internal absorption of concomitantly administerd medicines may be delayed by tannin containing-drugs. For this reason, the product should be taken 1 hour or more before or after intake of other medicinal products. Allergic reactions and mucous membrane irritation have been reported, patients susceptible to allergic reactions should use tannin-containing drugs carefully or not use them at all. Safety during pregnancy and lactation, as well as in children under the age of 18 has not been established, therefore, the use of these drugs during pregnancy and lactation, as well as in children under the age of 18 is not recommended. Their use is contraindicated in inflammatory bowel diseases and constipation, as well. Long-term use of tannin-containing drugs may be hepatotoxic. If the symptoms persist during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted in all cases.


gallic acid


glucogallin


octagalloyl glucose


m-trigallic acid


hexaoxydiphenic acid

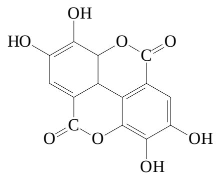
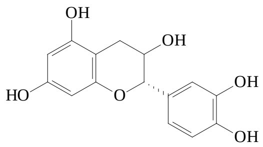
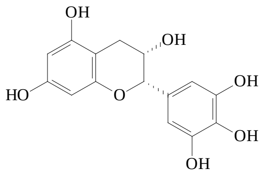
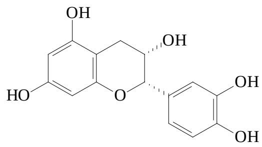
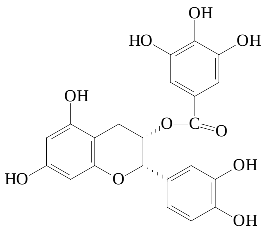

ellagic acid

Figure 14.1-6
Derivatives of gallic acid and ellagic acid.


catechin


epicatechin


epigallocatechin


epicatechin gallate

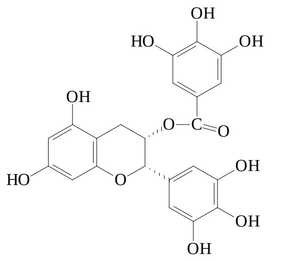

epigallocatechin gallate

Figure 14.7-11
Derivatives of catechin.

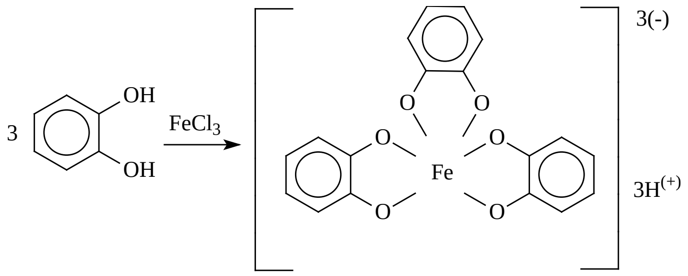


Figure 14.12
The complex developed after the reaction of phenolic OH-groups with $FeCl_3$.

Drugs

Quercus cortex

Plant

Quercus robur L. - Pedunculate oak, *Q. petraea* Liebl. - Sessile oak (Fagaceae)

These plants are native to Europe and the Caucasus. Oak bark is harvested in spring from March to April.

Figure 14.13
Pedunculate oak (*Quercus robur* L.)

Drug

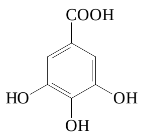
Quercus cortex (Oak bark, Ph. Eur)

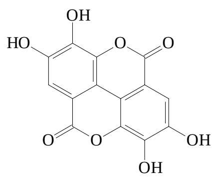
The drug is the cut and dried bark of the fresh young branches of *Quercus robur* L., *Q. petraea* (Matt.) Liebl. and *Q. pubescens* Willd. It contains not less than 3.0% of tannins, expressed as pyrogallol calculated with reference to the dried drug.

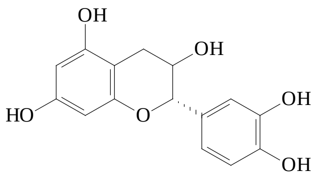
Figure 14.14
Quercus cortex (Oak bark)

Constituents

Oak bark contains 8-20% tannins, hydrolyzable (gallotannins and elagitannins), condensed tannins, flavano-ellagitannins (acutissimins A an B, eugenigrandin A, guajavin B, stenophyllanin), procyanidinoellagitannin (mongolicanin), oligomeric proanthocyanidins, triterpenes (friedelin, friedelinol, 3-friedelanol), insoluble lipid polyesters (suberins) and volatile acids (acetic and formic acid).


gallic acid


ellagic acid


catechin

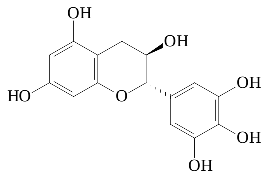

gallocatechin

Figure 14.15-18
The structure of gallic acid, ellagic acid, catechin and gallocatechin.

Uses

It is used internally in diarrhoea, externally against pharyngitis (inflammation of the throat) and stomatis (inflammation of the mucous membrane of the mouth), or hemorrhoids.

Dosage

Adult and elderly daily dose: 2 g of dried, ground drug should be boiled with 100 mL water for 5 minutes and filtered. This extract can be used to paint, gargle, or wash wounds, but it is recommended not to use for more than 1 week. Internally, in the case of severe diarrhoea, the single dose is 1 g, the maximum daily dose is 3 g, but do not use longer than 3 days. The dose of a dry extract is 140 mg, 4 times daily.

Children: The use in children and adolescents under 18 years of age is not recommended due to lack of adequate data.

Overdose: No case of overdose has been reported.

Interactions

Internal absorption of concomitantly administerd medicine may be delayed. For this reason, the product should be taken 1 hour or more before or after intake of other medicinal products.

Contra-indications

Allergic reactions have been reported, but their frequency is unknown.

Pregnancy and lactation

Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

Gall

Plant

Quercus infectoria Oliv. – Aleppo oak (Fagaceae)

Drug

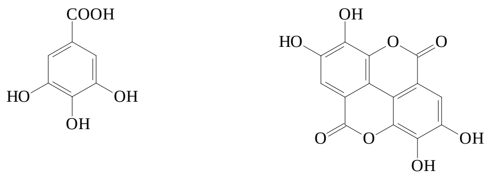
Galla (Gall)

It is an apple-like gall commonly found on many species of oak developing from the leaf buds due to chemicals injected by the larva of certain kinds of gall wasps.

Figure 14.19
Galla (Gall)

Constituents

The characteristic constituents are tannins (derivatives of gallic acid, 40-60%), gallic acid and ellagic acid. The drug also contains starch.



gallic acid ellagic acid

Figure 14.20-21
The structure of gallic acid and ellagic acid.

Uses

Externally the extract is traditionally used as adstringent, hemostatic, and for the treatment of thrush and gingivitis. However, the scientific documentation of these effects is sparse.

Dosage

Adult and elderly daily dose: Prepare a 1% decoction or tincture for a daily rinse.

Ratanhiae radix

Plant

Krameria triandra Ruiz et Pavon (syn: *Krameria lappacea* Burdet et Simpson) – Peruvian rhatany (Krameriaceae)

The plant is native to the mountain slopes of Peru and Bolivia.

Drug

Ratanhiae radix (Rhatany root, Ph. Eur.). **Other Drug** *Ratanhiae tictura* (Rhatany tincture, Ph. Eur.)

The drug is the dried root of Peruvian rhatany, a perennial shrub. Rhatany root, known as Peruvian rhatany, consists of the dried, usually fragmented, underground organs of *Krameria*

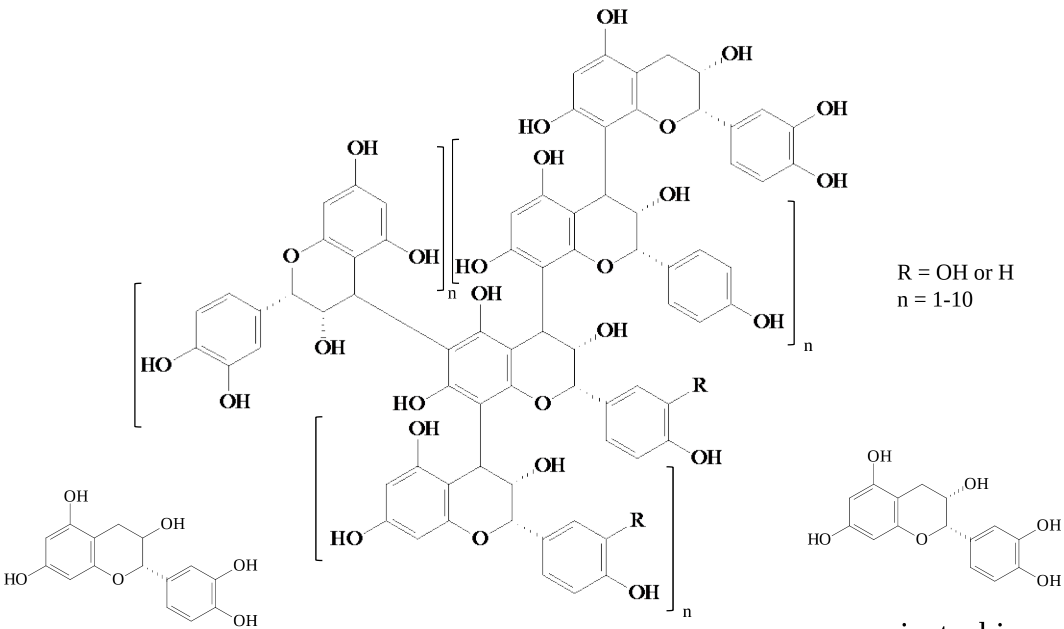
triandra Ruiz and Pavon. It contains not less than 5% of tannins, expressed as pyrogallol calculated with reference to the dried drug.

The tincture produced from Rhatany root contains not less than 1% m/m of tannins, expressed as pyrogallol.

Figure 14.22
Ratanhiae radix (Rhatany root)

Constituents

It contains 5-15% of catechin tannins, phlobaphenes („rhatania-red") and neolignans.



catechin ratanhia proanthocyanidin epicatechin

Figure 14.23-25
The structure of catechin, epicatechin and ratanhia proanthocyanidin.

Uses

It is traditionally used as adstringent, against stomatis, bleeding of the gums, gingivitis (inflammation of the gums), and pharyngitis (especially as a tincture). However, the scientific documentation of these effects is sparse.

Dosage

Adult and elderly daily dose: If rhatany root is used internally, the single dose is 0.5-1.5 g, and the maximum daily dose is 1.5-4.5 g, but it should be used internally only for a short period of time. For external use, a 2% extract should be prepared with 5 minutes of boiling.

Hamamelidis folium

Plant

Hamamelis virginiana L. - Virginian witch hazel (Hamamelidaceae)

The plant is a deciduous large shrub native to eastern North America.

Drug

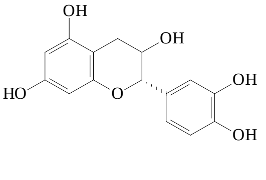
Hamamelidis folium (Hamamelis leaf, Ph. Eur.).

Hamamelis leaf consists of the whole or cut, dried leaf of *Hamamelis virginiana* L. It contains not less than 3% of tannins, expressed as pyrogallol, calculated with reference to the dried drug.

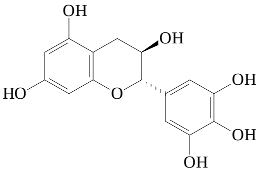
Figure 14.26
Hamamelidis folium (Hamamelis leaf)

Constituents

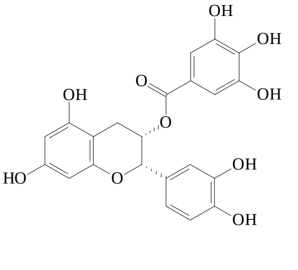
The characteristic constituents are tannins (5-10%), including condensed tannins, e.g. proanthocyanidin oligomers with catechin and/or gallocatechin units, hydrolysable tannins such as hamamelitannin, (+)-catechin, (+)-gallocatechin, (-)-epicatechin-gallate and (-)-epigallocatechin gallate. Other constituents are flavonoids, phenolic acids and essential oil.



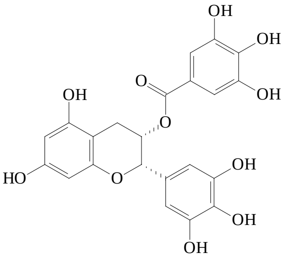
catechin



gallocatechin



epicatechin gallate



epigallocatechin gallate

Figure 14.27-30
The structure of catechin, gallocatechin, epicatechin gallate and epigallocatechin gallate.

Uses

It is traditionally used for relief of minor skin inflammation and dryness of the skin, for the temporary relief of the symptoms associated with hemorrhoids, such as itching, burning sensation or pain, and used as a mouthwash for relief of minor inflammatory conditions of the oral mucosa.

Dosage

Adult and elderly daily dose: For cutaneous use, the tincture should be used several times daily in a strength corresponding to 5-10% in semisolid preparations. The dry extract in a strength corresponding to 1.3% as an ointment should be used several times daily. The average duration of use is 1 week. For anorectal use, the tincture in a strength corresponding to 5-10% in semisolid and liquid preparations should be used several times daily. Comminuted herbal substances should be used as decoction: 5-10g/250 ml, up to 3 times a day as impregnated dressings. For rectal use, one suppository containing 66 mg of dry extract (5-7.7:1; ethanol 30% m/m) should be used two or three times a day. The recommended duration of use is 4 days. For gargles, 2-4 ml tincture (1:10; ethanol 45% (diluted (1:3) with water) should be used three times daily, or comminuted herbal substance as herbal tea: 2-3 g up to 3 times a day.

Children: Due to the lack of adequate data the use is not recommended in children and adolescents under 18 years of age.

Overdose: No case of overdose has been reported.

Contraindications

Hypersensitivity to the active substance(s). Allergic contact dermatitis has been reported. The frequency is not known. If other adverse reactions not mentioned above occur, a doctor or a qualified health care practitioner should be consulted. Available tests on carcinogenicity and genotoxicity did not give any reason for concern.

Pregnancy and lactation

Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

Tormentillae rhizoma

Plant

Potentilla erecta (L.) Räuschel (syn.: *Tormentilla* erecta L.) – Common tormentil (Rosaceae)

The plant is native to North and Middle Europe, as well as North Asia. It occurs frequently in the Hungarian Mountains and rarely in the Great Hungarian Plain. The plant can be cultivated.

Drug

Tormentillae rhizoma (Tormentil, Ph. Eur.). **Other Drug** *Tormentillae tinctura* (Tormentil tincture, Ph. Eur.)

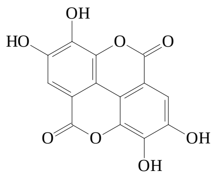
The drug is the whole or cut, dried rhizome of *Potentilla erecta* (L.) Raeusch. (*P. tormentilla* Stokes). It contains not less than 7% of tannins, expressed as pyrogallol, calculated with reference to the dried drug.

The drug has a bitter taste.

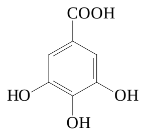
The tincture produced from *Tormentil* contains minimum 1.5% *m/m* of tannins, expressed as pyrogallol. The tincture is produced from 1 part of comminuted drug and 5 parts of ethanol (70 per cent *V/V*) by a suitable procedure. It is a red or reddish-brown liquid.

Constituents

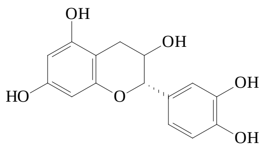
It contains 15-22% of total tannins (15-20% condensed tannins, about 3.5% hydrolysable tannins, plus 7% red, soluble phlobaphene), hydrolizable ellagitannins, flavonoids, phenolcarbonic acids, proanthocyanidins, triterpene saponins (e.g. tormentosid) and fatty acids.



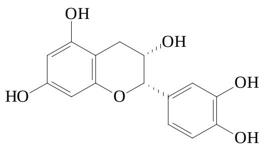
ellagic acid



gallic acid



catechin



epicatechin

Figure 14.31-34
The structure of ellagic acid, gallic acid, catechin and epicatechin.

Uses

It is traditionally used as an adstringent, antibacterial, antiviral, anti-inflammatory drug; internally as antidiarrhoeal, in the case of enterocolitis and dysentery; externally as gargle and mouth rinse. However, the scientific documentation of these effects is sparse.

Dosage

Adult and elderly daily dose: The daily internal dose of tormentil is 4-6 g in 2-3 portions, in the form of an infusion (made with 200 mL water, boiled for 10 minutes).

Children: There are no data from clinical trials or observational trials for the above mentioned herbal preparations available. Therefore the use should be restricted to adults. The use of the dry extract was allowed in Germany for adolescents in case of unspecific acute diarrhoea.

Contra-indications

The only reported side effects were mild gastrointestinal symptoms. The medicinal use of Tormentillae rhizoma can be regarded as safe.

Pregnancy and lactation

No data are available on the safe use during pregnancy and lactation. Therefore the use of tormentil is not recommended during pregnancy and lactation.

