Application of aerosols

Topics

- Types of aerosols
- Application of aerosols
- Biopharmaceutical aspects
  - Anatomy
- Preparations for inhalation
  - Liquid preparations
  - Solid preparations

Aerosols

Main types of aerosols:

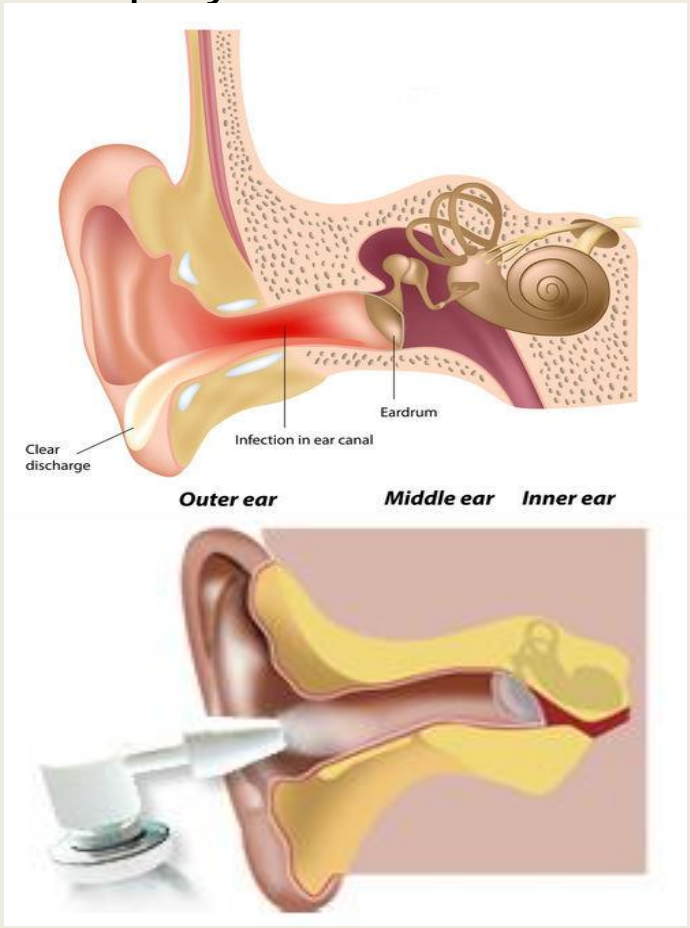
- Solution-based
- Water medium
- Suspension or dispersion systems
- Foam-based systems
  - Water-based, stable foams
  - Non-aqueous, stable foams
  - Quick-breaking foams
  - Temperature sensitive foams

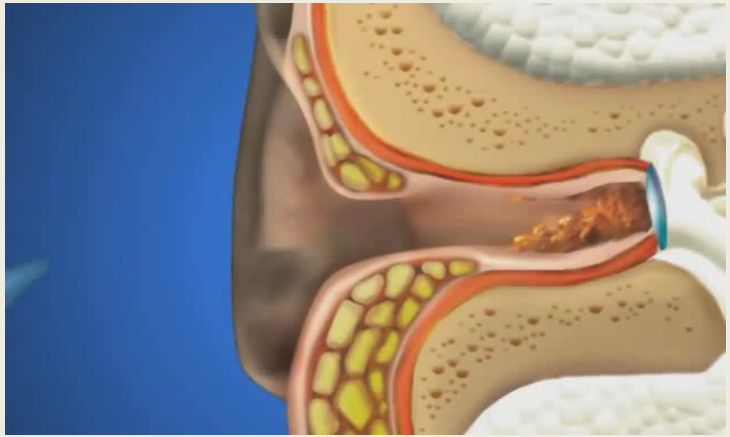
Application of aerosols

Air fresheners

Application of aerosols

Ear spray



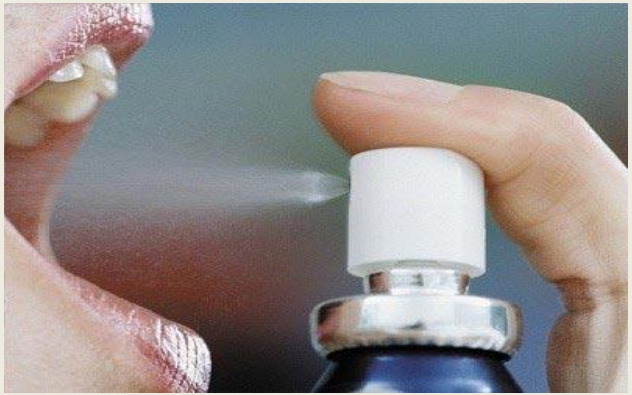


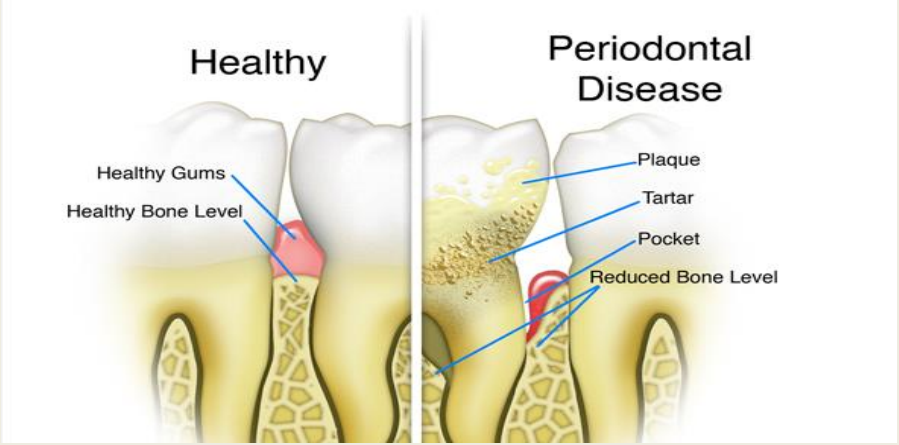
Application of aerosols

Nasal spray

Application of aerosols

Mouth spray





Application of aerosols

Throat treatment

Application of aerosols

Skin therapy

Pigmentation

Application of aerosols

Skin therapy

Sunburn

Application of aerosols

Skin therapy

Skin burning

Application of aerosols

Skin therapy

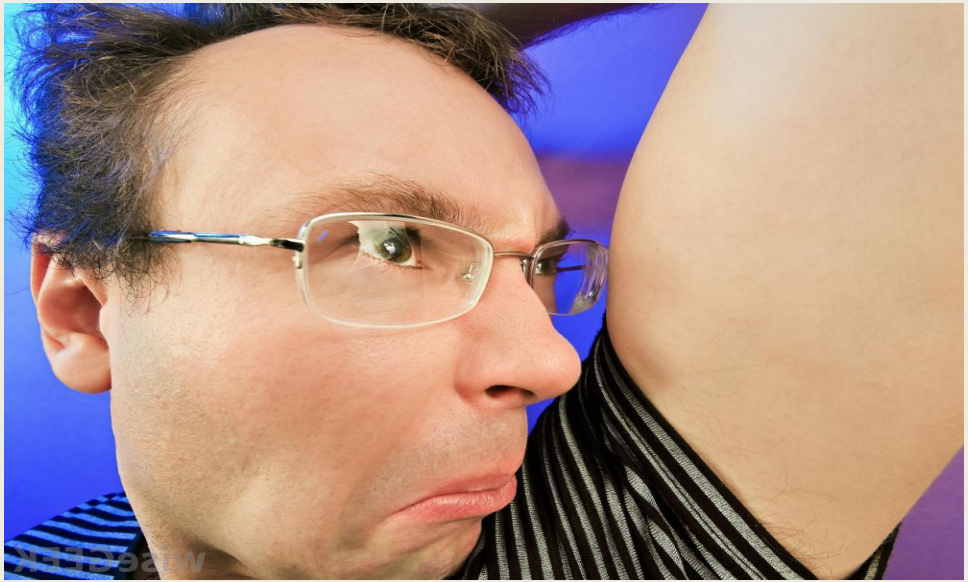
Eczema

Application of aerosols

Antianginal

Application of aerosols

Body odour



Application of aerosols

Foot & nail antifungal spray

Preparations for Inhalation (*Inhalanda*)

Preparations for inhalation

Definition

Preparations for inhalation are **liquid** or **solid** preparations intended for administration as **vapours** or **aerosols** to the **lungs** in order to obtain a **local** or **systemic** effect.