Anserinae herba

Plant

Potentilla anserina L. - Common silverweed (Rosaceae)

The plant is native throughout the temperate Northern Hemisphere.

Figure 14.35
Common silverweed (*Potentilla anserina* L.)

Drug

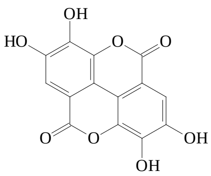
Anserinae herba (Silverweed flowering shoot, DAC). **Other Drug** *Anserinae radix* (Silverweed root)

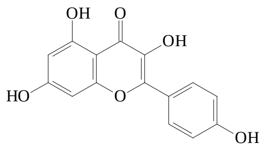
Silverweed flowering shoot consists of the dried aerial parts of *Potentilla anserina* L. collected during flowering.

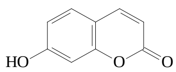
Figure 14.36
Anserinae herba (Silverweed flowering shoot)

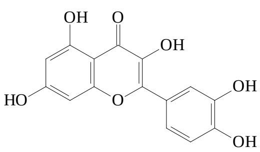
Constituents

The drug contains 6-10% of tannins (mainly ellagitannins), flavonoids, leucoanthocyanidins, coumarins (umbelliferon, scopoletin) and triterpenes.


ellagic acid


kaempferol


umbelliferone


quercetin

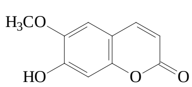

scopoletin

Figure 14.37-41
The structure of ellagic acid, kaempferol, quercetin, umbelliferone and scopoletin.

Uses

It is traditionally used as antibacterial, adstringent, anti-inflammatory in gastritis and enteritis (also in children). However, the scientific documentation of these effects is sparse.

Dosage

Adult and elderly daily dose: The maximal daily dose is 4 g prepared in 200 mL water in the form of infusion or decoction, in 2-3 portions.

Gei rhizoma et radix

Plant

Geum urbanum L. – Colewort (Rosaceae)

The plant is native to Europe, and the temperate regions of Asia and North Africa. It is a perennial herbaceous plant living in forests (especially in oak forests) and brushwoods.

Figure 14.42
Colewort (*Geum urbanum* L.)

Drug

Gei urbani rhizoma et radix (Colewort rhizome and root)

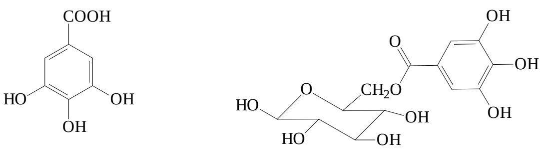
The drug consists of the dried underground parts of *Geum urbanum* L.

Figure 14.43
Gei urbani rhizoma et radix (Colewort root and rhizome)

Constituents

It contains 12-28% of tannins (mainly gallotannins and ellagitannins), catechin, caffeic acid, 0.02-0.3% of essential oil (eugenol in 50-89%, gein), triterpenes, phenolcarbonic acids, ascorbic acid, malic acid and sugars.

eugenol gein



gallic acid 6-galloyl-glucose

Figure 14.44-47
The structure of eugenol, gein, gallic acid and 6-galloyl-glucose.

Uses

The rhizome and the root is adstringent, antidiarrhoeal, antibacterial, anti-inflammatory, anti-haemorrhoidal. However, the scientific documentation of these effects is sparse. It is also processed by the liqueur industry.

Dosage

Adult and elderly daily dose: For internal use, an infusion (10 minutes) should be made from 0.5-1 g drug and 150-200 mL water. For external use, pour 200 mL lukewarm water to 0.5-1 g drug, and boil it for 5-10 minutes.

Agrimoniae herba

Plant

Agrimonia eupatoria L. - Common agrimony (Rosaceae)

The plant occurs both in grassy and shrubby habitats.

Figure 14.48
Common agrimony (*Agrimonia eupatoria* L.)

Drug

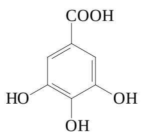
Agrimoniae herba (Agrimony, Ph. Eur.).

The drug is the dried flowering tops of *Agrimonia eupatoria* L. It contains not less than 2% of tannins, expressed as pyrogallol, calculated with reference to the dried drug.

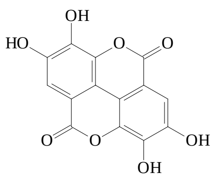
Figure 14.49
Agrimoniae herba (Agrimony)

Constituents

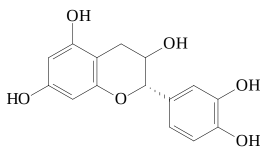
It contains 4-10% of catechin tannins, 5-6% of ellagitannins and gallotannins, triterpenes (mainly ursolic acid) and flavonoids.



gallic acid



ellagic acid



catechin

Figure 14.50-52
The structure of gallic acid, ellagic acid and catechin.

Uses

It is traditionally used as mild adstringent and antibacterial, therefore internally can be used in cases of gastroenteritis, cholecystitis (inflammation of the gallbladder) and cholangitis (inflammation of the bile ducts). It can also be used as a gargle. Its tea is particularly good for summer diarrhoea, enteritis and colitis. However, the scientific documentation of these effects is sparse.

Dosage

Adult and elderly daily dose: For treatment of skin disorders, it is used in the form of bath. The infusion (100 g of dried drug and 2 L water) should be added to the bath. For internal use, the daily dose is 1.5 g prepared with 150-200 mL water, as infusion or decoction. Long-term use is not recommended.

Fragariae folium

Plant

Fragaria vesca L. - Wild strawberry (Rosaceae)

The plant is native to Europe and Asia.

Figure 14.53
Wild strawberry (*Fragaria vesca* L.)

Drug

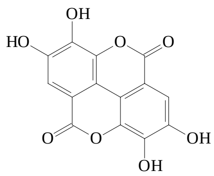
Fragariae folium (Wild strawberry leaf, DAC).

Strawberry leaf consists of the dried leaves of *Fragaria vesca* L.

Figure 14.54
Fragariae folium (Wild strawberry leaf)

Constituents

The drug contains 5-10% of ellagitannins, oligomeric proanthocyanidins, flavonoids, caffeic acid derivatives and traces of essential oil.



ellagic acid

Figure 14.55
The structure of ellagic acid.

Uses

It is traditionally used as adstringent in the case of diarrhoea, and as mild anti-inflammatory in inflammations of the mucous membrane of the mouth. However, the scientific documentation of these effects is sparse. Wild strawberry fruit is processed by the food industry (syrups, jams).

Dosage

Adult and elderly daily dose: 250 mL boiling water should be poured on 2 g drug, and filtered after 15 minutes.

Alchemillae herba

Plant

Alchemilla vulgaris L. - Lady's mantle/Alchemilla (Rosaceae)

The plant is native to meadows and sparse forests.

Figure 14.56
Lady's mantle/Alchemilla (*Alchemilla vulgaris* L.)

Drug

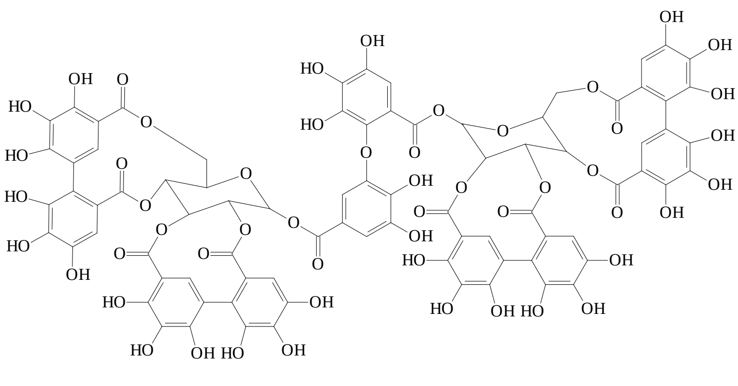
Alchemillae herba (Alchemilla, Ph. Eur.).

Alchemilla consists of the whole or cut, dried, flowering aerial parts of *Alchemilla vulgaris* L. s. l. It contains not less than 6% of tannins, expressed as pyrogallol, calculated with reference to the dried drug.

Figure 14.57
Alchemillae herba (Alchemilla)

Constituents

It contains 5-8% of gallic acid derivatives (the main component is agrimoniin), ellagic acid, pedunculagin, flavonoids and salicylic acid in traces.



agrimoniin

Figure 14.58-59
The structure of agrimoniin and pedunculagin.

Uses

It is traditionally used as adstringent, antidiarrhoeal, antiviral, antioxidant, and antimutagenic; internally in cases of diarrhoea, and as a gargle; externally as local hemostyptic, against eczema, rashes, or dermatitis. However, the scientific documentation of these effects is sparse.

Dosage

Adult and elderly daily dose: The daily dose is 5-10 g. The single dose is 2-4 g, which should be prepared with 200-250 mL boiling water as infusion, and filtered after 10 minutes.

Polygoni avicularis herba

Plant

Polygonum aviculare L. – Knotgrass (Polygonaceae)

The plant is native to Europe and Temperate Asia.

Figure 14.60
Knotgrass (*Polygonum aviculare* L.)

Drug

Polygoni avicularis herba (Knotgrass, Ph. Eur.).

The drug is the whole or cut dried flowering aerial parts of *Polygonum aviculare* L. s.l. It contains not less than 0.30% of flavonoids, expressed as hyperoside, calculated with reference to the dried drug.

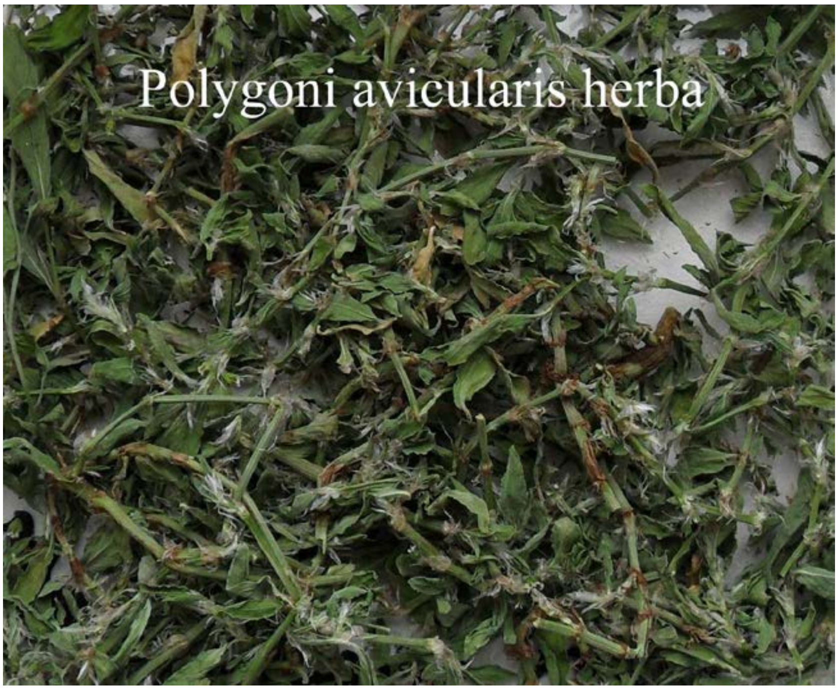
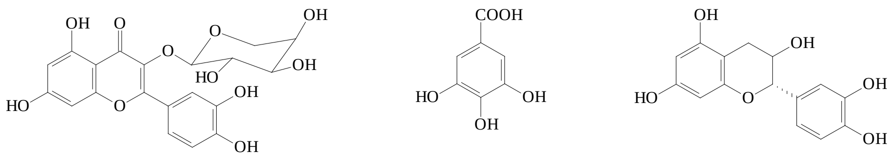


Figure 14.61
Polygoni avicularis herba (Knotgrass)

Constituents

The drug contains 3.6% of tannins (gallic acid and catechin derivatives), flavonoids (e.g. avicularin), mucilage and coumarins.



avicularin gallic acid catechin

Figure 14.62-64
The structure of avicularin, catechin and gallic acid.

Uses

It is traditionally used as expectorant, diuretic, and against mild inflammation of the respiratory tracts. However, the scientific documentation of these effects is sparse.

Dosage

Adult and elderly daily dose: Infusion should be made from 2 g drug with 200 mL water, which can be administered 2-3 times daily.

Rubi fruticosi folium

Plant

Rubus fruticosus L. - Blackberry (Rosaceae)

The plant is native to the northern hemisphere.

Figure 14.65
Blackberry (*Rubus fruticosus* L.)

Drug

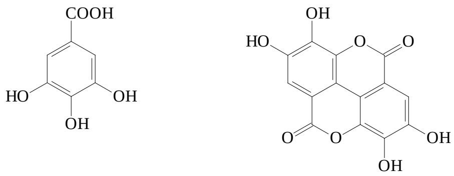
Rubi fruticosi folium (Blackberry leaf, DAC). **Other drugs:** *Rubi fruticosi fructus*, (Blackberry fruit), *Rubi fruticosi radix* (Blackberry root)

Blackberry leaf consists of the dried leaves of *Rubus fruticosus* L.

Figure 14.66
Rubi fruticosi folium (Blackberry leaf)

Constituents

In the leaf: 8-10% of hydrolyzable gallotannins, dimeric ellagitannins, organic acids, flavonoids, cyanidine glycosides, pentacyclic triterpene acids. *In the fruit*: special cyanidine glycosides, organic acids, alcohols and esters, sugars, pectin.



gallic acid ellagic acid

Figure 14.67-68
The structure of gallic acid and ellagic acid.

Uses

It is traditionally used as adstringent, antidiarrhoeal, diaphoretic, for gargle, and against mestrual cramps. However, the scientific documentation of these effects is sparse. It is the best alternative to caffeine containing types of tea. The raw fruits or the fruit juice and jam are rich in vitamins, trace elements and antioxidants.

Dosage

Adult and elderly daily dose: The daily dose is 200 mL decoction prepared from 1.5 g drug.

Rubi idaei folium

Plant

Rubus idaeus L. – Raspberry (Rosaceae)

The plant is native to the northern hemisphere. It can be cultivated.

Figure 14.69
Raspberry (*Rubus idaeus* L.)

Drug

Rubi idaei folium (Raspberry leaf, DAC). **Other drugs:** *Rubi idaei fructus* (Raspberry fruit).

Raspberry leaf consists of the dried leaves of *Rubus idaeus* L.

Figure 14.70
Rubi idaei folium (Raspberry leaf)

Constituents

Similar to those in blackberry. *In the fruit* there are special cyanidine glycosides, organic acids, alcohols and esters, sugars and pectin.

Uses

It is traditionally used for the symptomatic relief of minor spasms associated with menstrual periods, for the symptomatic treatment of mild inflammation in the mouth or throat, for the symptomatic treatment of mild diarrhoea. However, the scientific documentation of these effects is sparse and of questionable quality.

Dosage

Adult and elderly daily dose: For relief of minor spasms associated with menstrual periods, the single dose of dry extract is 113-226 mg up to 3 to 4 times daily. For the symptomatic treatment of mild inflammation in the mouth or throat, the single dose for an infusion for oromucosal use is 1.5-8 g of the comminuted herbal substance in 150 mL of boiling water 3 times daily. For the symptomatic treatment of mild diarrhoea, the single dose is 1.5-8 g of the comminuted herbal substance in 150 mL of boiling water as an infusion 3 times daily.

Children: The use in children and adolescents under 18 years of age has not been established due to lack of adequate data.

Overdose: No case of overdose has been reported.

Contraindications

Hypersensitivity to the active substance(s).

Pregnancy and lactation

Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

Coryli folium

Plant

Corylus avellana L. – (Common) hazel (Betulaceae)

The plant is native to Europe and Asia Minor. It is cultivated.

Figure 14.71
Fig. 14.71 Common hazel (*Corylus avellana* L.)

Drug

Coryli (avellanae) folium (Hazel leaf).

Hazel leaf consists of the dried leaves of *Corylus avellana* L.

Figure 14.72
Coryli folium (Hazel leaf)

Constituents

It contains 3-5% of tannins, flavonoids, chlorogenic acid, taraxasterol, β-sitosterol and essential oil.

Uses

It is traditionally used as anti-hemorrhoidal, anti-inflammatory (e.g. gingivitis), tissue regeneration inducing (wound healing) drug. However, the scientific documentation of these effects is sparse.

Dosage

Adult and elderly daily dose: The daily dose is 3-5 g, from which an infusion should be made, and it should be macerated for hours.

Myrtilli fructus

Plant

Vaccinium myrtillus L. – Bilberry / European blueberry (Ericaceae)

The plant is native to Europe, and Northwest Asia.

Figure 14.73
Bilberry / European blueberry (*Vaccinium myrtillus* L.)

Drug

Myrtilli fructus siccus (Bilberry fruit, dried, Ph. Eur.), *Myrtilli fructus recens* (Bilberry fruit, fresh, Ph. Eur.). **Other drugs:** *Myrtilli folium et fructus* (Bilberry leaves and berries)

The drug is the dried ripe fruit of *Vaccinium myrtillus* L. It contains not less than 1% of tannins, expressed as pyrogallol, and calculated with reference to the dried drug.

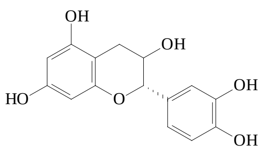
The drug is the fresh or frozen ripe fruit of *Vaccinium myrtillus* L. It contains not less than 0.30% of anthocyanins, expressed as cyanidin-3-glucoside chloride (chrysanthemin), and calculated with reference to the dried drug.

Figure 14.74
Myrtilli folium (Bilberry leaves)

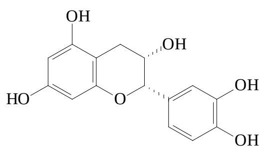
Figure 14.75
Myrtilli fructus siccus (Bilberry fruit, dried)

Constituents

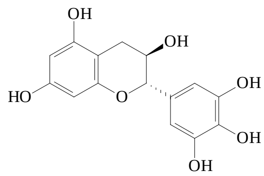
In the leaf: 0.8-6.7% catechin tannins, catechin, epicatechin, gallocatechin, proanthocyanidin, flavonoids, iridoids, phenolcarboxylic acids (chlorogenic acid) quinolizidine alkaloids (myrtine, epimyrtine), hydroquinone and arbutin, about 1 mg% chrome. *In the fruit*: about 1% of catechin tannins, anthocyanidins, flavonoid glycosides (e.g. astragalin), phenolcarboxylic acids, iridoids, inverted sugar, pectin, resveratrol.



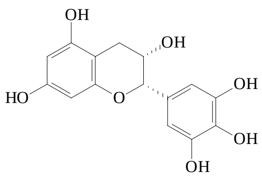
catechin



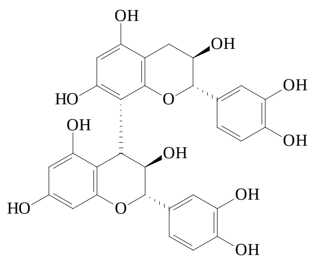
epicatechin



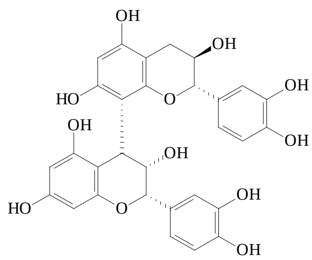
gallocatechin



epigallocatechin



procyanidin B-1



procyanidin B-2

Figure 14.76-81
The structure of catechin, epicatechin, gallocatechin, epigallocatechin, procyanidin B-1 and B-2.

Uses

For internal purposes the drug can be used for the symptomatic treatment of problems related to varicose veins such as painful and heavy legs. Dried bilberry fruit is used in the treatment of acute, non-specific diarrhoea. The drug is also applied in the topical treatment of mild inflammation of the mucous membranes of the mouth and throat.

Dosage

Adult and elderly daily dose: For internal use, the daily dose of the leaf is 1 g (infusion prepared with 200 mL water). Standardized extracts of bilberry fruit containing 36% of anthocyanidins: 320-480 mg/day; dried bilberry fruit: 20-60 g/day. For external use (washing or poultice), prepare an infusion from 1-2 g leaf with 250 mL water, and filter it after 15 minutes.

2.5-5.0 g fruit should be boiled with 150-200 mL water for 10 minutes, or macerated for 2-3 hours.

Pregnancy and lactation

Anthocyanins are well tolerated in pregnancy, they do not induce side-effects, but consultation with a doctor is always recommended.

Pelargonii radix

Plant

Pelargonium sidoides DC. – South African geranium, *Pelargonium reniforme* Curt. –, (Geraniaceae)

The plants are native to South Africa.

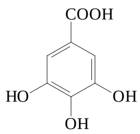
Drug

Pelargonii radix (Pelargonium root, Ph. Eur.).

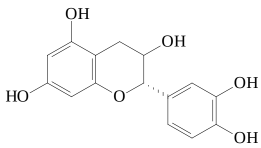
Pelargonium root consists of the dried, usually fragmented, underground organs of *Pelargonium sidoides* DC. and/or *Pelargonium reniforme* Curt. It contains not less than 2% of tannins, expressed as pyrogallol, and calculated with reference to the dried drug.

Constituents

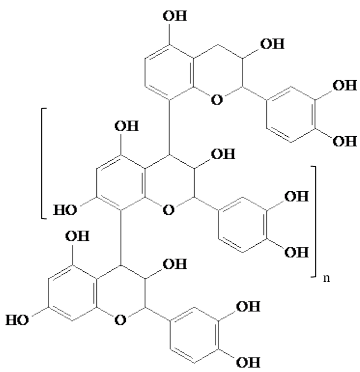
The drug contains gallic acid, catechin, procyanidin polymer composed of catechin monomers and procyanidin polymer composed of gallocatechin monomers. Other constituents include coumarins (e.g. scopoletin, 5,6,7-trimethoxycoumarin, 6,8-dihydroxy-7-methoxycoumarin, 6,8-dihydoxy-5,7-dimethoxycoumarine, umckalin-7-β-glucoside, 5,6-dimethoxycoumarin-7-sulfate), flavonoids and sterols.



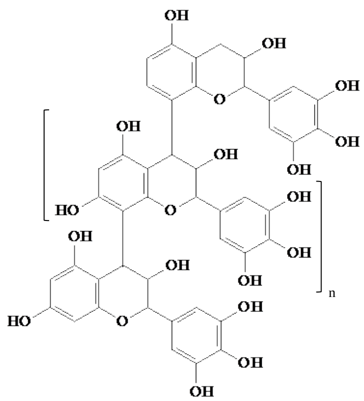
gallic acid



catechin



procyanidin polymer composed of catechin monomers



procyanidin polymer composed of gallocatechin monomers

Figure 14.82-85

The structure of gallic acid, catechin, procyanidin polymer composed of catechin monomers and procyanidin polymer composed of gallocatechin monomers.

Uses

It is traditionally used for the symptomatic treatment of common cold. Based on the available clinical data, the efficacy of *Pelargonii radix* in the symptomatic treatment of acute respiratory diseases, e.g. acute bronchitis, sinusitis, tonsillopharyngitis and common cold is not proven properly.

Dosage

Adult and elderly daily dose: Single dose: 1.14 g, 3 times daily.

Children: Single dose: 0.76 g, 3 times daily. The use in children under 6 years of age is not recommended due to lack of adequate data.

Overdose: No case of overdose has been reported.

Contra-indications

Hypersensitivity to the active substance(s). Although there is limited knowledge about pharmacokinetic parameters and toxicological data of Pelargonium extract, the current non-clinical results (including data regarding the constituents) suggest that the application of Pelargonium preparations is probably safe.

Pregnancy and lactation

Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

Cotini folium

Plant

Cotinus coggygria Scop. – Eurasian smoketree (Anacardiaceae)

The plant is native to Europe, Asia and China. In Hungary it can be found in karst scrub forests.

Figure 14.86
Eurasian smoketree (*Cotinus coggygria* Scop.)

Drug

Cotini folium (Smoke tree leaf)

The drug consists of the green summer leaves of the bush or small tree *Cotinus coggygria* (Scop.).

Figure 14.87
Cotini folium (Smoke tree leaf)

Constituents

The characteristic constituents of the drug are tannins (18-20%) including gallotannins, ellagic acid and catechin-derivatives. Other constituents include flavonoids and essential oil.

Uses

The drug has adstringent, hemostyptic and antibacterial activities. It is traditionally used for rinsing the mouth e.g. after tooth extraction and in gingivitis.

Index

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15 WHO Monographs on Selected Medicinal Plants. Volume 2. Geneva, World Health Organisation, 2002

16 WHO Monographs on Selected Medicinal Plants. Volume 3. Geneva, World Health Organisation, 2007

17 WHO Monographs on Selected Medicinal Plants. Volume 4. Geneva, World Health Organisation, 2009

Recommended homepages and databases

1 *Cochrane Library:* http://www.thecochranelibrary.com

2 *European Medicines Agency:* http://www.ema.europa.eu/ema/

3 *MedlinePlus:* http://www.nlm.nih.gov/medlineplus/druginfo/herb_All.html

4 *National Institute for Food and Nutrition Science:* www.oeti.hu

5 *National Institute for Quality- and Organizational Development in Healthcare and Medicines:* www.ogyi.hu

6 *US Food and Drug Administration:* http://www.fda.gov/

7 *World Health Organization:* http://www.who.int/en/

Appendices

Indications

Indications			
Latin name of species	*English name of species*	*Latin name of drug/drugs*	*English name of drug/drugs*
Vitamin A and D supplements			
Gadus morhua	Cod	Iecoris aselli oleum A, Iecoric aselli oleum B, Iecoris aselli oleum domestici	Cod-liver oil, Cod-liver oil (type A), Cod-liver oil (type B), Farmed cod-liver oil
Hemorrhoids			
Fagopyrum esculentum	Buckwheat	Fagopyri herba	Buckwheat herb
Hamamelis virginiana	Virginian witch-hazel	Hamamelidis folium	Hamamelis leaf
Melilotus officinalis	Sweet clover, Yellow melilot, Ribbed melilot, Common melilot	Meliloti herba	Melilot
Myroxylon balsamum var. pereirae	Peru balsam tree	Balsamum peruvianum	Peru balsam
Ruscus aculeatus	Butcher’s broom	Rusci rhizoma	Butcher's broom
Arterial occlusive disease			
Ginkgo biloba	Ginkgo	Ginkgonis folium, Ginkgonis extractum siccum raffinatum et quantificatum	Ginkgo leaf, Refined and quantified ginkgo dry extract
Atopic dermatitis			
Borago officinalis	Borage	Boragonis officinalis oleum raffinatum	Refined borage oil
Oenothera biennis	Evening primrose	Oenotherae oleum raffinatum	Refined evening primrose oil
Diverticulitis			
Linum usitatissimum	Flax	Lini semen	Flax seed (linseed)
Dermatitis, injuries or irritation of the skin			
Agrimonia eupatoria	Common agrimony	Agrimoniae herba	Agrimony
Chamaemelum nobile	Roman chamomile	Chamomillae romanae flos	Roman chamomile flower
Echinacea purpurea	Purple coneflower	Echinaceae purpureae radix, Echinaceae purpureae herba	Purple coneflower root, Purple coneflower herb
Hamamelis virginiana	Virginian witch-hazel	Hamamelidis folium	Hamamelis leaf
Lythrum salicaria	Purple loosestrife	Lythri herba	Loosestrife
Matricaria recutita	German chamomile	Matricariae flos, Matricariae aetheroleum, Matricariae extractum fluidum	Matricaria flower, Matricaria oil, Matricaria liquid extract

Indications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Persicaria bistorta	Common bistort, Snakeweed	Bistortae rhizoma	Bistort rhizome
Plantago lanceolata	Ribwort plantain	Plantaginis lanceolatae folium	Ribwort plantain
Quercus petraea	Sessile oak	Quercus cortex (externally)	Oak bark
Quercus pubescens	Downy/pubescent oak		
Quercus robur	Pedunculate oak		
Sanguisorba officinalis	Greater burnet	Sanguisorbae radix	Sanguisorba root
Viola arvensis	Field pansy	Violae herba cum floris	Wild pansy, flowering aerial parts
Viola tricolor	Heartsease		
Vitamin C supplements			
Rosa canina	Dog rose	Rosae pseudo-fructus	Rose hip
Rosa pendulina	Mountain rose		
Degenerative diseases of the locomotor system			
Harpagophytum procumbens	Devil’s claw	Harpagophyti radix, Harpagophyti extractum siccum	Devil's claw root, Devil's claw root dried extract
Harpagophytum zeyheri			
Depression			
Hypericum perforatum	St. John’s wort	Hyperici herba, Hyperici herba extractum siccum quantificatum	St. John's wort, Quantified hypericum dried extract
Burn injuries			
Hypericum perforatum	St. John’s wort	Hyperici herba, Hyperici herba extractum siccum quantificatum	St. John's wort, Quantified hypericum dried extract
Myroxylon balsamum var. pereirae	Peru balsam tree	Balsamum peruvianum	Peru balsam
Indigestion (dyspepsia)			
Hypericum perforatum	St. John’s wort	Hyperici herba, Hyperici herba extractum siccum quantificatum	St. John's wort, Quantified hypericum dried extract
Illicium verum	Star anise	Anisi stellati fructus, Anisi stellati aetheroleum	Star anise, Star anise oil
Juniperus communis	Common juniper	Iuniperi pseudo-fructus, Iuniperi aetheroleum	Juniper, Juniper oil
Marrubium vulgare	White / common horehound	Marrubii herba	White horehound
Melissa officinalis	Melissa, Lemon balm	Melissae folium, Melissae folii extractum siccum	Melissa leaf, Melissa leaves dried extract

Indications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Rosmarinus officinalis	Rosemary	Rosmarini folium, Rosmarini aetheroleum	Rosemary leaf, Rosemary oil
Taraxacum officinale	Dandelion	Taraxaci officinalis radix cum herba, Taraxaci officinalis radix	Dandelion root, Dandelion root with herb
Zingiber officinale	Ginger	Zingiberis rhizoma	Ginger
Gastrointestinal spasms			
Angelica archangelica	Garden angelica	Angelicae radix	Angelica root
Atropa belladonna	Deadly nightshade	Belladonnae folium, Belladonnae pulvis normatus, Belladonnae folii tinctura normata, Belladonnae folii extractum siccum normatum	Belladonna leaf, Belladonna, prepared, Belladonna leaf tincture, Standardized belladonna leaf dry extract
Carum carvi	Caraway	Carvi fructus, Carvi aetheroleum	Caraway fruit, Caraway oil
Chamaemelum nobile	Roman chamomile	Chamomillae romanae flos	Roman chamomile flower
Chelidonium majus	Greater celandine	Chelidonii herba	Greater celandine
Cinnamomum cassia	Cassia/Chinese cinnamon	Cinnamomi cassiae aetheroleum	Cassia oil
Cinnamomum zeylanicum	Ceylon cinnamon	Cinnamomi cortex, Cinnamomi zeylanici corticis aetheroleum, Cinnamomi zeylanici folii aetheroleum, Cinnamomi corticis tinctura	Cinnamon, Cinnamon bark oil, Cinnamon leaf oil, Cinnamon tincture
Datura stramonium	Thorn apple	Stramonii folium, Stramonii pulvis normatus	Stramonium leaf, Prepared stramonium
Foeniculum vulgare subsp. vulgare var. dulce	Sweet fennel	Foeniculi dulcis fructus	Sweet fennel
Foeniculum vulgare subsp. vulgare var. vulgare	Bitter fennel	Foeniculi amari fructus, Foeniculi amari fructus aetheroleum, Foeniculi amari herbae aetheroleum	Bitter fennel, Bitter-fennel fruit oil, Bitter fennel herb oil
Fumaria officinalis	Common fumitory	Fumariae herba	Common fumitory
Matricaria recutita	German chamomile	Matricariae flos, Matricariae aetheroleum, Matricariae extractum fluidum	Matricaria flower, Matricaria oil, Matricaria liquid extract

Indications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Mentha canadensis	Japanese mint	Menthae arvensis aetheroleum partim mentholi depletum	Japanese mint essential oil partially deprived of menthol
Mentha x piperita	Peppermint	Menthae piperitae folium, Menthae piperitae aetheroleum	Peppermint leaf, Peppermint oil
Peumus boldus	Boldo tree	Boldi folium	Boldo leaf
Pimpinella anisum	Aniseed	Anisi fructus, Anisi aetheroleum	Aniseed, Anise oil
Biliary colic			
Atropa belladonna	Deadly nightshade	Belladonnae folium, Belladonnae pulvis normatus, Belladonnae folii tinctura normata, Belladonnae folii extractum siccum normatum	Belladonna leaf, Belladonna, prepared, Belladonna leaf tincture, Standardized belladonna leaf dry extract
Chelidonium majus	Greater celandine	Chelidonii herba	Greater celandine
Datura stramonium	Thorn apple	Stramonii folium, Stramonii pulvis normatus	Stramonium leaf, Prepared stramonium
Fumaria officinalis	Common fumitory	Fumariae herba	Common fumitory
Mentha canadensis	Japanese mint	Menthae arvensis aetheroleum partim mentholi depletum	Japanese mint essential oil partially deprived of menthol
Mentha x piperita	Peppermint	Menthae piperitae folium, Menthae piperitae aetheroleum	Peppermint leaf, Peppermint oil
Disturbed bile secretion			
Artemisia absinthium	Absinthe wormwood	Absinthii herba	Wormwood
Curcuma xanthorrhiza	Javanese turmeric	Curcumae xanthorrhizae rhizoma	Javanese turmeric
Cynara scolimus	Artichoke	Cynarae folium, Cynarae folii extractus siccum	Artichoke leaf, Artichoke leaf dry extract
Fumaria officinalis	Common fumitory	Fumariae herba	Common fumitory
Mentha canadensis	Japanese mint	Menthae arvensis aetheroleum partim mentholi depletum	Japanese mint essential oil partially deprived of menthol
Mentha x piperita	Peppermint	Menthae piperitae folium, Menthae piperitae aetheroleum	Peppermint leaf, Peppermint oil
Peumus boldus	Boldo tree	Boldi folium	Boldo leaf
Taraxacum officinale	Dandelion	Taraxaci officinalis radix cum herba, Taraxaci officinalis radix	Dandelion root, Dandelion root with herb