They contain **one** or **more active substances** which may be **dissolved** or **dispersed** in a suitable vehicle.

Preparations for inhalation

Definition

Depending on the type of preparation, inhalation preparations may contain:

- **propellants,**
- **co-solvents,**
- **diluents,**
- **antimicrobial preservatives,**
- **solubilizing and**
- **stabilizing agents, etc.**

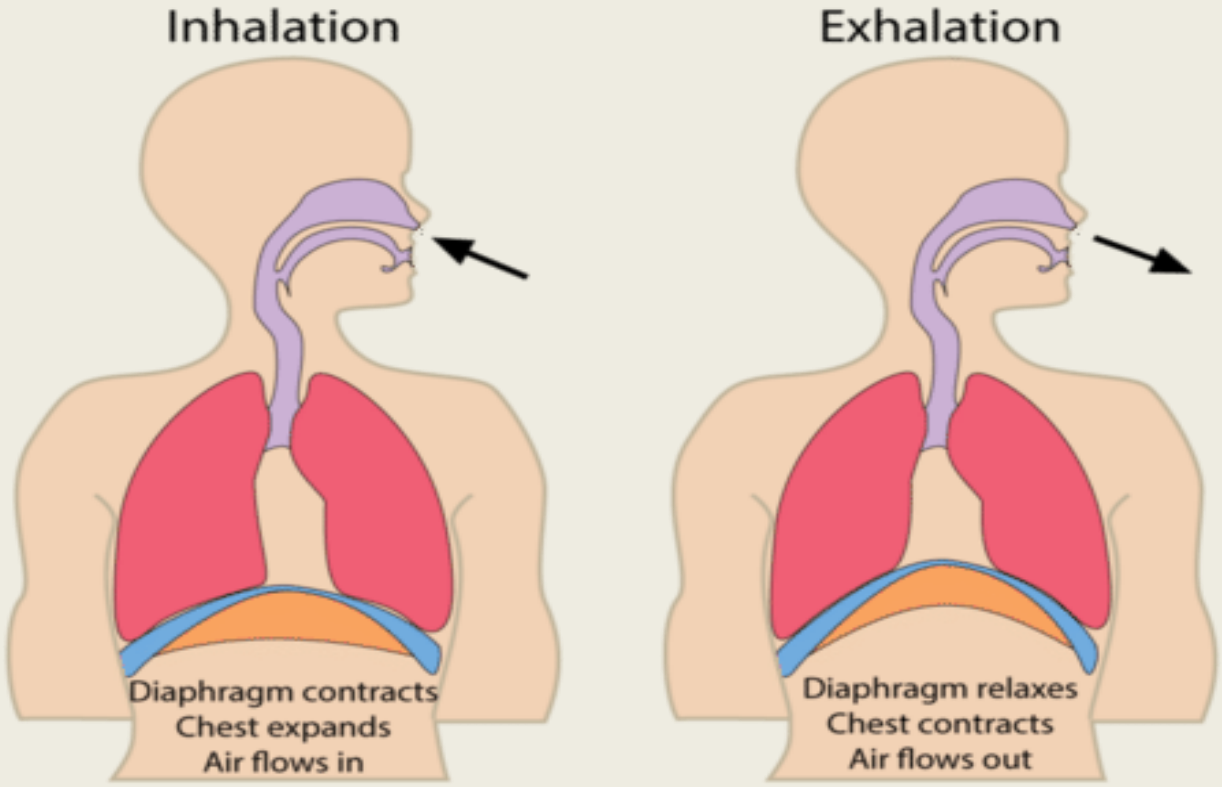
These excipients **do not adversely affect the functions** of the mucosa of the respiratory tract or its cilia.

Preparations for inhalation are supplied in **single** or **multi-dose** containers.