Indications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Loss of appetite			
Achillea millefolium	Yarrow	Millefolii herba	Yarrow
Angelica archangelica	Garden angelica	Angelicae radix	Angelica root
Artemisia absinthium	Absinthe wormwood	Absinthii herba	Wormwood
Centaurium erythraea	Common / European centaury	Centaurii herba	Centaury
Cetraria islandica	Iceland moss	Lichen islandicus	Iceland moss
Cinchona calisaya	Cinchona	Cinchonae cortex, Cinchonae extractum fluidum normatum	Cinchona bark, Standardised cinchona liquid extract
Cinchona ledgeriana			
Cinchona pubescens	Quinine tree		
Cinnamomum cassia	Cassia/Chinese cinnamon	Cinnamomi cassiae aetheroleum	Cassia oil
Cinnamomum zeylanicum	Ceylon cinnamon	Cinnamomi cortex, Cinnamomi zeylanici corticis aetheroleum, Cinnamomi zeylanici folii aetheroleum, Cinnamomi corticis tinctura	Cinnamon, Cinnamon bark oil, Cinnamon leaf oil, Cinnamon tincture
Citrus aurantium subsp. aurantium	Bitter orange	Aurantii amari epicarpium et mesocarpium	Bitter-orange epicarp and mesocarp
Coriandrum sativum	Coriander	Coriandri fructus, Coriandri aetheroleum	Coriander, Coriander oil
Gentiana lutea	Great yellow gentian	Gentianae radix, Gentianae tinctura	Gentian root, Gentian tincture
Harpagophytum procumbens	Devil’s claw	Harpagophyti radix, Harpagophyti extractum siccum	Devil's claw root, Devil's claw root dried extract
Harpagophytum zeypheri			
Marrubium vulgare	White / common horehound	Marrubii herba	White horehound
Menyanthes trifoliata	Bogbean	Menyanthidis trifoliatae folium	Bogbean leaf
Origanum onites	Cretan oregano	Origani herba	Oregano
Origanum vulgare subsp. hirtum	Common (greek) oregano		
Taraxacum officinale	Dandelion	Taraxaci officinalis radix cum herba, Taraxaci officinalis radix	Dandelion root with herb, Dandelion root
Trigonella foenum-graecum	Fenugreek	Trigonellae foenugraeci semen	Fenugreek
Frostbite			
Myroxylon balsamum var. pereirae	Peru balsam tree	Balsamum peruvianum	Peru balsam

Indications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Fatigue			
Cola acuminata		Colae semen	Cola
Cola nitida			
Eleutherococcus senticosus	Siberian ginseng	Eleuterococci radix	Eleutherococcus
Panax ginseng	Korean ginseng	Ginseng radix	Ginseng
Schisandra chinensis	Schizandra	Schisandrae chinensis fructus	Schisandra fruit
Headache (cephalalgia), migraine			
Salix daphnoides	Violet willow	Salicis cortex, Salicis corticis extractum siccum	Willow bark
Salix fragilis	Crack willow		
Salix purpurea	Purple willow		
Mentha canadensis	Japanese mint	Menthae arvensis aetheroleum partim mentholi depletum	Japanese mint essential oil partially deprived of menthol
Mentha x piperita	Peppermint	Menthae piperitae folium, Menthae piperitae aetheroleum	Peppermint leaf, Peppermint oil
Tanacetum parthenium	Feverfew	Tanaceti parthenii herba	Feverfew
Catarrh of the upper respiratory tract, bronchitis, productive cough			
Cephaëlis acuminata		Ipecacuanhae radix, Ipecacuanhae pulvis normatus, Ipecacuanhae fluidum normatum, Ipecacuanhae tinctura normata	Ipecacuanha, Prepared ipecacuanha, Standardized ipecacuanha liquid extract, Standardized ipecacuanha tincture
Cephaëlis ipecacuanha			
Eucalyptus globulus	Eucalyptus	Eucalyptus globulus: Eucalypti folium, Eucalypti aetheroleum	Eucalyptus leaf, Eucalyptus oil
Eucalyptus polybractea	Blue mallee		
Eucalyptus smithii	Gully gum		
Foeniculum vulgare subsp. vulgare var. dulce	Sweet fennel	Foeniculi dulcis fructus	Sweet fennel
Foeniculum vulgare subsp. vulgare var. vulgare	Bitter fennel	Foeniculi amari fructus, Foeniculi amari fructus aetheroleum, Foeniculi amari herbae aetheroleum	Bitter fennel, Bitter-fennel fruit oil, Bitter fennel herb oil
Glycyrrhiza glabra	Licorice, Liquorice	Liquiritiae radix, Liquiritiae extractum fluidum ethanolicum normatum, Liquiritiae extractum siccum ad saporandum	Liquorice root, Standardized liquorice ethanolic liquid extract, Liquorice root dry extract as a flavouring
Hedera helix	Common ivy	Hederae folium	Ivy leaf

Indications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Illicium verum	Star anise	Anisi stellati fructus, Anisi stellati aetheroleum	Star anise, Star anise oil
Mentha canadensis	Japanese mint	Menthae arvensis aetheroleum partim mentholi depletum	Japanese mint essential oil partially deprived of menthol
Mentha x piperita	Peppermint	Menthae piperitae folium, Menthae piperitae aetheroleum	Peppermint leaf, Peppermint oil
Myroxylon balsamum var. pereirae	Peru balsam tree	Balsamum peruvianum	Peru balsam
Pimpinella anisum	Aniseed	Anisi fructus, Anisi aetheroleum	Aniseed, Anise oil
Pinus mugo	Mugo pine	Pini pumilionis aetheroleum	Dwarf pine needle oil
Pinus pinaster	Maritime pine	Terebinthae aetheroleum ab Pinum pinastrum	Pinus pinaster type turpentine oil
Pinus sylvestris	Scots pine	Pini sylvestris aetheroleum	Pine sylvestris oil
Plantago lanceolata	Ribwort plantain	Plantaginis lanceolatae folium	Ribwort plantain
Polygala senega	Seneca snakeroot	Polygalae radix	Senega root
Polygonum aviculare	Common knotgrass	Polygoni avicularis herba	Knotgrass
Primula elatior	Oxlip	Primulae radix	Primula root
Primula veris	Cowslip		
Thymus serpyllum	Wild thyme	Serpylli herba	Wild thyme
Thymus vulgaris	Common thyme	Thymi herba, Thymi aetheroleum	Thyme, Thyme oil
Thymus zygis	Spanish thyme		
Verbascum densiflorum	Dense-flowered mullein	Verbasci flos	Mullein flower
Verbascum phlomoides	Orange mullein		
Verbascum thapsus	Great/common mullein		
Excessive sweating (hyperhydrosis)			
Salvia officinalis	Sage	Salviae officinalis folium, Salviae tinctura	Sage leaf, Sage tincture
Tinnitus			
Ginkgo biloba	Ginkgo	Ginkgonis folium, Ginkgonis extractum siccum raffinatum et quantificatum	Ginkgo leaf, Refined and quantified ginkgo dry extract

Indications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Fungal infections			
Melaleuca alternifolia	Narrow-leaved tea tree	Melaleucae aetheroleum	Tea tree oil
Melaleuca dissitiflora	Creek tea–tree		
Melaleuca linariifolia	Snow-in-Summer, Cajeput tree, Flax-leaved paperbark		
Gastritis and peptic ulcers			
Althaea officinalis	Marshmallow	Althaeae folium, Althaeae radix	Marshmallow leaf, Marshmallow root
Glycyrrhiza glabra	Licorice, Liquorice	Liquiritiae radix, Liquiritiae extractum fluidum ethanolicum normatum, Liquiritiae extractum siccum ad saporandum	Liquorice root, Standardized liquorice ethanolic liquid extract, Liquorice root dry extract as a flavouring
Linum usitatissimum	Flax	Lini semen	Flax seed (linseed)
Malva neglecta	Common mallow	Malvae folium	Mallow leaf
Malva sylvestris	Mallow		
Diarrhoea			
Agrimonia eupatoria	Common agrimony	Agrimoniae herba	Agrimony
Alchemilla vulgaris	Lady's mantle	Alchemillae herba	Alchemilla
Lythrum salicaria	Purple loosestrife	Lythri herba	Loosestrife
Papaver somniferum	Opium poppy	Opium crudum, Opii pulvis normatus, Opii extractum siccum normatum, Opii tinctura normata	Raw opium, Prepared opium, Opium dry extract, Opium tincture standardized
Persicaria bistorta	Common bistort, Snakeweed	Bistortae rhizoma	Bistort rhizome
Plantago afra	Psyllium	Psylli semen	Psyllium seed
Plantago indica	French psyllium, Sand plantain		
Plantago ovata	Desert indianwheat	Plantaginis ovatae semen, Plantaginis ovatae seminis tegumentum	Ispaghula seed, Ispaghula husk
Potentilla erecta	Common tormentil	Tormentillae rhizoma, Tormentillae tinctura	Tormentil, Tormentil tincture
Quercus petrea	Sessile oak	Quercus cortex (externally)	Oak bark
Quercus pubescens	Downy/pubescent oak		
Quercus robur	Pedunculate oak		
Sanguisorba officinalis	Greater burnet	Sanguisorbae radix	Sanguisorba root
Vaccinium myrtillus	Bilberry	Myrtilli fructus siccus, Myrtilli fructus recens	Dried bilberry fruit, Fresh bilberry fruit

Indications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Local anesthesia			
Syzygium aromaticum	Clove tree	Caryophylli flos, Caryophylli floris aetheroleum	Clove, Clove oil
Urinary tract infection and inflammation			
Arctostaphylos uva-ursi	Bearberry	Uvae ursi folium	Bearberry leaf
Echinacea angustifolia	Narrow-leaved purple coneflower	Echinaceae angustifoliae radix	Narrow-leaved purple coneflower root
Echinacea pallida	Pale purple coneflower	Echinaceae pallidae radix	Pale purple coneflower root
Echinacea purpurea	Purple coneflower	Echinaceae purpureae radix, Echinaceae purpureae herba	Purple coneflower root, Purple coneflower herb
Taraxacum officinale	Dandelion	Taraxaci officinalis radix cum herba, Taraxaci officinalis radix	Dandelion root, Dandelion root with herb
Neuralgia			
Mentha canadensis	Japanese mint	Menthae arvensis aetheroleum partim mentholi depletum	Japanese mint essential oil partially deprived of menthol
Mentha x piperita	Peppermint	Menthae piperitae folium, Menthae piperitae aetheroleum	Peppermint leaf, Peppermint oil
Pinus mugo	Mugo pine	Pini pumilionis aetheroleum	Dwarf pine needle oil
Pinus pinaster	Maritime pine	Terebinthae aetheroleum ab Pinum pinastrum	Pinus pinaster type turpentine oil
Pinus sylvestris	Scots pine	Pini sylvestris aetheroleum	Pine sylvestris oil
Capsicum annuum var. minimum	Cayenne pepper	Capsici fructus, Capsici oleoresina raffinata et quantificata, Capsici tinctura normata	Capsicum, Refined and quantified capsicum oleoresin, Capsicum tincture
Capsicum frutescens	Chili pepper		
Anxiety related upset stomach			
Lavandula angustifolia	True (narrow-leaved) lavender	Lavandulae flos, Lavandulae aetheroleum	Lavender flower, Lavender oil
Melissa officinalis	Melissa, Lemon balm	Melissae folium, Melissae folii extractum siccum	Melissa leaf, Melissa leaves dried extract

Indications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Irritable bowel syndrome			
Linum usitatissimum	Flax	Lini semen	Flax seed (linseed)
Mentha canadensis	Japanese mint	Menthae arvensis aetheroleum partim mentholi depletum	Japanese mint essential oil partially deprived of menthol
Mentha x piperita	Peppermint	Menthae piperitae folium, Menthae piperitae aetheroleum	Peppermint leaf, Peppermint oil
Plantago afra	Psyllium	Psylli semen	Psyllium seed
Plantago indica	French psyllium, Sand plantain		
Plantago ovata	Desert indianwheat	Plantaginis ovatae semen, Plantaginis ovatae seminis tegumentum	Ispaghula seed, Ispaghula husk
Muscle pain (myalgia)			
Arnica montana	Mountain arnica / wolf's bane	Arnicae flos, Arnicae tinctura	Arnica flower, Arnica tincture
Eucalyptus globulus	Eucalyptus	Eucalyptus globulus: Eucalypti folium, Eucalypti aetheroleum	Eucalyptus leaf, Eucalyptus oil
Eucalyptus polybractea	Blue mallee		
Eucalyptus smithii	Gully gum		
Mentha canadensis	Japanese mint	Menthae arvensis aetheroleum partim mentholi depletum	Japanese mint essential oil partially deprived of menthol
Mentha x piperita	Peppermint	Menthae piperitae folium, Menthae piperitae aetheroleum	Peppermint leaf, Peppermint oil
Pinus mugo	Mugo pine	Pini pumilionis aetheroleum	Dwarf pine needle oil
Pinus pinaster	Maritime pine	Terebinthae aetheroleum ab Pinum pinastrum	Pinus pinaster type turpentine oil
Pinus sylvestris	Scots pine	Pini sylvestris aetheroleum	Pine sylvestris oil
Rosmarinus officinalis	Rosemary	Rosmarini folium, Rosmarini aetheroleum	Rosemary leaf, Rosemary oil
Muscle cramp			
Capsicum annuum var. minimum	Cayenne pepper	Capsici fructus, Capsici oleoresina raffinata et quantificata, Capsici tinctura normata	Capsicum, Refined and quantified capsicum oleoresin, Capsicum tincture
Capsicum frutescens	Chili pepper		

Indications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Joint pain (arthralgia)			
Arnica montana	Mountain arnica / wolf's bane	Arnicae flos, Arnicae tinctura	Arnica flower, Arnica tincture
Capsicum annuum var. minimum	Cayenne pepper	Capsici fructus, Capsici oleoresina raffinata et quantificata, Capsici tinctura normata	Capsicum, Refined and quantified capsicum oleoresin, Capsicum tincture
Capsicum frutescens	Chili pepper		
Eucalyptus globulus	Eucalyptus	Eucalyptus globulus: Eucalypti folium, Eucalypti aetheroleum	Eucalyptus leaf, Eucalyptus oil
Eucalyptus polybractea	Blue mallee		
Eucalyptus smithii	Gully gum		
Harpagophytum procumbens	Devil's claw	Harpagophyti radix, Harpagophyti extractum siccum	Devil's claw root, Devil's claw root dried extract
Harpagophytum zeypheri			
Pinus mugo	Mugo pine	Pini pumilionis aetheroleum	Dwarf pine needle oil
Pinus pinaster	Maritime pine	Terebinthae aetheroleum ab Pinum pinastrum	Pinus pinaster type turpentine oil
Pinus sylvestris	Scots pine	Pini sylvestris aetheroleum	Pine sylvestris oil
Rosmarinus officinalis	Rosemary	Rosmarini folium, Rosmarini aetheroleum	Rosemary leaf, Rosemary oil
Salix daphnoides	Violet willow	Salicis cortex, Salicis corticis extractum siccum	Willow bark, Willow bark dried extract
Salix fragilis	Crack willow		
Salix purpurea	Purple willow		
Iodine supplements			
Ascophyllum nodosum	Knotted wrack	Fucus vel Ascophyllum	Kelp
Fucus serratus / serratulatus?	Serrated wrack		
Fucus vesiculosus	Bladder wrack		
Benign prostatic hyperplasia (BPH)			
Prunus africana	Red stinkwood	Pruni africanae cortex	Pygeum africanum bark
Serenoa repens	Saw palmetto	Sabalis serrulatae fructus	Saw palmetto fruit
Exhaustion, reconvalescence			
Eleutherococcus senticosus	Siberian ginseng	Eleuterococci radix	Eleutherococcus
Panax ginseng	Korean ginseng	Ginseng radix	Ginseng
Schisandra chinensis	Schizandra	Schisandrae chinensis fructus	Schisandra fruit

Indications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Venous ulcers (ulcus cruris)			
Calendula officinalis	Calendula	Calendulae flos	Calendula flower
Centella asiatica	Pot marigold	Centellae asiaticae herba	Centella
Matricaria recutita	German chamomile	Matricariae flos, Matricariae aetheroleum, Matricariae extractum fluidum	Matricaria flower, Matricaria oil, Matricaria liquid extract
Myroxylon balsamum var. pereirae	Peru balsam tree	Balsamum peruvianum	Peru balsam
Fever (pyrexia)			
Salix daphnoides	Violet willow	Salicis cortex, Salicis corticis extractum siccum	Willow bark, Willow bark dried extract
Salix fragilis	Crack willow		
Salix purpurea	Purple willow		
Reduction of cholesterol level and cardiovascular risk			
Allium sativum	Garlic	Allii sativi bulbi pulvis	Garlic powder
Cynara scolimus	Artichoke	Cynarae folium, Cynarae folii extractus siccum	Artichoke leaf, Artichoke leaf dry extract
Plantago afra	Psyllium	Psylli semen	Psyllium seed
Plantago indica	French psyllium, Sand plantain		
Plantago ovata	Desert indianwheat	Plantaginis ovatae semen, Plantaginis ovatae seminis tegumentum	Ispaghula seed, Ispaghula husk
Salmo salar	Atlantic salmon	Salmonis domestici oleum	Farmed salmon oil
		Piscis oleum omega-3 acidis abundans	Fish oil rich in Omega-3-acids
Liver failure			
Schisandra chinensis	Schizandra	Schisandrae chinensis fructus	Schisandra fruit
Silybum marianum	Milk thistle	Silybi mariani fructus, Silybi mariani extractum siccum raffinatum et normatum	Milk-thistle fruit, Preset (standardised) purified milk thistle dried extract
Common cold, influenza			
Apis mellifera	Honey bee	Mel	
Echinacea angustifolia	Narrow-leaved purple coneflower	Echinaceae angustifoliae radix	Narrow-leaved purple coneflower root
Echinacea pallida	Pale purple coneflower	Echinaceae pallidae radix	Pale purple coneflower root

Indications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Echinacea purpurea	Purple coneflower	Echinaceae purpureae radix, Echinaceae purpureae herba	Purple coneflower root, Purple coneflower herb
Filipendula ulmaria	Meadowsweet	Filipendulae ulmariae herba	Meadowsweet
Pelargonium reniforme	Geranium	Pelargonii radix	Pelargonium
Pelargonium sidoides	South African geranium		
Sambucus nigra	Black elder	Sambuci flos	Elder flower
Tilia cordata	Small-leaved linden/lime	Tiliae flos	Lime flower
Tilia platyphyllos	Large-leaved linden/lime		
Tilia x vulgaris	Common lime		
Decreased memory functions			
Ginkgo biloba	Ginkgo	Ginkgonis folium, Ginkgonis extractum siccum raffinatum et quantificatum	Ginkgo leaf, Refined and quantified ginkgo dry extract
Mucous membrane irritation			
Althaea officinalis	Marshmallow	Althaeae folium, Althaeae radix	Marshmallow leaf, Marshmallow root
Hamamelis virginiana	Virginian witch-hazel	Hamamelidis folium	Hamamelis leaf
Malva neglecta	Common mallow	Malvae folium	Mallow leaf
Malva sylvestris	Mallow		
Malva sylvestris	Mallow	Malvae sylvestris flos	Mallow flower
Matricaria recutita	German chamomile	Matricariae flos, Matricariae aetheroleum, Matricariae extractum fluidum	Matricaria flower, Matricaria oil, Matricaria liquid extract
Plantago lanceolata	Ribwort plantain	Plantaginis lanceolatae folium	Ribwort plantain
Premenstrual syndrome, menstrual disorders and cramps			
Achillea millefolium	Yarrow	Millefolii herba	Yarrow
Vitex agnus-castus	Agnus castus	Agni casti fructus	Agnus castus fruit
Inflation, distension			
Angelica archangelica	Garden angelica	Angelicae radix	Angelica root
Carum carvi	Caraway	Carvi fructus, Carvi aetheroleum	Caraway fruit, Caraway oil
Chamaemelum nobile	Roman chamomile	Chamomillae romanae flos	Roman chamomile flower
Cinnamomum cassia	Cassia/Chinese cinnamon	Cinnamomi cassiae aetheroleum	Cassia oil

Indications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Cinnamomum zeylanicum	Ceylon cinnamon	Cinnamomi cortex, Cinnamomi zeylanici corticis aetheroleum, Cinnamomi zeylanici folii aetheroleum, Cinnamomi corticis tinctura	Cinnamon, Cinnamon bark oil, Cinnamon leaf oil, Cinnamon tincture
Foeniculum vulgare subsp. vulgare var. dulce	Sweet fennel	Foeniculi dulcis fructus	Sweet fennel
Foeniculum vulgare subsp. vulgare var. vulgare	Bitter fennel	Foeniculi amari fructus, Foeniculi amari fructus aetheroleum, Foeniculi amari herbae aetheroleum	Bitter fennel, Bitter-fennel fruit oil, Bitter fennel herb oil
Pimpinella anisum	Aniseed	Anisi fructus, Anisi aetheroleum	Aniseed, Anise oil
Rheumatism			
Arnica montana	Mountain arnica / wolf's bane	Arnicae flos, Arnicae tinctura	Arnica flower, Arnica tincture
Betula pendula	Silver birch	Betulae folium	Birch leaf
Betula pubescens	Downy/white birch		
Capsicum annuum var. minimum	Cayenne pepper	Capsici fructus, Capsici oleoresina raffinata et quantificata, Capsici tinctura normata	Capsicum, Refined and quantified capsicum oleoresin, Capsicum tincture
Capsicum frutescens	Chili pepper		
Eucalyptus globulus	Eucalyptus	Eucalyptus globulus: Eucalypti folium, Eucalypti aetheroleum	Eucalyptus leaf, Eucalyptus oil
Eucalyptus polybrachtea	Blue mallee		
Eucalyptus smithii	Gully gum		
Pinus mugo	Mugo pine	Pini pumilionis aetheroleum	Dwarf pine needle oil
Pinus pinaster	Maritime pine	Terebinthae aetheroleum ab Pinum pinastrum	Pinus pinaster type turpentine oil
Pinus sylvestris	Scots pine	Pini sylvestris aetheroleum	Pine sylvestris oil
Rosmarinus officinalis	Rosemary	Rosmarini folium, Rosmarini aetheroleum	Rosemary leaf
Salix daphnoides	Violet willow	Salicis cortex, Salicis corticis extractum siccum	Willow bark
Salix fragilis	Crack willow		
Salix purpurea	Purple willow		
Urtica dioica	Stinging nettle	Urticae folium	Nettle leaf
Urtica urens	Annual nettle, Dwarf nettle or Small Nettle		

Indications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Wounds			
Calendula officinalis	Calendula	Calendulae flos	Calendula flower
Echinacea purpurea	Purple coneflower	Echinaceae purpureae radix, Echinaceae purpureae herba	Purple coneflower root, Purple coneflower herb
Equisetum arvense	Field horsetail	Equiseti herba	Equisetum stem
Myroxylon balsamum var. pereirae	Peru balsam tree	Balsamum peruvianum	Peru balsam
Inflammation of the mouth or throat (pharyngitis)			
Agrimonia eupatoria	Common agrimony	Agrimoniae herba	Agrimony
Althaea officinalis	Marshmallow	Althaeae folium, Althaeae radix	Marshmallow leaf, Marshmallow root
Arnica montana	Mountain arnica / wolf's bane	Arnicae flos, Arnicae tinctura	Arnica flower, Arnica tincture
Calendula officinalis	Calendula	Calendulae flos	Calendula flower
Cetraria islandica	Iceland moss	Lichen islandicus	Iceland moss
Commiphora molmol	Common myrrh, Gum myrrh	Myrrha, Myrrhae tinctura	Myrrh, Myrrh tincture
Krameria triandra	Peruvian rhatany	Ratanhiae radix, Ratanhiae tinctura	Rhatany root, Rhatany tincture
Malva neglecta	Common mallow	Malvae folium	Mallow leaf
Malva sylvestris	Mallow		
Malva sylvestris	Mallow	Malvae sylvestris flos	Mallow flower
Matricaria recutita	German chamomile	Matricariae flos, Matricariae aetheroleum, Matricariae extractum fluidum	Matricaria flower, Matricaria oil, Matricaria liquid extract
Mentha x piperita	Peppermint	Menthae piperitae folium, Menthae piperitae aetheroleum	Peppermint leaf, Peppermint oil
Persicaria bistorta	Common bistort, Snakeweed	Bistortae rhizoma	Bistort rhizome
Plantago lanceolata	Ribwort plantain	Plantaginis lanceolatae folium	Ribwort plantain
Polygonum aviculare	Common knotgrass	Polygoni avicularis herba	Knotgrass
Potentilla erecta	Common tormentil	Tormentillae rhizoma, Tormentillae tinctura	Tormentil, Tormentil tincture
Quercus petraea	Sessile oak	Quercus cortex (externally)	Oak bark
Quercus pubescens	Downy/pubescent oak		
Quercus robur	Pedunculate oak		
Salvia fruticosa	Greek sage	Salviae trilobae folium	Three-lobed sage leaf
Salvia officinalis	Sage	Salviae officinalis folium, Salviae tinctura	Sage leaf, Sage tincture

Indications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Styrax benzoin		Benzoë sumatranus, Benzoë sumatrani tinctura	Sumatra benzoin, Sumatra benzoin tincture
Styrax tonkinensis		Benzoë tonkinensis, Benzoë tonkinensis tinctura	Siam benzoin, Siam benzoin tincture
Syzygium aromaticum	Clove tree	Caryophylli flos, Caryophylli floris aetheroleum	Clove, Clove oil
Vaccinium myrtillus	Bilberry	Myrtilli fructus siccus, Myrtilli fructus recens	Dried bilberry fruit, Fresh bilberry fruit
Whooping cough (pertussis)			
Thymus serpyllum	Wild thyme	Serpylli herba	Wild thyme
Thymus vulgaris	Common thyme	Thymi herba, Thymi aetheroleum	Thyme, Thyme oil
Thymus zygis	Spanish thyme		
Dry cough			
Althaea officinalis	Marshmallow	Althaeae folium, Althaeae radix	Marshmallow leaf, Marshmallow root
Cetraria islandica	Iceland moss	Lichen islandicus	Iceland moss
Malva neglecta	Common mallow	Malvae folium	Mallow leaf
Malva sylvestris	Mallow		
Malva sylvestris	Mallow	Malvae sylvestris flos	Mallow flower
Plantago lanceolata	Ribwort plantain	Plantaginis lanceolatae folium	Ribwort plantain
Tilia cordata	Small-leaved linden/lime	Tiliae flos	Lime flower
Tilia platyphyllos	Large-leaved linden/lime		
Tilia x vulgaris	Common lime		
Verbascum densiflorum	Dense-flowered mullein	Verbasci flos	Mullein flower
Verbasum phlomoides	Orange mullein		
Verbascum thapsus	Great/common mullein		
Dizziness (vertigo)			
Ginkgo biloba	Ginkgo	Ginkgonis folium, Ginkgonis extractum siccum raffinatum et quantificatum	Ginkgo leaf, Refined and quantified ginkgo dry extract
Constipation			
Aloë barbadensis	True/medicinal aloe	Aloë barbadensis, Aloë capensis, Aloës extractum siccum normatum	Cape aloes, Barbados aloes, Standardized aloes dry extract
Aloë ferox	Cape aloe, Bitter aloe, Red aloe, Tap aloe		
Cassia angustifolia	Tinnevelly senna	Sennae fructus angustifoliae	Tinnevelly senna pods

Indications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Cassia senna	Alexandrian senna	Sennae fructus acutifoliae	Alexandrian senna pods
Cassia angustifolia	Tinnevelly senna	Sennae folium, Sennae folii extractum siccum normatum	Senna leaf, Senna leaf dry extract
Cassia senna	Alexandrian senna		
Linum usitatissimum	Flax	Lini semen	Flax seed (linseed)
Plantago afra	Psyllium	Psylli semen	Psyllium seed
Plantago indica	French psyllium, Sand plantain		
Plantago ovata	Desert indianwheat	Plantaginis ovatae semen, Plantaginis ovatae seminis tegumentum	Ispaghula seed, Ispaghula husk
Rhamnus frangula	Alder buckthorn	Frangulae cortex, Frangulae cortex extractum siccum normatum	Frangula bark, Standardized frangula bark dry extract
Rhamnus purshiana	Cascara buckthorn	Rhamni purshianae extractum siccum normatum	Cascara
Rheum officinale	Rhubarb	Rhei radix	Rhubarb
Rheum palmatum	Chinese rhubarb		
Ricinus communis	Castor oil plant	Ricini oleum virginale, Ricini oleum hydrogenatum, Ricini oleum raffinatum	Virgin Castor oil, Hydrogenated castor oil, Refined castor oil
Heart failure (cardiac insufficiency)			
Crataegus azarolus	Azarole	Crataegi folium cum flore, Crataegi folii cum flore extractum siccum, Crataegi fructus	Hawthorn leaf and flower, Hawthorn leaf and flower dry extract, Hawthorn berries
Crataegus laevigata	Woodland hawthorn		
Crataegus monogyna	Common hawthorn		
Crataegus nigra	Hungarian hawthorn		
Crataegus pentagyna	Small-flowered black hawthorn		
Digitalis purpurea	Common foxglove, Purple foxglove	Digitalis purpureae folium	Digitalis leaf
Anxiety, sleep disorders			
Humulus lupulus	Common hop	Lupuli flos	Hop strobile
Lavandula angustifolia	True (narrow-leaved) lavender	Lavandulae flos, Lavandulae aetheroleum	Lavender flower, Lavender oil
Melissa officinalis	Melissa, Lemon balm	Melissae folium, Melissae folii extractum siccum	Melissa leaf, Melissa leaves dried extract
Passiflora incarnata	Purple passion flower	Passiflorae herba, Passiflorae herbae extractum siccum	Passion flower, Passion flower dry extract

Indications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Valeriana officinalis	Valerian	Valerianae radix, Valerianae radix minuta, Valerianae extractum hydroalcoholicum siccum, Valerianae extractum aquosum siccum, Valerianae tinctura ?	Valerian root, Valerian dry hydroalcoholic extract, Valerian dry aqueous extract, Valerian tincture
Tachycardia			
Leonurus cardiaca	Motherwort	Leonuri cardiacae herba	Motherwort
Galactogogues			
Foeniculum vulgare subsp. vulgare var. dulce	Sweet fennel	Foeniculi dulcis fructus	Sweet fennel
Foeniculum vulgare subsp. vulgare var. vulgare	Bitter fennel	Foeniculi amari fructus, Foeniculi amari fructus aetheroleum, Foeniculi amari herbae aetheroleum	Bitter fennel, Bitter-fennel fruit oil, Bitter fennel herb oil
Pimpinella anisum	Aniseed	Anisi fructus, Anisi aetheroleum	Aniseed, Anise oil
Sore throat			
Agrimonia eupatoria	Common agrimony	Agrimoniae herba	Agrimony
Althaea officinalis	Marshmallow	Althaeae folium, Althaeae radix	Marshmallow leaf, Marshmallow root
Arnica montana	Mountain arnica / wolf's bane	Arnicae flos, Arnicae tinctura	Arnica flower, Arnica tincture
Calendula officinalis	Calendula	Calendulae flos	Calendula flower
Cetraria islandica	Iceland moss	Lichen islandicus	Iceland moss
Malva neglecta	Common mallow	Malvae folium	Mallow leaf
Malva sylvestris	Mallow		
Malva sylvestris	Mallow	Malvae sylvestris flos	Mallow flower
Polygonum aviculare	Common knotgrass	Polygoni avicularis herba	Knotgrass
Quercus petraea	Sessile oak	Quercus cortex (externally)	Oak bark
Quercus pubescens	Downy/pubescent oak		
Quercus robur	Pedunculate oak		
Syzygium aromaticum	Clove tree	Caryophylli flos, Caryophylli floris aetheroleum	Clove
Seasickness			
Zingiber officinale	Ginger	Zingiberis rhizoma	Ginger

Indications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Venous insufficiency and leg swelling (oedema)			
Centella asiatica	Pot marigold	Centellae asiaticae herba	Centella
Fagopyrum esculentum	Buckwheat	Fagopyri herba	Buckwheat herb
Melilotus officinalis	Sweet clover, Yellow melilot, Ribbed melilot, Common melilot	Meliloti herba	Melilot
Ruscus aculeatus	Butcher’s broom	Rusci rhizoma	Butcher's broom
Phlebitis			
Arnica montana	Mountain arnica / wolf’s bane	Arnicae flos, Arnicae tinctura	Arnica flower, Arnica tincture
Melilotus officinalis	Sweet clover, Yellow melilot, Ribbed melilot, Common melilot	Meliloti herba	Melilot
Diuretics			
Agropyron repens	Couch grass	Graminis rhizoma	Couch grass rhizome
Betula pendula	Silver birch	Betulae folium	Birch leaf
Betula pubescens	Downy/white birch		
Equisetum arvense	Field horsetail	Equiseti herba	Equisetum stem
Levisticum officinale	Lovage	Levistici radix	Lovage root
Ononis spinosa	Spiny restharrow	Ononidis radix	Restharrow root
Orthosiphon stamineus	Cat's Whiskers, Java Tea	Orthosiphonis folium	Java tea
Solidago canadensis	Canada goldenrod	Solidaginis herba	Goldenrod
Solidago giganthea	Giant goldenrod		
Solidago virgaurea	European goldenrod	Solidaginis virgaureae herba	European goldenrod
Urtica dioica	Stinging nettle	Urticae folium	Nettle leaf
Urtica urens	Annual nettle, Dwarf nettle or Small Nettle		
Bruise (contusion) and dislocation			
Arnica montana	Mountain arnica / wolf’s bane	Arnicae flos, Arnicae tinctura	Arnica flower, Arnica tincture
Hypericum perforatum	St. John’s wort	Hyperici herba, Hyperici herba extractum siccum quantificatum	St. John's wort
Melilotus officinalis	Sweet clover, Yellow melilot, Ribbed melilot, Common melilot	Meliloti herba	Melilot