Biopharmaceutical aspects

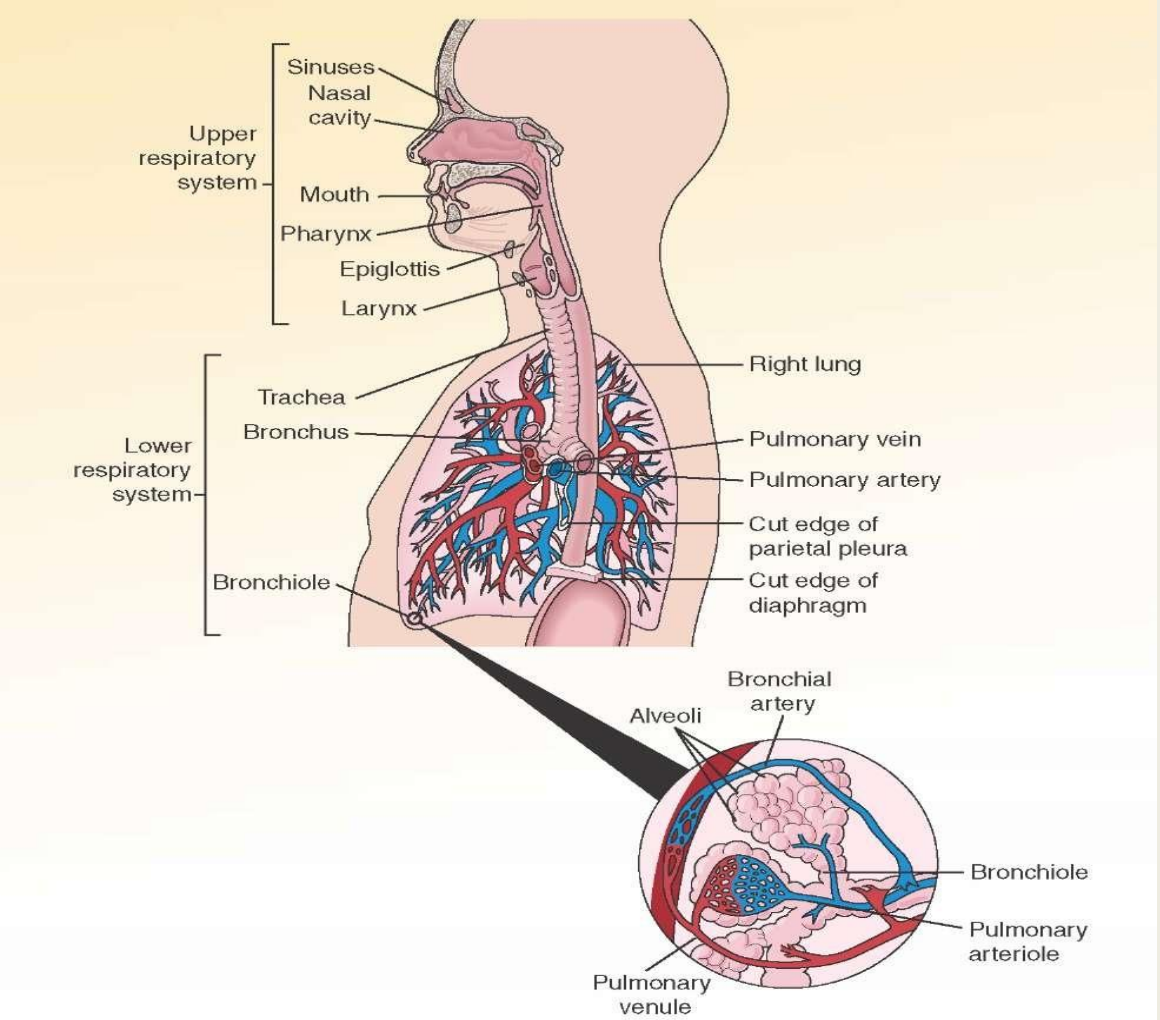
Respiratory system

The breathing



Respiratory system

Airway anatomy



Respiratory system

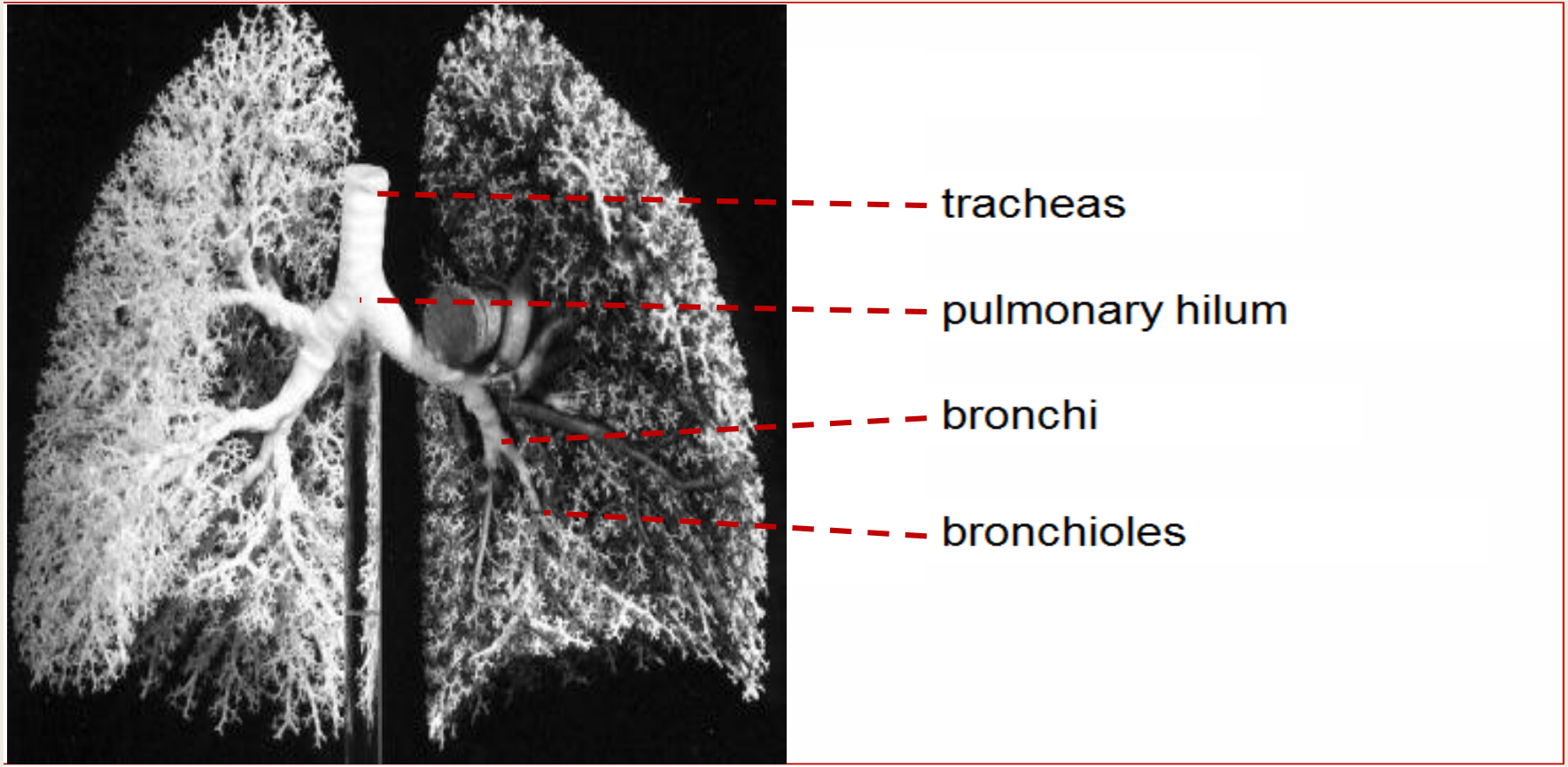
Anatomy of the airways

- Air enters the nostrils
- passes through the nasopharynx,
- the oral pharynx
- through the glottis
- into the trachea
- into the right and left bronchi, which branches and rebranches into
- bronchioles, each of which terminates in a cluster of
- alveoli.

Only in the alveoli does actual gas exchange takes place.
There are some **300 million alveoli** in adult lungs.
These provide a surface area of some 160 m^2.
(Almost equal to the area of a tennis court and 80 times more than the area of our skin!).

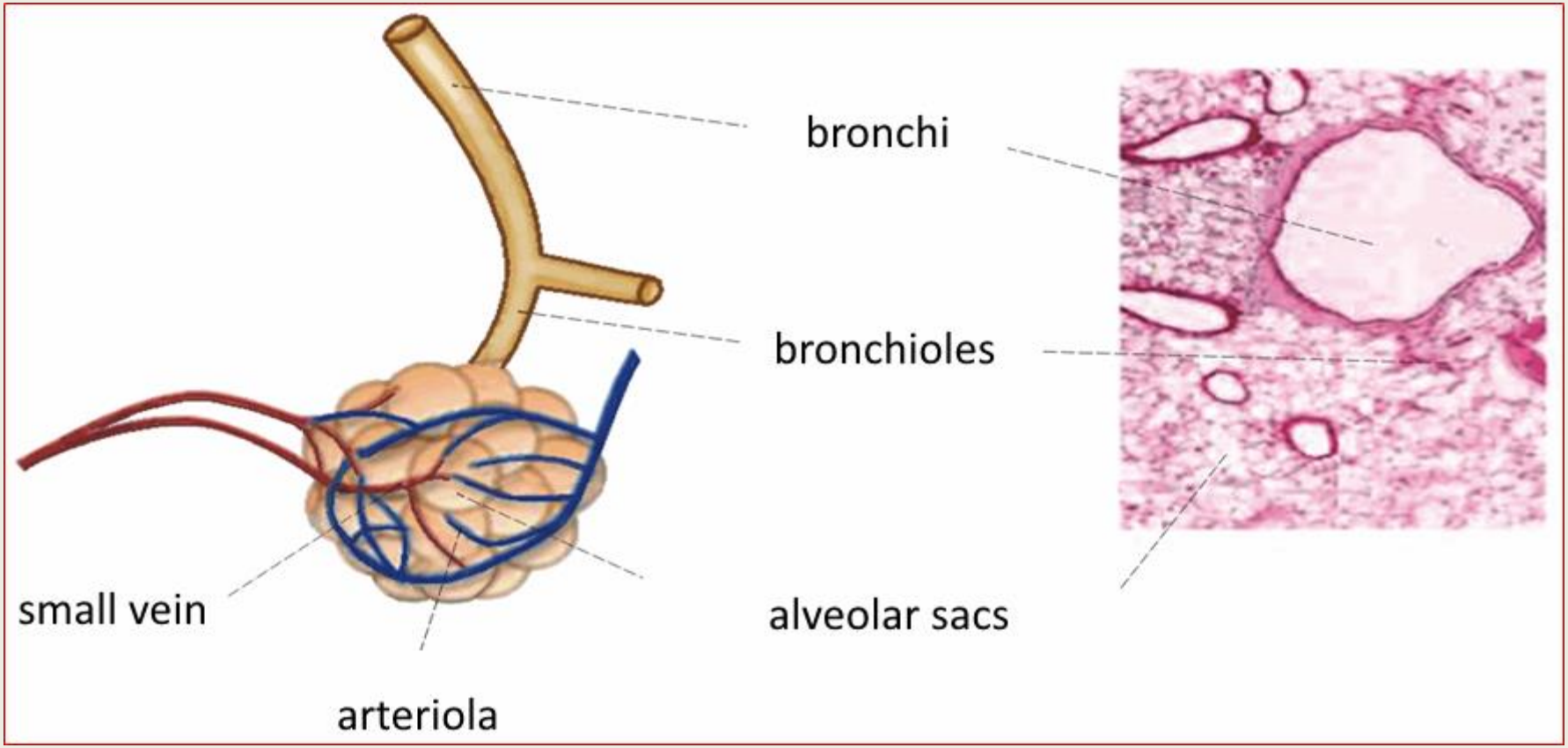
Respiratory system

Anatomy of the airways

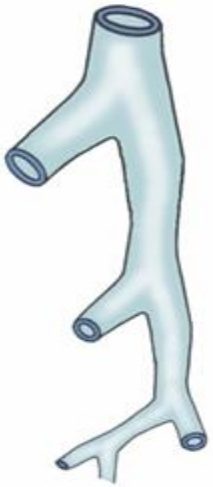


Respiratory system

Anatomy of the airways



Particles in respiratory system

	Surface (m^2)	Dumped particle sizes (μm)
trachea  bronchus	0,03	5 – 20 μm
bronchiolus 	5 – 7,5	1–5 μm
ductus alveolaris alveolus pulmonalis 	100 – 150	

Particles in respiratory system

The mechanism of **deposition** of inhaled particles affect the

- **size,**
- **sedimentation,**
- **density,**
- **shape,**
- **surface charge,**
- **surface tension,**
- **the particles hygroscopicity.**

These properties influenced by the

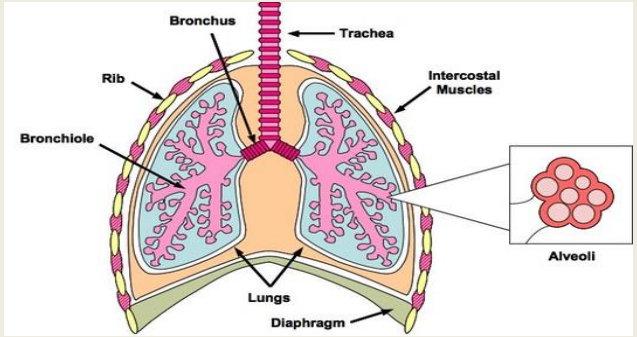
- **excipients,**
- **mode of administration and**
- **the atomizing parameters.**

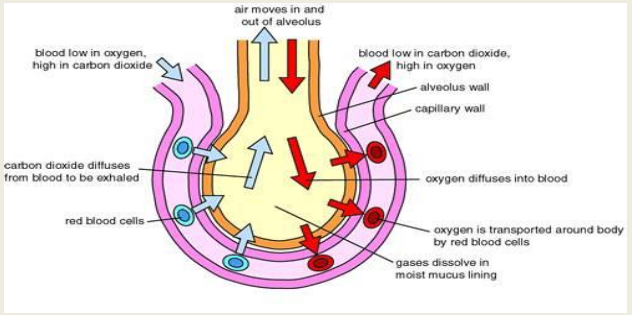
Particles in respiratory system

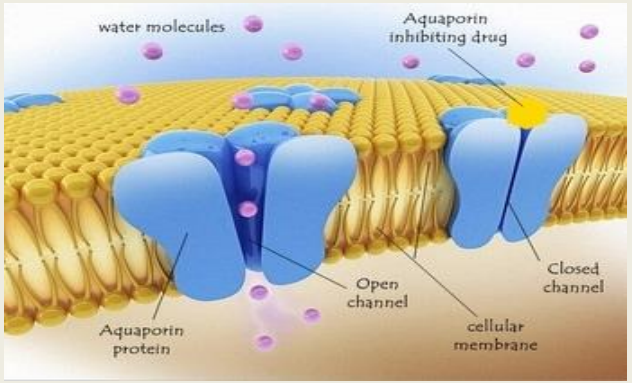
Mechanism of drug absorption

The absorption of drugs may occur by:

- drug **diffusion** through alveoli,
- absorption through aqueous pores by **carrier mediated transport** (aquaporin channel),
- **phagocytosis** of **insoluble particles** allow absorption of compounds with low lipophilicity or high molecular weight.







Preparations for inhalation

Liquid preparations

Liquid preparations

Definition

Liquid preparations for inhalation are **solutions** or **dispersions**.

Liquid preparations for inhalation may be distinguished:

1. preparations intended to be **converted into vapour**,
2. liquid preparations for **nebulisation**,
3. **pressurised metered-dose** preparations for inhalation.

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Liquid preparations

Preparations intended to be converted into vapour

Preparations intended to be converted into **vapour** are

- solutions,
- dispersions or
- solid preparations.

They are usually added to hot water and the vapour generated is inhaled.

Liquid preparations

Liquid preparations for nebulisation

Liquid preparations for inhalation intended to be converted into aerosols by continuously operating nebulisers or metered-dose nebulisers are

- solutions,
- suspensions or
- emulsions.

Suitable co-solvents or solubilisers may be used to increase the solubility of the active substances.

Liquid preparations for nebulisation in concentrated form for use in continuously operating nebulisers are diluted to the prescribed volume with the prescribed liquid before use.

Liquids for nebulisation may also be prepared from powders.

Liquid preparations

Liquid preparations for inhalation

A. Preparations for steaming

- they may be solutions, dispersions or solids. Such formulations are usually added to hot water and the vapour formed must be inhaled.

B. Liquid for nebulization

- aerosolized with a continuous nebulizer or metering valve nebulizer, in the form of solutions, suspensions or emulsions. The solubility of the active ingredient may be increased by the use of a suitable co-solvent or solubilizer.

C. Pressurized inhaled metered dose

- solutions, suspensions or emulsions in dosing valves marketed in special containers which are pressurized with a suitable mixture of propellants or liquefied propellants, whether or not they may be used as solvents. Addition of cosolvents and solubilizers is permitted.

Liquid preparations

Liquid preparations for nebulization
Continuously operating nebulizers

The pH of the liquid preparations for use in **continuously operating nebulizers** is not **lower than pH 3** and **not higher than pH 8.5**.

Suspensions and emulsions are readily dispersible on shaking and they remain sufficiently stable to enable the correct dose to be delivered.

Aqueous preparations for nebulization supplied in **multidose** containers may contain a suitable **antimicrobial preservative** at a suitable concentration except where the preparation itself has adequate antimicrobial properties.

Continuously operating nebulizers are devices that **convert liquids into aerosols** by **high-pressure gases, ultrasonic vibration** or other methods. They allow the dose to be inhaled at an appropriate rate and particle size which ensures deposition of the preparation in the lungs.

Liquid preparations

Liquid preparations for nebulisation

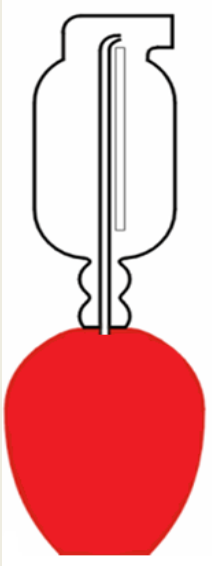
Continuously operating nebulisers

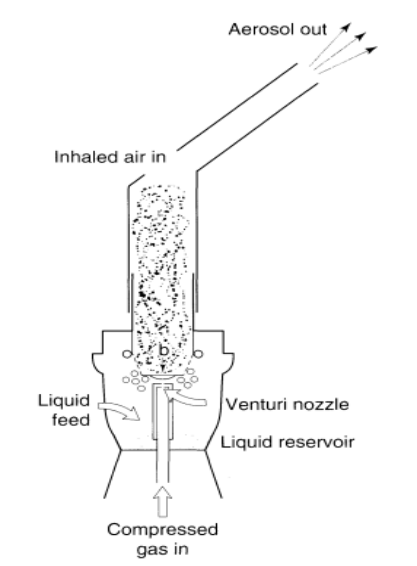
The power injectors with oxygen, compressed air, or ultrasonically produced spray.