Contraindications

Contraindications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Asthma			
Pimpinella anisum	Aniseed	Anisi fructus, Anisi aetheroleum	Aniseed, Anise oil
Pinus mugo	Mugo pine	Pini pumilionis aetheroleum	Dwarf pine needle oil
Pinus sylvestris	Scots pine	Pini sylvestris aetheroleum	Pine sylvestris oil
Salix daphnoides	Violet willow	Salicis cortex, Salicis corticis extractum siccum	Willow bark, Willow bark dried extract
Salix fragilis	Crack willow		
Salix purpurea	Purple willow		
Gastrointestinal obstructions			
Aloë barbadensis	True/medicinal aloe	Aloë barbadensis, Aloë capensis, Aloës extractum siccum normatum	Cape aloes, Barbados aloes, Standardized aloes dry extract
Aloë ferox	Cape aloe, Bitter aloe, Red aloe, Tap aloe		
Atropa belladonna	Deadly nightshade	Belladonnae folium, Belladonnae pulvis normatus, Belladonnae folii tinctura normata, Belladonnae folii extractum siccum normatum	Belladonna leaf, Belladonna, prepared, Belladonna leaf tincture, Standardized belladonna leaf dry extract
Cassia angustifolia	Tinnevelly senna	Sennae fructus angustifoliae	Tinnevelly senna pods
Cassia senna	Alexandrian senna	Sennae fructus acutifoliae	Alexandrian senna pods
Cassia angustifolia	Tinnevelly senna	Sennae folium, Sennae folii extractum siccum normatum	Senna leaf, Senna leaf dry extract
Cassia senna	Alexandrian senna		
Linum usitatissimum	Flax	Lini semen	Flax seed (linseed)
Plantago afra	Psyllium	Psylli semen	Psyllium seed
Plantago indica	French psyllium, Sand plantain		
Plantago ovata	Desert indianwheat	Plantaginis ovatae semen, Plantaginis ovatae seminis tegumentum	Ispaghula seed, Ispaghula husk
Rhamnus frangula	Alder buckthorn	Frangulae cortex, Frangulae cortex extractum siccum normatum	Frangula bark, Standardized frangula bark dry extract
Rhamnus purshiana	Cascara buckthorn	Rhamni purshianae extractum siccum normatum	Cascara
Rheum officinale	Rhubarb	Rhei radix	Rhubarb
Rheum palmatum	Chinese rhubarb		

Contraindications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Skin injuries			
Capsicum annuum var. minimum	Cayenne pepper	Capsici fructus, Capsici oleoresina raffinata et quantificata, Capsici tinctura normata	Capsicum, Refined and quantified capsicum oleoresin, Capsicum tincture
Capsicum frutescens	Chili pepper		
Ulcerative colitis, Crohn's disease			
Aloë barbadensis	True/medicinal aloe	Aloë barbadensis, Aloë capensis, Aloës extractum siccum normatum	Cape aloes, Barbados aloes, Standardized aloes dry extract
Aloë ferox	Cape aloe, Bitter aloe, Red aloe, Tap aloe		
Cassia angustifolia	Tinnevelly senna	Sennae fructus angustifoliae	Tinnevelly senna pods
Cassia senna	Alexandrian senna	Sennae fructus acutifoliae	Alexandrian senna pods
Cassia angustifolia	Tinnevelly senna	Sennae folium, Sennae folii extractum siccum normatum	Senna leaf, Senna leaf dry extract
Cassia senna	Alexandrian senna		
Rhamnus frangula	Alder buckthorn	Frangulae cortex, Frangulae cortex extractum siccum normatum	Frangula bark, Standardized frangula bark dry extract
Rhamnus purshiana	Cascara buckthorn	Rhamni purshianae extractum siccum normatum	Cascara
Rheum officinale	Rhubarb	Rhei radix	Rhubarb
Rheum palmatum	Chinese rhubarb		
Diabetes			
Ephedra sinica	Ephedra, Ma Huang	Ephedrae herba	Ephedra
Ephedra intermedia	Zhong Ma Huang		
Ephedra equisetina	Muzei Ma Huang		
Intestinal stricture			
Atropa belladonna	Deadly nightshade	Belladonnae folium, Belladonnae pulvis normatus, Belladonnae folii tinctura normata, Belladonnae folii extractum siccum normatum	Belladonna leaf, Belladonna, prepared, Belladonna leaf tincture, Standardized belladonna leaf dry extract
Datura stramonium	Thorn apple	Stramonii folium, Stramonii pulvis normatus	Stramonium leaf, Prepared stramonium
Plantago afra	Psyllium	Psylli semen	Psyllium seed
Plantago indica	French psyllium, Sand plantain		
Plantago ovata	Desert indianwheat	Plantaginis ovatae semen, Plantaginis ovatae seminis tegumentum	Ispaghula seed, Ispaghula husk

Contraindications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Inflammation of the gallbladder (cholecystitis), gallstone (cholelithiasis)			
Curcuma xanthorrhiza	Javanese turmeric	Curcumae xanthorrhizae rhizoma	Javanese turmeric
Cynara scolymus	Artichoke	Cynarae folium, Cynarae folii extractus siccum	Artichoke leaf, Artichoke leaf dry extract
Harpagophytum procumbens	Devil's claw	Harpagophyti radix, Harpagophyti extractum siccum	Devil's claw root, Devil's claw root dried extract
Harpagophytum zeypheri			
Mentha canadensis	Japanese mint	Menthae arvensis aetheroleum partim mentholi depletum	Japanese mint essential oil partially deprived of menthol
Mentha x piperita	Peppermint	Menthae piperitae folium, Menthae piperitae aetheroleum	Peppermint leaf, Peppermint oil
Peumus boldus	Boldo tree	Boldi folium	Boldo leaf
Zingiber officinale	Ginger	Zingiberis rhizoma	Ginger
Cholestatic liver disease			
Glycyrrhiza glabra	Licorice, Liquorice	Liquiritiae radix, Liquiritiae extractum fluidum ethanolicum normatum, Liquiritiae extractum siccum ad saporandum	Liquorice root, Standardized liquorice ethanolic liquid extract, Liquorice root dry extract as a flavouring
Inflammation and blockage of the bile ducts (cholangitis and biliary obstruction)			
Curcuma xanthorrhiza	Javanese turmeric	Curcumae xanthorrhizae rhizoma	Javanese turmeric
Cynara scolymus	Artichoke	Cynarae folium, Cynarae folii extractus siccum	Artichoke leaf, Artichoke leaf dry extract
Eucalyptus globulus	Eucalyptus	Eucalyptus globulus: Eucalypti folium, Eucalypti aetheroleum	Eucalyptus leaf, Eucalyptus oil
Eucalyptus polybractea	Blue mallee		
Eucalyptus smithii	Gully gum		
Mentha canadensis	Japanese mint	Menthae arvensis aetheroleum partim mentholi depletum	Japanese mint essential oil partially deprived of menthol
Mentha x piperita	Peppermint	Menthae piperitae folium, Menthae piperitae aetheroleum	Peppermint leaf, Peppermint oil
Olea europaea	Olive	Oleae folium, Oleae folii extractum siccum	Olive leaf, Olive tree leaves dried extract
Peumus boldus	Boldo tree	Boldi folium	Boldo leaf
Taraxacum officinale	Dandelion	Taraxaci officinalis radix cum herba, Taraxaci officinalis radix	Dandelion root, Dandelion root with herb

Contraindications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Infancy and childhood			
Aloë barbadensis	True/medicinal aloe	Aloë barbadensis, Aloë capensis, Aloës extractum siccum normatum	Cape aloes, Barbados aloes, Standardized aloes dry extract
Aloë ferox	Cape aloe, Bitter aloe, Red aloe, Tap aloe		
Cassia angustifolia	Tinnevelly senna	Sennae fructus angustifoliae	Tinnevelly senna pods
Cassia senna	Alexandrian senna	Sennae fructus acutifoliae	Alexandrian senna pods
Cassia angustifolia	Tinnevelly senna	Sennae folium, Sennae folii extractum siccum normatum	Senna leaf, Senna leaf dry extract
Cassia senna	Alexandrian senna		
Eucalyptus globulus	Eucalyptus	Eucalyptus globulus: Eucalypti folium, Eucalypti aetheroleum	Eucalyptus leaf, Eucalyptus oil
Eucalyptus polybractea	Blue mallee		
Mentha canadensis	Japanese mint	Menthae arvensis aetheroleum partim mentholi depletum	Japanese mint essential oil partially deprived of menthol
Mentha x piperita	Peppermint	Menthae piperitae folium, Menthae piperitae aetheroleum	Peppermint leaf, Peppermint oil
Rhamnus frangula	Alder buckthorn	Frangulae cortex, Frangulae cortex extractum siccum normatum	Frangula bark, Standardized frangula bark dry extract
Rhamnus purshiana	Cascara buckthorn	Rhamni purshianae extractum siccum normatum	Cascara
Rheum officinale	Rhubarb	Rhei radix	Rhubarb
Rheum palmatum	Chinese rhubarb		
Salix daphnoides	Violet willow	Salicis cortex, Salicis corticis extractum siccum	Willow bark, Willow bark dried extract
Salix fragilis	Crack willow		
Salix purpurea	Purple willow		
Gastric and duodenal ulcers			
Artemisia absinthium	Absinthe wormwood	Absinthii herba	Wormwood
Cola acuminata		Colae semen	Cola
Cola nitida			
Gentiana lutea	Great yellow gentian	Gentianae radix, Gentianae tinctura	Gentian root, Gentian tincture
Harpagophytum procumbens	Devil’s claw	Harpagophyti radix, Harpagophyti extractum siccum	Devil's claw root, Devil's claw root dried extract
Harpagophytum zeypheri			
Menyanthes trifoliata	Bogbean	Menyanthidis trifoliatae folium	Bogbean leaf

Contraindications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Hypokalemia			
Glycyrrhiza glabra	Licorice, Liquorice	Liquiritiae radix, Liquiritiae extractum fluidum ethanolicum normatum, Liquiritiae extractum siccum ad saporandum	Liquorice root, Standardized liquorice ethanolic liquid extract, Liquorice root dry extract as a flavouring
Abdominal pain of unknown origin			
Aloë barbadensis	True/medicinal aloe	Aloë barbadensis, Aloë capensis, Aloës extractum siccum normatum	Cape aloes, Barbados aloes, Standardized aloes dry extract
Aloë ferox	Cape aloe, Bitter aloe, Red aloe, Tap aloe		
Cassia angustifolia	Tinnevelly senna	Sennae fructus angustifoliae	Tinnevelly senna pods
Cassia senna	Alexandrian senna	Sennae fructus acutifoliae	Alexandrian senna pods
Cassia angustifolia	Tinnevelly senna	Sennae folium, Sennae folii extractum siccum normatum	Senna leaf, Senna leaf dry extract
Cassia senna	Alexandrian senna		
Rhamnus frangula	Alder buckthorn	Frangulae cortex, Frangulae cortex extractum siccum normatum	Frangula bark, Standardized frangula bark dry extract
Rhamnus purshiana	Cascara buckthorn	Rhamni purshianae extractum siccum normatum	Cascara
Rheum officinale	Rhubarb	Rhei radix	Rhubarb
Rheum palmatum	Chinese rhubarb		
Megacolon			
Atropa belladonna	Deadly nightshade	Belladonnae folium, Belladonnae pulvis normatus, Belladonnae folii tinctura normata, Belladonnae folii extractum siccum normatum	Belladonna leaf, Belladonna, prepared, Belladonna leaf tincture, Standardized belladonna leaf dry extract
Datura stramonium	Thorn apple	Stramonii folium, Stramonii pulvis normatus	Stramonium leaf, Prepared stramonium
Chronic progressive diseases (e.g. tuberculosis, multiple sclerosis, leukaemia, HIV infection, collagen diseases)			
Echinacea angustifolia	Narrow-leaved purple coneflower	Echinaceae angustifoliae radix	Narrow-leaved purple coneflower root
Echinacea pallida	Pale purple coneflower	Echinaceae pallidae radix	Pale purple coneflower root
Echinacea purpurea	Purple coneflower	Echinaceae purpureae radix, Echinaceae purpureae herba	Purple coneflower root, Purple coneflower herb

Contraindications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
High blood pressure (hypertension)			
Eleutherococcus senticosus	Siberian ginseng	Eleuterococci radix	Eleutherococcus
Ephedra sinica	Ephedra, Ma Huang	Ephedrae herba	Ephedra
Ephedra intermedia	Zhong Ma Huang		
Ephedra equisetina	Muzei Ma Huang		
Glycyrrhiza glabra	Licorice, Liquorice	Liquiritiae radix, Liquiritiae extractum fluidum ethanolicum normatum, Liquiritiae extractum siccum ad saporandum	Liquorice root, Standardized liquorice ethanolic liquid extract, Liquorice root dry extract as a flavouring
Panax ginseng	Korean ginseng	Ginseng radix	Ginseng
Cirrhosis of the liver			
Glycyrrhiza glabra	Licorice, Liquorice	Liquiritiae radix, Liquiritiae extractum fluidum ethanolicum normatum, Liquiritiae extractum siccum ad saporandum	Liquorice root, Standardized liquorice ethanolic liquid extract, Liquorice root dry extract as a flavouring
Esophageal stricture			
Plantago afra	Psyllium	Psylli semen	Psyllium seed
Plantago indica	French psyllium, Sand plantain		
Plantago ovata	Desert indianwheat	Plantaginis ovatae semen, Plantaginis ovatae seminis tegumentum	Ispaghula seed, Ispaghula husk
Enlarged prostate			
Atropa belladonna	Deadly nightshade	Belladonnae folium, Belladonnae pulvis normatus, Belladonnae folii tinctura normata, Belladonnae folii extractum siccum normatum	Belladonna leaf, Belladonna, prepared, Belladonna leaf tincture, Standardized belladonna leaf dry extract
Datura stramonium	Thorn apple	Stramonii folium, Stramonii pulvis normatus	Stramonium leaf, Prepared stramonium
Whooping cough (pertussis)			
Pinus mugo	Mugo pine	Pini pumilionis aetheroleum	Dwarf pine needle oil
Pinus sylvestris	Scots pine	Pini sylvestris aetheroleum	Pine sylvestris oil

Contraindications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Oedema of cardiac or renal origin			
Agropyron repens	Couch grass	Graminis rhizoma	Couch grass rhizome
Betula pendula	Silver birch	Betulae folium	Birch leaf
Betula pubescens	Downy/white birch		
Ephedra sinica	Ephedra, Ma Huang	Ephedrae herba	Ephedra
Ephedra intermedia	Zhong Ma Huang		
Ephedra equisetina	Muzei Ma Huang		
Levisticum officinale	Lovage	Levistici radix	Lovage root
Ononis spinosa	Spiny restharrow	Ononidis radix	Restharrow root
Orthosiphon stamineus	Cat's Whiskers, Java Tea	Orthosiphonis folium	Java tea
Solidago canadensis	Canada goldenrod	Solidaginis herba	Goldenrod
Solidago gigantea	Giant goldenrod		
Solidago virgaurea	European goldenrod	Solidaginis virgaureae herba	European goldenrod
Taraxacum officinale	Dandelion	Taraxaci officinalis radix cum herba, Taraxaci officinalis radix	Dandelion root, Dandelion root with herb
Urtica dioica	Stinging nettle	Urticae folium	Nettle leaf
Urtica urens	Annual nettle, Dwarf nettle or Small Nettle		
Arrhythmia			
Atropa belladonna	Deadly nightshade	Belladonnae folium, Belladonnae pulvis normatus, Belladonnae folii tinctura normata, Belladonnae folii extractum siccum normatum	Belladonna leaf, Belladonna, prepared, Belladonna leaf tincture, Standardized belladonna leaf dry extract
Datura stramonium	Thorn apple	Stramonii folium, Stramonii pulvis normatus	Stramonium leaf, Prepared stramonium
Ephedra sinica	Ephedra, Ma Huang	Ephedrae herba	Ephedra
Ephedra intermedia	Zhong Ma Huang		
Ephedra equisetina	Muzei Ma Huang		
Breastfeeding			
Aloë barbadensis	True/medicinal aloe	Aloë barbadensis, Aloë capensis, Aloës extractum siccum normatum	Cape aloes, Barbados aloes, Standardized aloes dry extract
Aloë ferox	Cape aloe, Bitter aloe, Red aloe, Tap aloe		
Arctostaphylos uva-ursi	Bearberry	Uvae ursi folium	Bearberry leaf
Astragalus membranaceus	Huang qi	Astragali mongholici radix	Membranous milk-vetch root ?