Liquid preparations

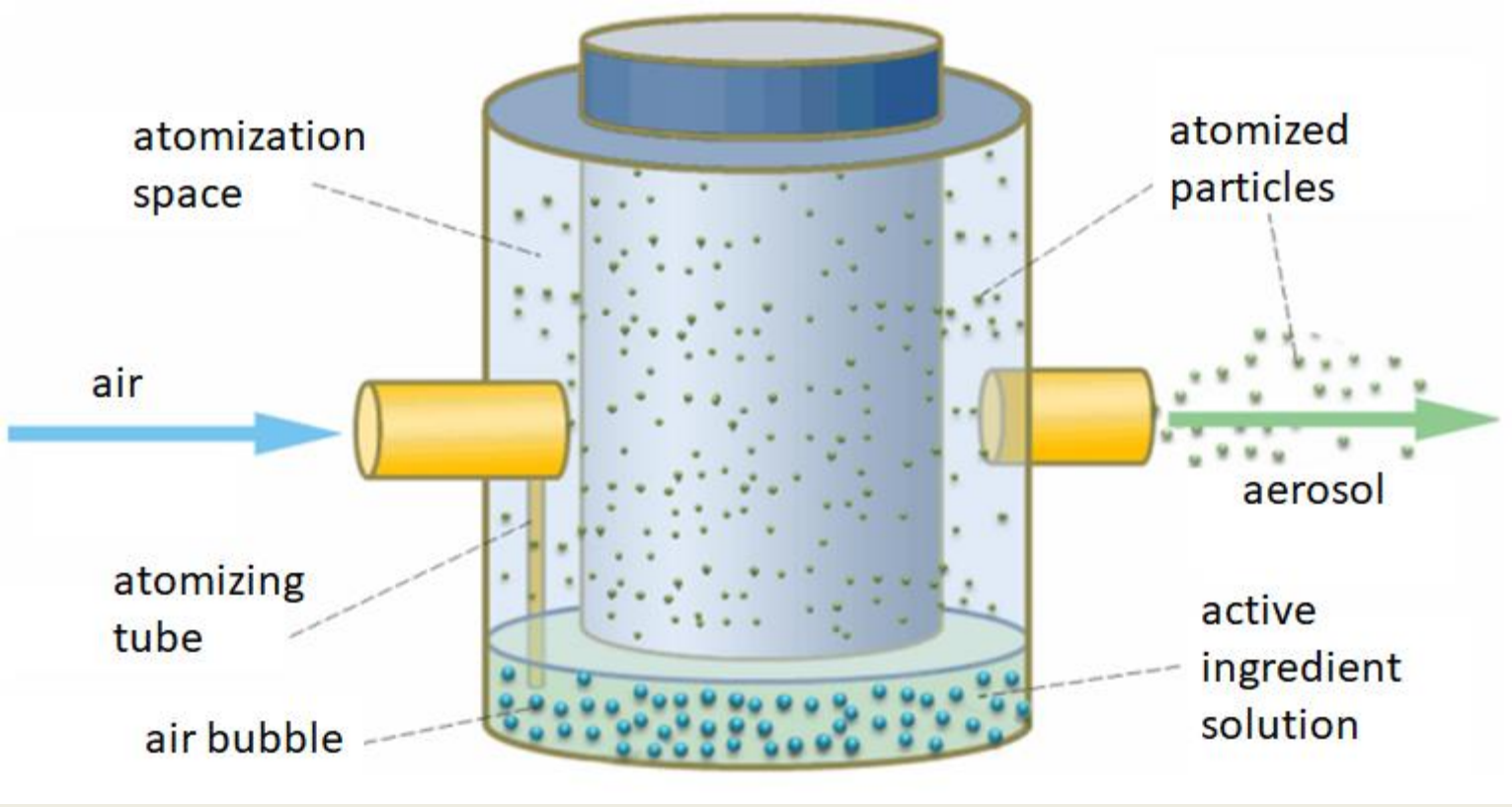
Liquid preparations for nebulisation

Handy nebulizer





Liquid preparations



Inhalation nebulizer equipment

Liquid preparations

Jet nebulizer

Machine sprayers produce spray with oxygen, pressurized air, or ultrasound.

Liquid preparations

Pressurised metered-dose preparations for inhalation

Pressurised metered-dose preparations for inhalation are

- **solutions,**
- **suspensions or**
- **emulsions**

supplied in special containers equipped with a metering valve and which are held under pressure with suitable propellants or suitable mixtures of liquefied propellants, which can act also as solvents.

Liquid preparations

Pressurised metered-dose preparations for inhalation

Suitable **co-solvents**, **solubilisers** and **stabilisers** may be added.

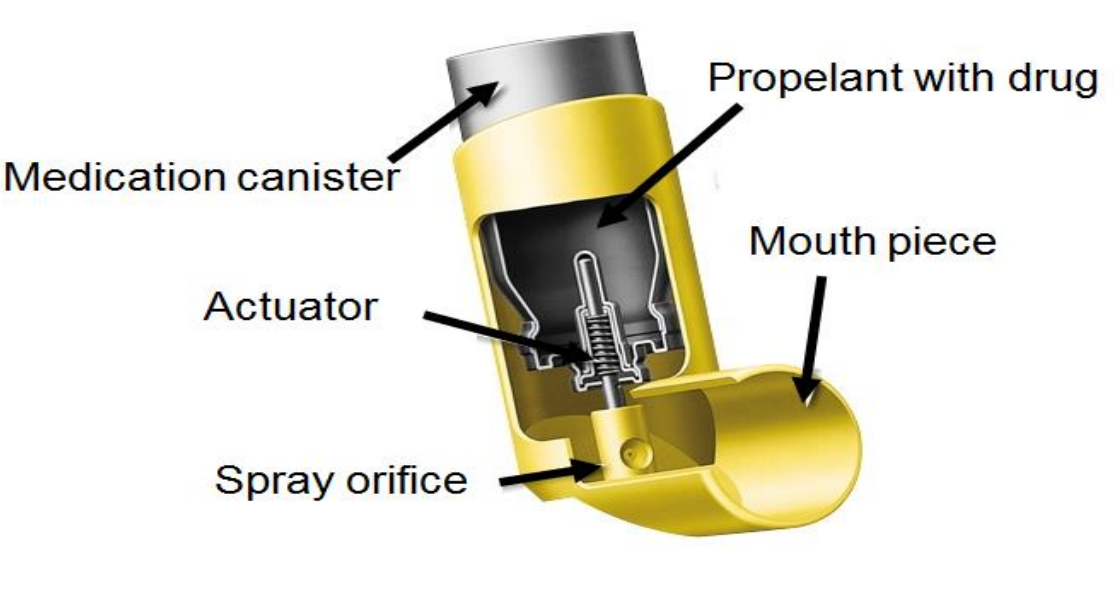
The delivered dose is the dose delivered from the inhaler to the patient.

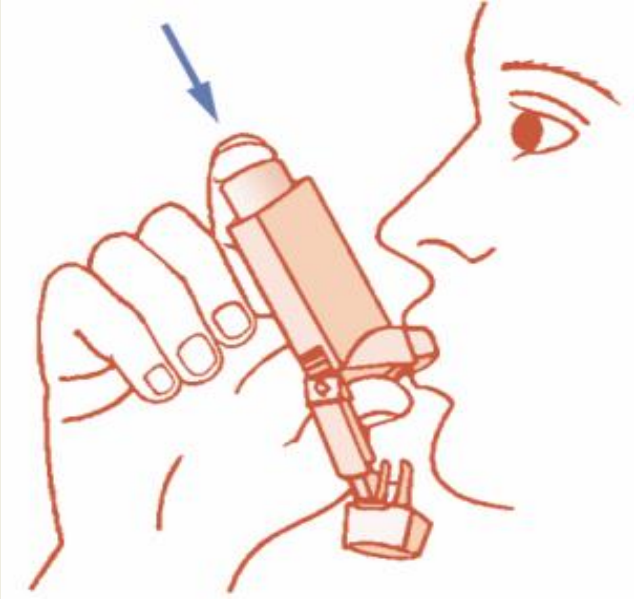
For some preparations, the dose has been established as a **metered-dose.**

The metered-dose is determined by adding the amount deposited within the device to the delivered dose. It may also be determined directly.

Liquid preparations

Pressurised metered-dose preparations for inhalation





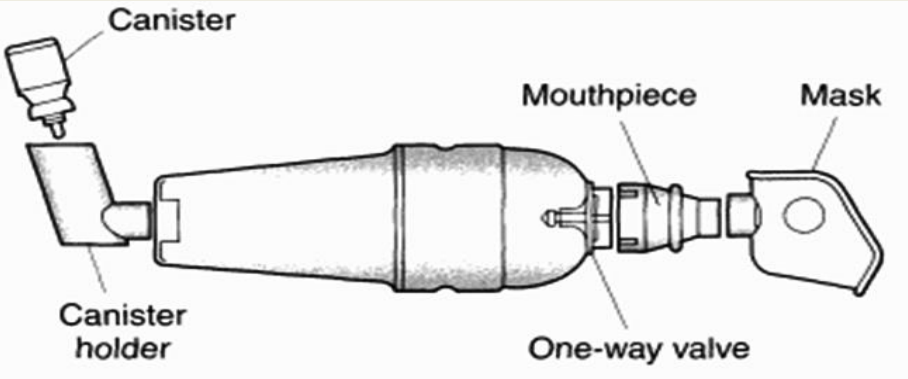
Metered-dose nebulisers are devices that convert liquids into aerosols by high-pressure gases, ultrasonic vibration or other methods.

The volume of liquid to be nebulised is metered so that the aerosol dose can be inhaled with one breath.

Liquid preparations

Pressurised metered-dose preparations for inhalation

Spacer device

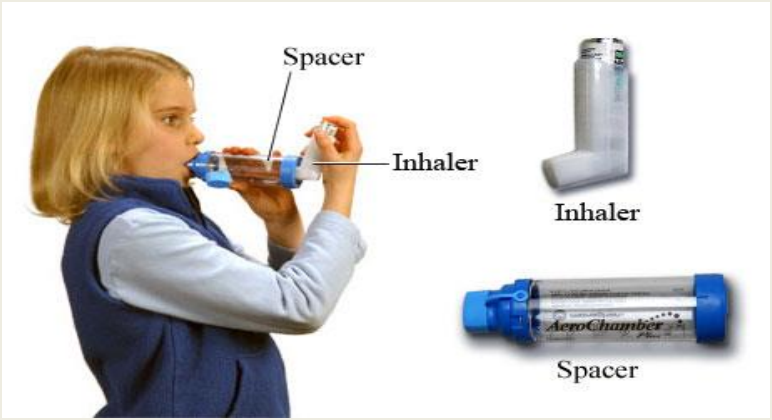


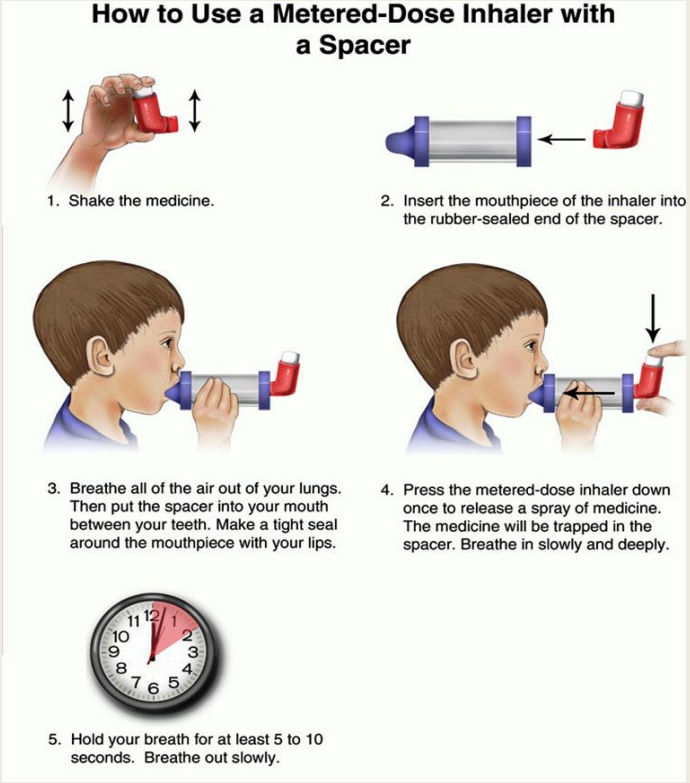
The Nebuhaler® spacer device fitted with a facemask for use by a child

Liquid preparations

Pressurised metered-dose preparations for inhalation

Spacer device





Liquid preparations

Pressurised metered-dose preparations for inhalation

One of the most crucial components of a metered-dose inhaler (MDI) its propellant. The propellant provides the force to generate the aerosol cloud and is also the medium in which the active component must be suspended or dissolved. Propellants in MDIs typically make up more than 99% of the delivered dose, so it is the properties of the propellant that dominate more than any other individual factor.

Suitable propellants must:

- have a boiling point in the range -100 to +30°C
- have a density of approximately 1.2 to 1.5 g cm−3 (approximately that of the drug to be suspended or dissolved)
- have a vapour pressure of 40 to 80 psig
- have no toxicity to the patient
- be non flammable
- be able to dissolve common additives.

Active ingredients should be either fully soluble or fully insoluble.

Liquid preparations

Advantages of metered-dose pressurized preparations

- Easy to carry
- Easy to use
- It does not contaminate during use
- It is aseptically rechargeable and maintains its purity
- Protection from light, oxygen and moisture
- The goal is not-contact during application

Liquid preparations

Disadvantages of pressurized preparations

- Risk of explosion
- Output may be reduced during use
- Limited security
  - *Flammable*
  - *Overpressure*
  - *Unintentional inhalation*
- Insufficient application - in some cases
- Local and nasal sprays can not be water based systems

Pressurised inhalation solutions

- ALVESCO 160 µg
- ATROVENT N 21 µg/dose
- ATIMOS 12 µg/dose
- FOSTER 100 µg/6 µg