Contraindications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Cassia angustifolia	Tinnevelly senna	Sennae fructus angustifoliae	Tinnevelly senna pods
Cassia senna	Alexandrian senna	Sennae fructus acutifoliae	Alexandrian senna pods
Cassia angustifolia	Tinnevelly senna	Sennae folium, Sennae folii extractum siccum normatum	Senna leaf, Senna leaf dry extract
Cassia senna	Alexandrian senna		
Ephedra sinica	Ephedra, Ma Huang	Ephedrae herba	Ephedra
Ephedra intermedia	Zhong Ma Huang		
Ephedra equisetina	Muzei Ma Huang		
Rhamnus frangula	Alder buckthorn	Frangulae cortex, Frangulae cortex extractum siccum normatum	Frangula bark, Standardized frangula bark dry extract
Rhamnus purshiana	Cascara buckthorn	Rhamni purshianae extractum siccum normatum	Cascara
Rheum officinale	Rhubarb	Rhei radix	Rhubarb
Rheum palmatum	Chinese rhubarb		
Schisandra chinensis	Schizandra	Schisandrae chinensis fructus	Schisandra fruit
Scutellaria baicalensis	Baikal Skullcap	Scutellariae tetrandrae radix	Tetrandra root
Stephania tetrandra		Stephaniae radix	Stephania Root
Vitex agnus-castus	Agnus castus	Agni casti fructus	Agnus castus fruit
Pregnancy			
Aloë barbadensis	True/medicinal aloe	Aloë barbadensis, Aloë capensis, Aloës extractum siccum normatum	Cape aloes, Barbados aloes, Standardized aloes dry extract
Aloë ferox	Cape aloe, Bitter aloe, Red aloe, Tap aloe		
Arctostaphylos uva-ursi	Bearberry	Uvae ursi folium	Bearberry leaf
Artemisia absinthium	Absinthe wormwood	Absinthii herba	Wormwood
Astragalus membranaceus	Huang qi	Astragali mongholici radix	Membranous milk-vetch root ?
Cassia angustifolia	Tinnevelly senna	Sennae fructus angustifoliae	Tinnevelly senna pods
Cassia senna	Alexandrian senna	Sennae fructus acutifoliae	Alexandrian senna pods
Cassia angustifolia	Tinnevelly senna	Sennae folium, Sennae folii extractum siccum normatum	Senna leaf, Senna leaf dry extract
Cassia senna	Alexandrian senna		
Cinchona calisaya	Cinchona	Cinchonae cortex, Cinchonae extractum fluidum normatum	Cinchona bark, Standardised cinchona liquid extract
Cinchona ledgeriana			
Cinchona pubescens	Quinine tree		

Contraindications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Cinnamomum cassia	Cassia/Chinese cinnamon	Cinnamomi cassiae aetheroleum	Cassia oil
Cinnamomum zeylanicum	Ceylon cinnamon	Cinnamomi cortex, Cinnamomi zeylanici corticis aetheroleum, Cinnamomi zeylanici folii aetheroleum, Cinnamomi corticis tinctura	Cinnamon, Cinnamon bark oil, Cinnamon leaf oil, Cinnamon tincture
Echinacea angustifolia	Narrow-leaved purple coneflower	Echinaceae angustifoliae radix	Narrow-leaved purple coneflower root
Echinacea pallida	Pale purple coneflower	Echinaceae pallidae radix	Pale purple coneflower root
Echinacea purpurea	Purple coneflower	Echinaceae purpureae radix, Echinaceae purpureae herba	Purple coneflower root, Purple coneflower herb
Ephedra sinica	Ephedra, Ma Huang	Ephedrae herba	Ephedra
Ephedra intermedia	Zhong Ma Huang		
Ephedra equisetina	Muzei Ma Huang		
Glycyrrhiza glabra	Licorice, Liquorice	Liquiritiae radix, Liquiritiae extractum fluidum ethanolicum normatum, Liquiritiae extractum siccum ad saporandum	Liquorice root, Standardized liquorice ethanolic liquid extract, Liquorice root dry extract as a flavouring
Juniperus communis	Common juniper	Iuniperi pseudo-fructus, Iuniperi aetheroleum	Juniper, Juniper oil
Myristica fragrans	Nutmeg	Myristicae fragrantis aetheroleum	Nutmeg oil
Rhamnus frangula	Alder buckthorn	Frangulae cortex, Frangulae cortex extractum siccum normatum	Frangula bark, Standardized frangula bark dry extract
Rhamnus purshiana	Cascara buckthorn	Rhamni purshianae extractum siccum normatum	Cascara
Rheum officinale	Rhubarb	Rhei radix	Rhubarb
Rheum palmatum	Chinese rhubarb		
Salvia officinalis	Sage	Salviae officinalis folium, Salviae tinctura	Sage leaf, Sage tincture
Schisandra chinensis	Schizandra	Schisandrae chinensis fructus	Schisandra fruit
Scutellaria baicalensis	Baikal Skullcap	Scutellariae tetrandrae radix	Tetrandra root
Stephania tetrandra		Stephaniae radix	Stephania root
Vitex agnus-castus	Agnus castus	Agni casti fructus	Agnus castus fruit
Zingiber officinale	Ginger	Zingiberis rhizoma	Ginger

Contraindications			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Pulmonary oedema			
Atropa belladonna	Deadly nightshade	Belladonnae folium, Belladonnae pulvis normatus, Belladonnae folii tinctura normata, Belladonnae folii extractum siccum normatum	Belladonna leaf, Belladonna, prepared, Belladonna leaf tincture, Standardized belladonna leaf dry extract
Datura stramonium	Thorn apple	Stramonii folium, Stramonii pulvis normatus	Stramonium leaf, Prepared stramonium
Inflammation of the kidney			
Glycyrrhiza glabra	Licorice, Liquorice	Liquiritiae radix, Liquiritiae extractum fluidum ethanolicum normatum, Liquiritiae extractum siccum ad saporandum	Liquorice root, Standardized liquorice ethanolic liquid extract, Liquorice root dry extract as a flavouring
Juniperus communis	Common juniper	Iuniperi pseudo-fructus, Iuniperi aetheroleum	Juniper, Juniper oil
Levisticum officinale	Lovage	Levistici radix	Lovage root
Glaucoma			
Atropa belladonna	Deadly nightshade	Belladonnae folium, Belladonnae pulvis normatus, Belladonnae folii tinctura normata, Belladonnae folii extractum siccum normatum	Belladonna leaf, Belladonna, prepared, Belladonna leaf tincture, Standardized belladonna leaf dry extract
Datura stramonium	Thorn apple	Stramonii folium, Stramonii pulvis normatus	Stramonium leaf, Prepared stramonium
Ephedra sinica	Ephedra, Ma Huang	Ephedrae herba	Ephedra
Ephedra intermedia	Zhong Ma Huang		
Ephedra equisetina	Muzei Ma Huang		

Side effects

Side effects			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Visual accommodation disturbance			
Atropa belladonna	Deadly nightshade	Belladonnae folium, Belladonnae pulvis normatus, Belladonnae folii tinctura normata, Belladonnae folii extractum siccum normatum	Belladonna leaf, Belladonna, prepared, Belladonna leaf tincture, Standardized belladonna leaf dry extract
Datura stramonium	Thorn apple	Stramonii folium, Stramonii pulvis normatus	Stramonium leaf, Prepared stramonium
Sleep disorders			
Cola acuminata		Colae semen	Cola
Cola nitida			
Contact allergy to herbal teas derived from the Asteraceae plant family			
Achillea millefolium	Yarrow	Millefolii herba	Yarrow
Arnica montana	Mountain arnica / wolf's bane	Arnicae flos, Arnicae tinctura	Arnica flower, Arnica tincture
Artemisia absinthium	Absinthe wormwood	Absinthii herba	Wormwood
Calendula officinalis	Calendula	Calendulae flos	Calendula flower
Carthamus tinctorius	Safflower	Carthami flos, Carthami oleum raffinatum	Carthamus flower, Safflower flower, Refined safflower oil
Chamaemelum nobile	Roman chamomile	Chamomillae romanae flos	Roman chamomile flower
Cynara scolymus	Artichoke	Cynarae folium, Cynarae folii extractus siccum	Artichoke leaf, Artichoke leaf dry extract
Echinacea angustifolia	Narrow-leaved purple coneflower	Echinaceae angustifoliae radix	Narrow-leaved purple coneflower root
Echinacea pallida	Pale purple coneflower	Echinaceae pallidae radix	Pale purple coneflower root
Echinacea purpurea	Purple coneflower	Echinaceae purpureae radix, Echinaceae purpureae herba	Purple coneflower root, Purple coneflower herb
Matricaria recutita	German chamomile	Matricariae flos, Matricariae aetheroleum, Matricariae extractum fluidum	Matricaria flower, Matricaria oil, Matricaria liquid extract
Solidago canadensis	Canada goldenrod	Solidaginis herba	Goldenrod
Solidago gigantea	Giant goldenrod		
Solidago virgaurea	European goldenrod	Solidaginis virgaureae herba	European goldenrod

Side effects			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Silybum marianum	Milk thistle	Silybi mariani fructus, Silybi mariani extractum siccum raffinatum et normatum	Milk-thistle fruit, Preset (standardised) purified milk thistle dried extract
Tanacetum parthenium	Feverfew	Tanaceti parthenii herba	Feverfew
Taraxacum officinale	Dandelion	Taraxaci officinalis radix cum herba, Taraxaci officinalis radix	Dandelion root, Dandelion root with herb
Changes in the natural intestinal flora			
Allium sativum	Garlic	Allii sativi bulbi pulvis	Garlic powder
Deficient peristalsis			
Aloë barbadensis	True/medicinal aloe	Aloë barbadensis, Aloë capensis, Aloës extractum siccum normatum	Cape aloes, Barbados aloes, Standardized aloes dry extract
Aloë ferox	Cape aloe, Bitter aloe, Red aloe, Tap aloe		
Cassia angustifolia	Tinnevelly senna	Sennae fructus angustifoliae	Tinnevelly senna pods
Cassia senna	Alexandrian senna	Sennae fructus acutifoliae	Alexandrian senna pods
Cassia angustifolia	Tinnevelly senna	Sennae folium, Sennae folii extractum siccum normatum	Senna leaf, Senna leaf dry extract
Cassia senna	Alexandrian senna		
Rhamnus frangula	Alder buckthorn	Frangulae cortex, Frangulae cortex extractum siccum normatum	Frangula bark, Standardized frangula bark dry extract
Rhamnus purshiana	Cascara buckthorn	Rhamni purshianae extractum siccum normatum	Cascara
Rheum officinale	Rhubarb	Rhei radix	Rhubarb
Rheum palmatum	Chinese rhubarb		
Allergic skin reactions			
Cinchona calisaya	Cinchona	Cinchonae cortex, Cinchonae extractum fluidum normatum	Cinchona bark, Standardised cinchona liquid extract
Cinchona ledgeriana			
Cinchona pubescens	Quinine tree		
Cinnamomum cassia	Cassia/Chinese cinnamon	Cinnamomi cassiae aetheroleum	Cassia oil
Cinnamomum zeylanicum	Ceylon cinnamon	Cinnamomi cortex, Cinnamomi zeylanici corticis aetheroleum, Cinnamomi zeylanici folii aetheroleum, Cinnamomi corticis tinctura	Cinnamon, Cinnamon bark oil, Cinnamon leaf oil, Cinnamon tincture

Side effects			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Cymbopogon winterianus	Citronella grass, Java grass, Cymbopogon grass	Citronellae aetheroleum	Citronella oil
Foeniculum vulgare subsp. vulgare var. dulce	Sweet fennel	Foeniculi dulcis fructus	Sweet fennel
Foeniculum vulgare subsp. vulgare var. vulgare	Bitter fennel	Foeniculi amari fructus, Foeniculi amari fructus aetheroleum, Foeniculi amari herbae aetheroleum	Bitter fennel, Bitter-fennel fruit oil, Bitter fennel herb oil
Myroxylon balsamum var. pereirae	Peru balsam tree	Balsamum peruvianum	Peru balsam
Pimpinella anisum	Aniseed	Anisi fructus, Anisi aetheroleum	Aniseed, Anise oil
Dermatitis			
Capsicum annuum var. minimum	Cayenne pepper	Capsici fructus, Capsici oleoresina raffinata et quantificata, Capsici tinctura normata	Capsicum, Refined and quantified capsicum oleoresin, Capsicum tincture
Capsicum frutescens	Chili pepper		
Pinus mugo	Mugo pine	Pini pumilionis aetheroleum	Dwarf pine needle oil
Pinus sylvestris	Scots pine	Pini sylvestris aetheroleum	Pine sylvestris oil
Disturbed electrolyte homeostasis			
Aloë barbadensis	True/medicinal aloe	Aloë barbadensis, Aloë capensis, Aloës extractum siccum normatum	Cape aloes, Barbados aloes, Standardized aloes dry extract
Aloë ferox	Cape aloe, Bitter aloe, Red aloe, Tap aloe		
Cassia angustifolia	Tinnevelly senna	Sennae fructus angustifoliae	Tinnevelly senna pods
Cassia senna	Alexandrian senna	Sennae fructus acutifoliae	Alexandrian senna pods
Cassia angustifolia	Tinnevelly senna	Sennae folium, Sennae folii extractum siccum normatum	Senna leaf, Senna leaf dry extract
Cassia senna	Alexandrian senna		
Glycyrrhiza glabra	Licorice, Liquorice	Liquiritiae radix, Liquiritiae extractum fluidum ethanolicum normatum, Liquiritiae extractum siccum ad saporandum	Liquorice root, Standardized liquorice ethanolic liquid extract, Liquorice root dry extract as a flavouring
Rhamnus frangula	Alder buckthorn	Frangulae cortex, Frangulae cortex extractum siccum normatum	Frangula bark, Standardized frangula bark dry extract
Rhamnus purshiana	Cascara buckthorn	Rhamni purshianae extractum siccum normatum	Cascara

Side effects			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Rheum officinale	Rhubarb	Rhei radix	Rhubarb
Rheum palmatum	Chinese rhubarb		
Allergic reactions of the gastrointestinal system			
Pimpinella anisum	Aniseed	Anisi fructus, Anisi aetheroleum	Aniseed, Anise oil
Gastrointestinal disorders			
Agrimonia eupatoria	Common agrimony	Agrimoniae herba	Agrimony
Alchemilla vulgaris	Lady's mantle	Alchemillae herba	Alchemilla
Allium sativum	Garlic	Allii sativi bulbi pulvis	Garlic powder
Cola acuminata		Colae semen	Cola
Cola nitida			
Curcuma xanthorrhiza	Javanese turmeric	Curcumae xanthorrhizae rhizoma	Javanese turmeric
Eucalyptus globulus	Eucalyptus	Eucalyptus globulus: Eucalypti folium, Eucalypti aetheroleum	Eucalyptus leaf, Eucalyptus oil
Eucalyptus polybractea	Blue mallee		
Eucalyptus smithii	Gully gum		
Lythrum salicaria	Purple loosestrife	Lythri herba	Loosestrife
Mentha canadensis	Japanese mint	Menthae arvensis aetheroleum partim mentholi depletum	Japanese mint essential oil partially deprived of menthol
Mentha x piperita	Peppermint	Menthae piperitae folium, Menthae piperitae aetheroleum	Peppermint leaf, Peppermint oil
Persicaria bistorta	Common bistort, Snakeweed	Bistortae rhizoma	Bistort rhizome
Plantago afra	Psyllium	Psylli semen	Psyllium seed
Plantago indica	French psyllium, Sand plantain		
Plantago ovata	Desert indianwheat	Plantaginis ovatae semen, Plantaginis ovatae seminis tegumentum	Ispaghula seed, Ispaghula husk
Polygala senega	Seneca snakeroot	Polygalae radix	Senega root
Potentilla erecta	Common tormentil	Tormentillae rhizoma, Tormentillae tinctura	Tormentil, Tormentil tincture
Primula elatior	Oxlip	Primulae radix	Primula root
Primula veris	Cowslip		
Quercus petraea	Sessile oak	Quercus cortex (externally)	Oak bark
Quercus pubescens	Downy/pubescent oak		
Quercus robur	Pedunculate oak		
Ruscus aculeatus	Butcher's broom	Rusci rhizoma	Butcher's broom
Sanguisorba minor	Salad burnet, Garden burnet, Small burnet	Sanguisorbae radix	Sanguisorbae radix