Pressurized inhalation suspensions

ECOSAL

VENTOLIN Evohaler

SEREVENT EVOHALER 25 µg/dose

FLIXOTIDE EVOHALER 125 µg/dose

FLIXOTIDE EVOHALER 250 µg/dose

SYMBICORT forte SERETIDE Evohaler 25/50 µg/dose

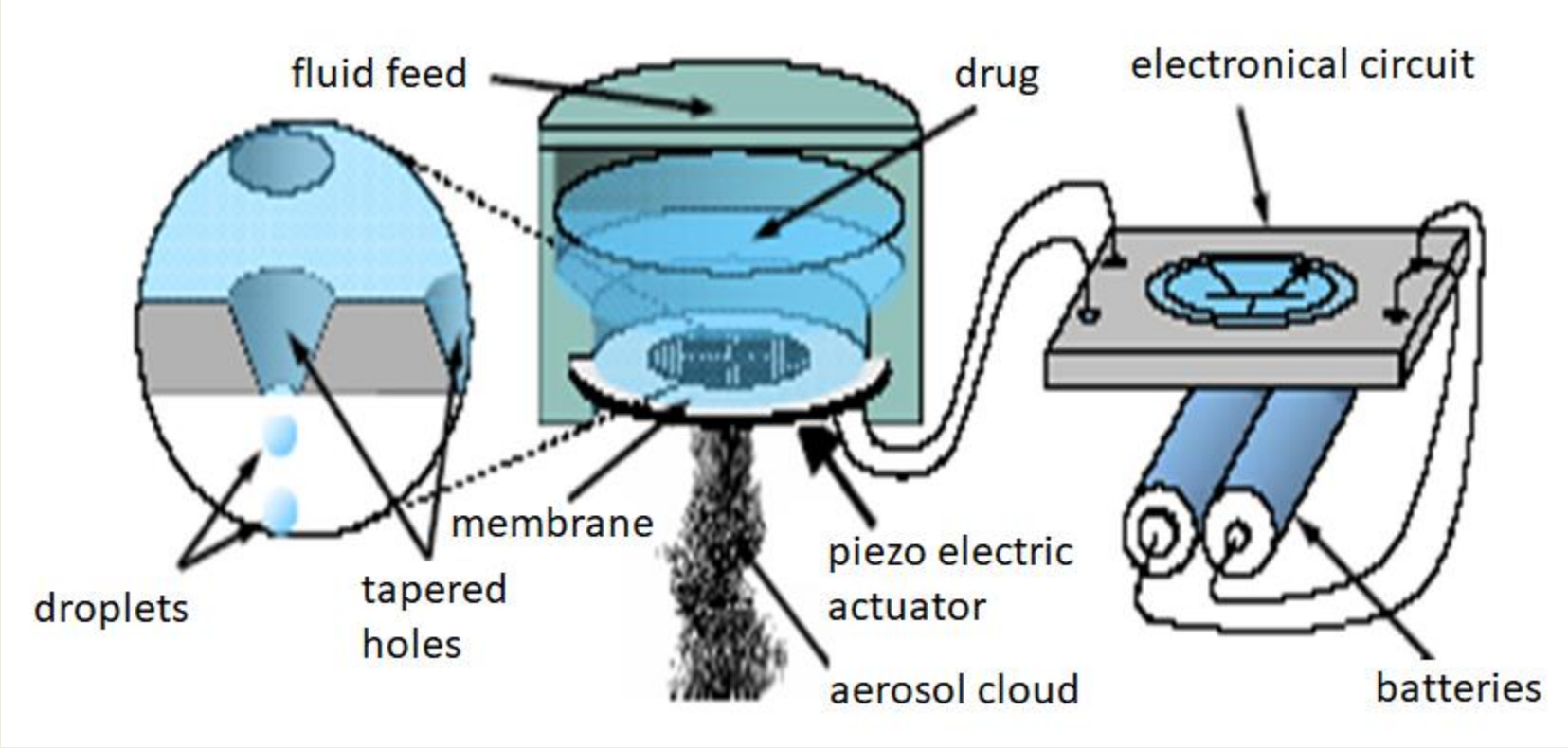
SERETIDE Evohaler 25/125 µg/dose

SERETIDE Evohaler 25/250 µg/dose

Special atomizing

Process:

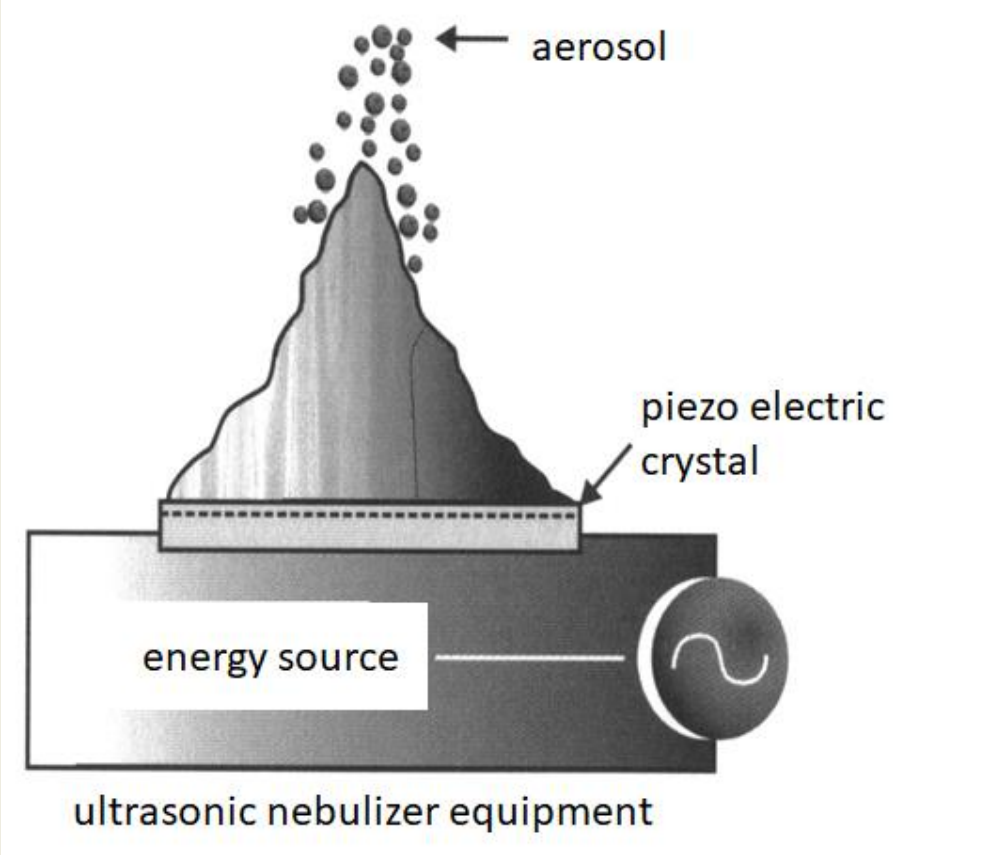
piezoelectric - membrane - atomized droplets



Special atomizing

Process:

Ultrasonic nebulizer – Propellant free



ultrasonic nebulizer equipment

Preparations for Inhalation

Solid preparations

Inhalation powders

Powder inhalation

DPI= dry powder inhalers

SINGLE-DOSE DPIs

Aerolizer

HandiHaler

MULTI UNIT-DOSE DPI

Diskhaler

MULTI-DOSE DPIs

Twisthaler

Flexhaler

Diskus

Tudorza Pressair

Solid preparations

Powders for inhalation

Dry powder inhaler is drug is inhaled as a cloud of fine particles. Powders for inhalation are presented as **single-dose** powders or **multidose** powders. To facilitate their use, active substances may be combined with a suitable carrier.

In pre-metered systems, the inhaler is loaded with powders pre-dispensed in capsules or other suitable pharmaceutical forms.
For devices using a powder reservoir, the dose is created by a metering mechanism within the inhaler. The delivered dose is the dose delivered from the inhaler.

Solid preparations

Powders for inhalation

Ideal preparation:

- Effective dosing
  - uniform dose
  - targeted delivery
  - operable at low inhalation flow rates
- Efficient device
- Easy to use

Solid preparations

Powders for inhalation

Advantages:

- Propellant free design
- Less need for patient coordination
- Less potential for formulation problems
- Environmental sustainability
- Less potential for extractable from device components