Side effects			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Vaccinium myrtillus	Bilberry	Myrtilli fructus siccus, Myrtilli fructus recens	Dried bilberry fruit, Fresh bilberry fruit
Albuminuria			
Aloë barbadensis	True/medicinal aloe	Aloë barbadensis, Aloë capensis, Aloës extractum siccum normatum	Cape aloes, Barbados aloes, Standardized aloes dry extract
Aloë ferox	Cape aloe, Bitter aloe, Red aloe, Tap aloe		
Cassia angustifolia	Tinnevelly senna	Sennae fructus angustifoliae	Tinnevelly senna pods
Cassia senna	Alexandrian senna	Sennae fructus acutifoliae	Alexandrian senna pods
Cassia angustifolia	Tinnevelly senna	Sennae folium, Sennae folii extractum siccum normatum	Senna leaf, Senna leaf dry extract
Cassia senna	Alexandrian senna		
Rhamnus frangula	Alder buckthorn	Frangulae cortex, Frangulae cortex extractum siccum normatum	Frangula bark, Standardized frangula bark dry extract
Rhamnus purshiana	Cascara buckthorn	Rhamni purshianae extractum siccum normatum	Cascara
Rheum officinale	Rhubarb	Rhei radix	Rhubarb
Rheum palmatum	Chinese rhubarb		
Headache (cephalalgia)			
Gentiana lutea	Great yellow gentian	Gentianae radix, Gentianae tinctura	Gentian root, Gentian tincture
Ginkgo biloba	Ginkgo	Ginkgonis folium, Ginkgonis extractum siccum raffinatum et quantificatum	Ginkgo leaf, Refined and quantified ginkgo dry extract
Melilotus officinalis	Sweet clover, Yellow melilot, Ribbed melilot, Common melilot	Meliloti herba	Melilot
Photosensitisation			
Angelica archangelica	Garden angelica	Angelicae radix	Angelica root
Citrus aurantium subsp. aurantium	Bitter orange	Aurantii amari epicarpium et mesocarpium	Bitter-orange epicarp and mesocarp
Hypericum perforatum	St. John’s wort	Hyperici herba, Hyperici herba extractum siccum quantificatum	St. John's wort, Quantified hypericum dried extract
Levisticum officinale	Lovage	Levistici radix	Lovage root

Side effects			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Fluid retention			
Glycyrrhiza glabra	Licorice, Liquorice	Liquiritiae radix, Liquiritiae extractum fluidum ethanolicum normatum, Liquiritiae extractum siccum ad saporandum	Liquorice root, Standardized liquorice ethanolic liquid extract, Liquorice root dry extract as a flavouring
Hallucination			
Atropa belladonna	Deadly nightshade	Belladonnae folium, Belladonnae pulvis normatus, Belladonnae folii tinctura normata, Belladonnae folii extractum siccum normatum	Belladonna leaf, Belladonna, prepared, Belladonna leaf tincture, Standardized belladonna leaf dry extract
Datura stramonium	Thorn apple	Stramonii folium, Stramonii pulvis normatus	Stramonium leaf, Prepared stramonium
Myristica fragrans	Nutmeg	Myristicae fragrantis aetheroleum	Nutmeg oil
Nausea and vomiting			
Arctostaphylos uva-ursi	Bearberry	Uvae ursi folium	Bearberry leaf
Eucalyptus globulus	Eucalyptus	Eucalyptus globulus: Eucalypti folium, Eucalypti aetheroleum	Eucalyptus leaf, Eucalyptus oil
Eucalyptus polybractea	Blue mallee		
Eucalyptus smithii	Gully gum		
Polygala senega	Seneca snakeroot	Polygalae radix	Senega root
Primula elatior	Oxlip	Primulae radix	Primula root
Primula veris	Cowslip		
Ruscus aculeatus	Butcher’s broom	Rusci rhizoma	Butcher's broom
Abdominal cramps			
Aloë barbadensis	True/medicinal aloe	Aloë barbadensis, Aloë capensis, Aloës extractum siccum normatum	Cape aloes, Barbados aloes, Standardized aloes dry extract
Aloë ferox	Cape aloe, Bitter aloe, Red aloe, Tap aloe		
Cassia angustifolia	Tinnevelly senna	Sennae fructus angustifoliae	Tinnevelly senna pods
Cassia senna	Alexandrian senna	Sennae fructus acutifoliae	Alexandrian senna pods
Cassia angustifolia	Tinnevelly senna	Sennae folium, Sennae folii extractum siccum normatum	Senna leaf, Senna leaf dry extract
Cassia senna	Alexandrian senna		
Rhamnus frangula	Alder buckthorn	Frangulae cortex, Frangulae cortex extractum siccum normatum	Frangula bark, Standardized frangula bark dry extract

Side effects			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Rhamnus purshiana	Cascara buckthorn	Rhamni purshianae extractum siccum normatum	Cascara
Rheum officinale	Rhubarb	Rhei radix	Rhubarb
Rheum palmatum	Chinese rhubarb		
Increased risk for bronchial constriction			
Pinus mugo	Mugo pine	Pini pumilionis aetheroleum	Dwarf pine needle oil
Pinus sylvestris	Scots pine	Pini sylvestris aetheroleum	Pine sylvestris oil
Mentha canadensis	Japanese mint	Menthae arvensis aetheroleum partim mentholi depletum	Japanese mint essential oil partially deprived of menthol
Mentha x piperita	Peppermint	Menthae piperitae folium, Menthae piperitae aetheroleum	Peppermint leaf, Peppermint oil
Irritability, excitement, restlessness			
Cola acuminata		Colae semen	Cola
Cola nitida			
Muscle cramp			
Atropa belladonna	Deadly nightshade	Belladonnae folium, Belladonnae pulvis normatus, Belladonnae folii tinctura normata, Belladonnae folii extractum siccum normatum	Belladonna leaf, Belladonna, prepared, Belladonna leaf tincture, Standardized belladonna leaf dry extract
Datura stramonium	Thorn apple	Stramonii folium, Stramonii pulvis normatus	Stramonium leaf, Prepared stramonium
Potassium deficiency			
Aloë barbadensis	True/medicinal aloe	Aloë barbadensis, Aloë capensis, Aloës extractum siccum normatum	Cape aloes, Barbados aloes, Standardized aloes dry extract
Aloë ferox	Cape aloe, Bitter aloe, Red aloe, Tap aloe		
Cassia angustifolia	Tinnevelly senna	Sennae fructus angustifoliae	Tinnevelly senna pods
Cassia senna	Alexandrian senna	Sennae fructus acutifoliae	Alexandrian senna pods
Cassia angustifolia	Tinnevelly senna	Sennae folium, Sennae folii extractum siccum normatum	Senna leaf, Senna leaf dry extract
Cassia senna	Alexandrian senna		
Glycyrrhiza glabra	Licorice, Liquorice	Liquiritiae radix, Liquiritiae extractum fluidum ethanolicum normatum, Liquiritiae extractum siccum ad saporandum	Liquorice root, Standardized liquorice ethanolic liquid extract, Liquorice root dry extract as a flavouring

Side effects			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Rhamnus frangula	Alder buckthorn	Frangulae cortex, Frangulae cortex extractum siccum normatum	Frangula bark, Standardized frangula bark dry extract
Rhamnus purshiana	Cascara buckthorn	Rhamni purshianae extractum siccum normatum	Cascara
Rheum officinale	Rhubarb	Rhei radix	Rhubarb
Rheum palmatum	Chinese rhubarb		
Allergic reactions of the respiratory system			
Foeniculum vulgare subsp. vulgare var. dulce	Sweet fennel	Foeniculi dulcis fructus	Sweet fennel
Foeniculum vulgare subsp. vulgare var. vulgare	Bitter fennel	Foeniculi amari fructus, Foeniculi amari fructus aetheroleum, Foeniculi amari herbae aetheroleum	Bitter fennel, Bitter-fennel fruit oil, Bitter fennel herb oil
Mentha canadensis	Japanese mint	Menthae arvensis aetheroleum partim mentholi depletum	Japanese mint essential oil partially deprived of menthol
Mentha x piperita	Peppermint	Menthae piperitae folium, Menthae piperitae aetheroleum	Peppermint leaf, Peppermint oil
Pimpinella anisum	Aniseed	Anisi fructus, Anisi aetheroleum	Aniseed, Anise oil
High blood pressure (hypertension)			
Ephedra sinica	Ephedra, Ma Huang	Ephedrae herba	Ephedra
Ephedra intermedia	Zhong Ma Huang		
Ephedra equisetina	Muzei Ma Huang		
Glycyrrhiza glabra	Licorice, Liquorice	Liquiritiae radix, Liquiritiae extractum fluidum ethanolicum normatum, Liquiritiae extractum siccum ad saporandum	Liquorice root, Standardized liquorice ethanolic liquid extract, Liquorice root dry extract as a flavouring
Sodium retention			
Glycyrrhiza glabra	Licorice, Liquorice	Liquiritiae radix, Liquiritiae extractum fluidum ethanolicum normatum, Liquiritiae extractum siccum ad saporandum	Liquorice root, Standardized liquorice ethanolic liquid extract, Liquorice root dry extract as a flavouring

Side effects			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Hyperthermia			
Atropa belladonna	Deadly nightshade	Belladonnae folium, Belladonnae pulvis normatus, Belladonnae folii tinctura normata, Belladonnae folii extractum siccum normatum	Belladonna leaf, Belladonna, prepared, Belladonna leaf tincture, Standardized belladonna leaf dry extract
Cinchona calisaya	Cinchona	Cinchonae cortex, Cinchonae extractum fluidum normatum	Cinchona bark, Standardised cinchona liquid extract
Cinchona ledgeriana			
Cinchona pubescens	Quinine tree		
Datura stramonium	Thorn apple	Stramonii folium, Stramonii pulvis normatus	Stramonium leaf, Prepared stramonium
Irritations and allergic reactions of the mucous membranes			
Cinnamomum cassia	Cassia/Chinese cinnamon	Cinnamomi cassiae aetheroleum	Cassia oil
Cinnamomum zeylanicum	Ceylon cinnamon	Cinnamomi cortex, Cinnamomi zeylanici corticis aetheroleum, Cinnamomi zeylanici folii aetheroleum, Cinnamomi corticis tinctura	Cinnamon, Cinnamon bark oil, Cinnamon leaf oil, Cinnamon tincture
Krameria triandra	Peruvian rhatany	Ratanhiae radix, Ratanhiae tinctura	Rhatany root, Rhatany tincture
Pinus mugo	Mugo pine	Pini pumilionis aetheroleum	Dwarf pine needle oil
Pinus sylvestris	Scots pine	Pini sylvestris aetheroleum	Pine sylvestris oil
Syzygium aromaticum	Clove tree	Caryophylli flos, Caryophylli floris aetheroleum	Clove
Oedema			
Glycyrrhiza glabra	Licorice, Liquorice	Liquiritiae radix, Liquiritiae extractum fluidum ethanolicum normatum, Liquiritiae extractum siccum ad saporandum	Liquorice root, Standardized liquorice ethanolic liquid extract, Liquorice root dry extract as a flavouring
Hyperthyroidism			
Ephedra sinica	Ephedra, Ma Huang	Ephedrae herba	Ephedra
Ephedra intermedia	Zhong Ma Huang		
Ephedra equisetina	Muzei Ma Huang		

Side effects			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Dry mouth (xerostomia)			
Atropa belladonna	Deadly nightshade	Belladonnae folium, Belladonnae pulvis normatus, Belladonnae folii tinctura normata, Belladonnae folii extractum siccum normatum	Belladonna leaf, Belladonna, prepared, Belladonna leaf tincture, Standardized belladonna leaf dry extract
Datura stramonium	Thorn apple	Stramonii folium, Stramonii pulvis normatus	Stramonium leaf, Prepared stramonium
Cardiovascular diseases			
Aloë barbadensis	True/medicinal aloe	Aloë barbadensis, Aloë capensis, Aloës extractum siccum normatum	Cape aloes, Barbados aloes, Standardized aloes dry extract
Aloë ferox	Cape aloe, Bitter aloe, Red aloe, Tap aloe		
Cassia angustifolia	Tinnevelly senna	Sennae fructus angustifoliae	Tinnevelly senna pods
Cassia senna	Alexandrian senna	Sennae fructus acutifoliae	Alexandrian senna pods
Cassia angustifolia	Tinnevelly senna	Sennae folium, Sennae folii extractum siccum normatum	Senna leaf, Senna leaf dry extract
Cassia senna	Alexandrian senna		
Ephedra sinica	Ephedra, Ma Huang	Ephedrae herba	Ephedra
Ephedra intermedia	Zhong Ma Huang		
Ephedra equisetina	Muzei Ma Huang		
Rhamnus frangula	Alder buckthorn	Frangulae cortex, Frangulae cortex extractum siccum normatum	Frangula bark, Standardized frangula bark dry extract
Rhamnus purshiana	Cascara buckthorn	Rhamni purshianae extractum siccum normatum	Cascara
Rheum officinale	Rhubarb	Rhei radix	Rhubarb
Rheum palmatum	Chinese rhubarb		
Tachycardia			
Atropa belladonna	Deadly nightshade	Belladonnae folium, Belladonnae pulvis normatus, Belladonnae folii tinctura normata, Belladonnae folii extractum siccum normatum	Belladonna leaf, Belladonna, prepared, Belladonna leaf tincture, Standardized belladonna leaf dry extract
Datura stramonium	Thorn apple	Stramonii folium, Stramonii pulvis normatus	Stramonium leaf, Prepared stramonium

Side effects			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Ephedra sinica	Ephedra, Ma Huang	Ephedrae herba	Ephedra
Ephedra intermedia	Zhong Ma Huang		
Ephedra equisetina	Muzei Ma Huang		
Thrombocytopenia			
Cinchona calisaya	Cinchona	Cinchonae cortex, Cinchonae extractum fluidum normatum	Cinchona bark, Standardised cinchona liquid extract
Cinchona ledgeriana			
Cinchona pubescens	Quinine tree		
Inflammation of the kidney (nephritis), kidney damaging effects			
Juniperus communis	Common juniper	Iuniperi pseudo-fructus, Iuniperi aetheroleum	Juniper, Juniper oil
Pinus pinaster	Maritime pine	Terebinthae aetheroleum ab Pinum pinastrum	Pinus pinaster type turpentine oil
Increased risk of miscarriage			
Aloë barbadensis	True/medicinal aloe	Aloë barbadensis, Aloë capensis, Aloës extractum siccum normatum	Cape aloes, Barbados aloes, Standardized aloes dry extract
Aloë ferox	Cape aloe, Bitter aloe, Red aloe, Tap aloe		
Cassia angustifolia	Tinnevelly senna	Sennae fructus angustifoliae	Tinnevelly senna pods
Cassia senna	Alexandrian senna	Sennae fructus acutifoliae	Alexandrian senna pods
Cassia angustifolia	Tinnevelly senna	Sennae folium, Sennae folii extractum siccum normatum	Senna leaf, Senna leaf dry extract
Cassia senna	Alexandrian senna		
Myristica fragrans	Nutmeg	Myristicae fragrantis aetheroleum	Nutmeg oil
Rhamnus frangula	Alder buckthorn	Frangulae cortex, Frangulae cortex extractum siccum normatum	Frangula bark, Standardized frangula bark dry extract
Rhamnus purshiana	Cascara buckthorn	Rhamni purshianae extractum siccum normatum	Cascara
Rheum officinale	Rhubarb	Rhei radix	Rhubarb
Rheum palmatum	Chinese rhubarb		
Ricinus communis	Castor oil plant	Ricini oleum virginale, Ricini oleum hydrogenatum, Ricini oleum raffinatum	Virgin Castor oil, Hydrogenated castor oil, Refined castor oil

Side effects			
Latin name of species	***English name of species***	***Latin name of drug/drugs***	***English name of drug/drugs***
Urine discoloration			
Aloë barbadensis	True/medicinal aloe	Aloë barbadensis, Aloë capensis, Aloës extractum siccum normatum	Cape aloes, Barbados aloes, Standardized aloes dry extract
Aloë ferox	Cape aloe, Bitter aloe, Red aloe, Tap aloe		
Cassia angustifolia	Tinnevelly senna	Sennae fructus angustifoliae	Tinnevelly senna pods
Cassia senna	Alexandrian senna	Sennae fructus acutifoliae	Alexandrian senna pods
Cassia angustifolia	Tinnevelly senna	Sennae folium, Sennae folii extractum siccum normatum	Senna leaf, Senna leaf dry extract
Cassia senna	Alexandrian senna		
Rhamnus frangula	Alder buckthorn	Frangulae cortex, Frangulae cortex extractum siccum normatum	Frangula bark, Standardized frangula bark dry extract
Rhamnus purshiana	Cascara buckthorn	Rhamni purshianae extractum siccum normatum	Cascara
Rheum officinale	Rhubarb	Rhei radix	Rhubarb
Rheum palmatum	Chinese rhubarb		
Difficulty with urination			
Atropa belladonna	Deadly nightshade	Belladonnae folium, Belladonnae pulvis normatus, Belladonnae folii tinctura normata, Belladonnae folii extractum siccum normatum	Belladonna leaf, Belladonna, prepared, Belladonna leaf tincture, Standardized belladonna leaf dry extract
Datura stramonium	Thorn apple	Stramonii folium, Stramonii pulvis normatus	Stramonium leaf, Prepared stramonium

Figures

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