Solid preparations

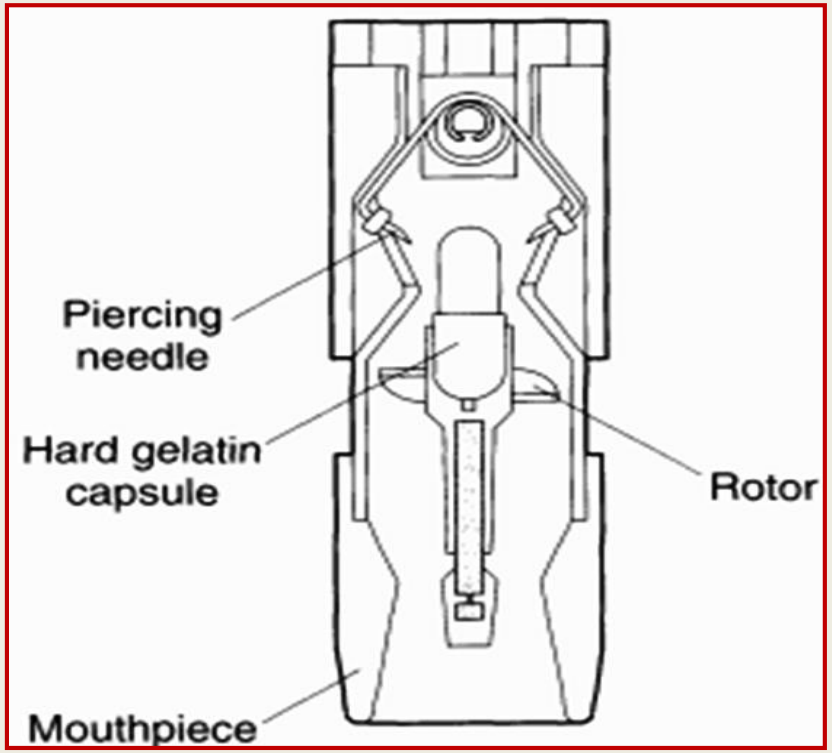
Powders for inhalation

Disadvantages:

- Dependency on patient inspiration flow rate and profile
- Device resistance and other device issues
- More expensive than pressurized MDI
- Complex development and manufacture
- Not available world wide
- Greater potential problems in dose uniformity

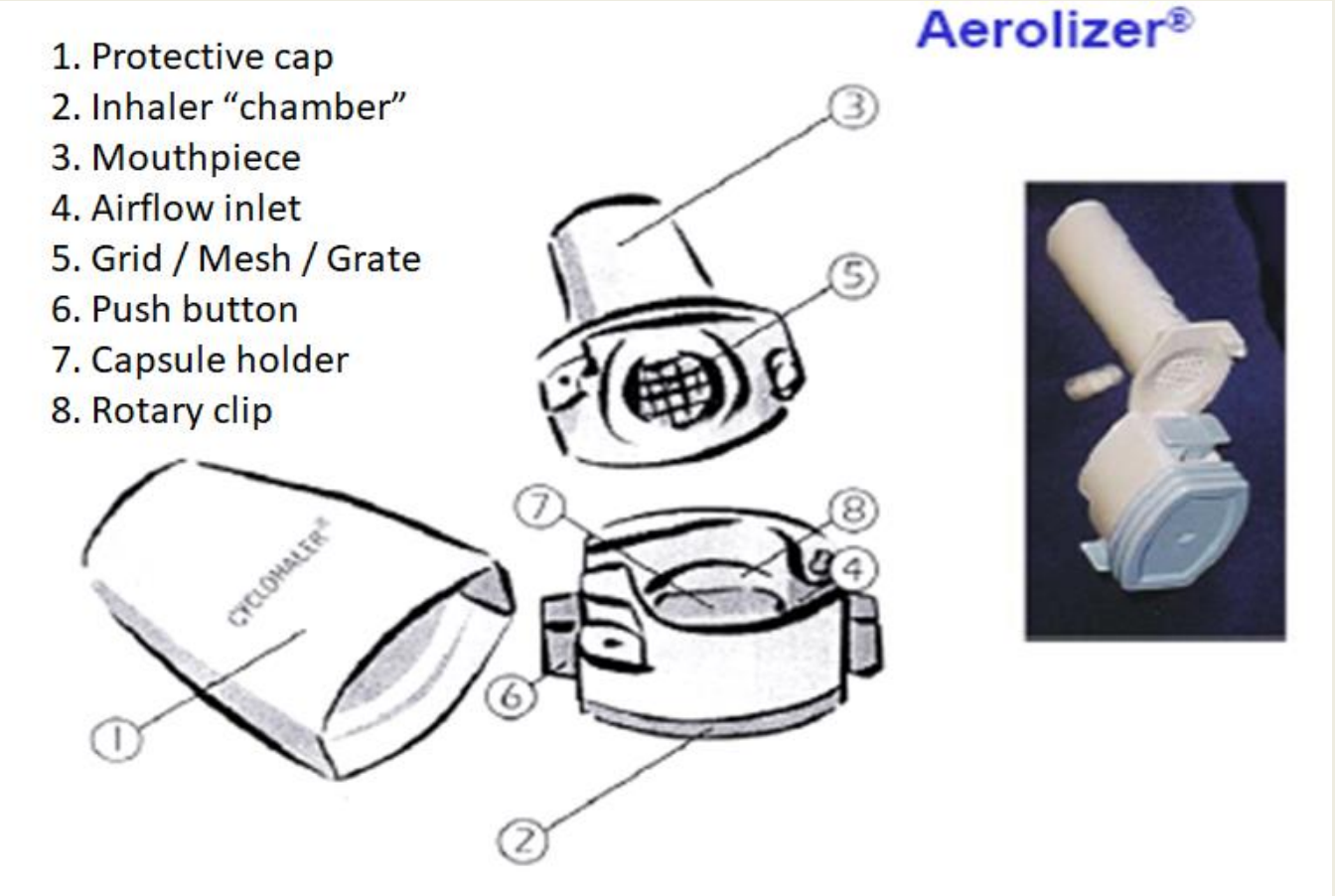
Solid preparations

Powders for inhalation - Spinhaler



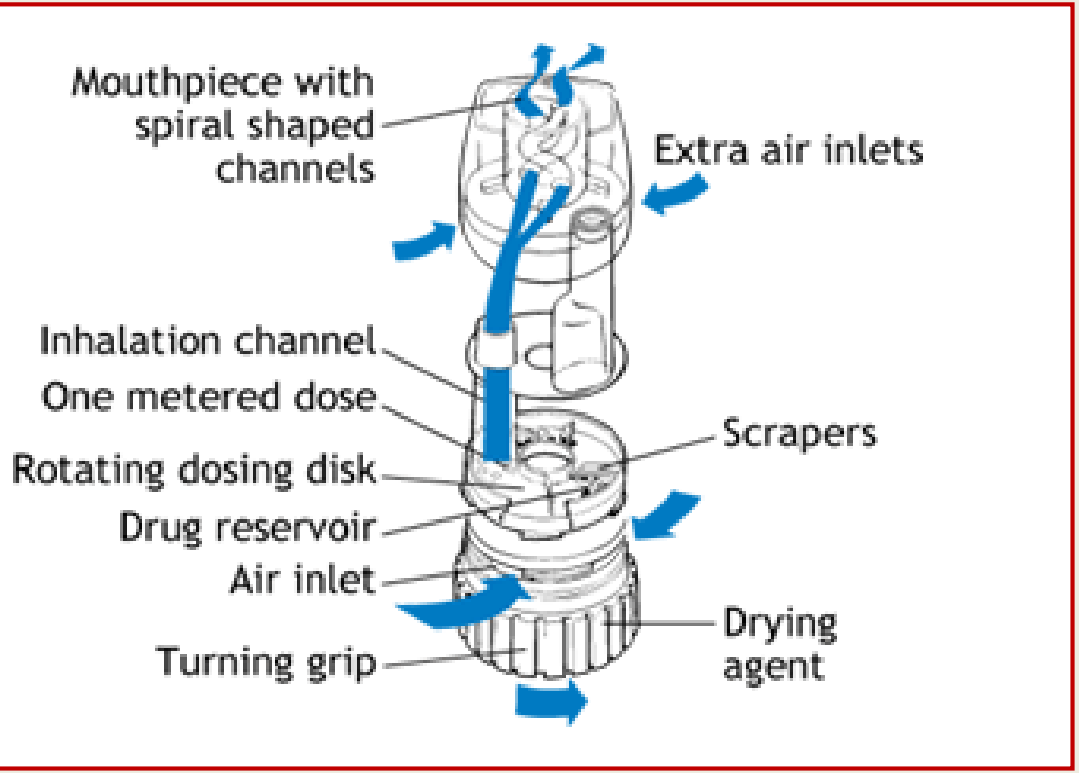
Solid preparations

Powders for inhalation - Aerolizer



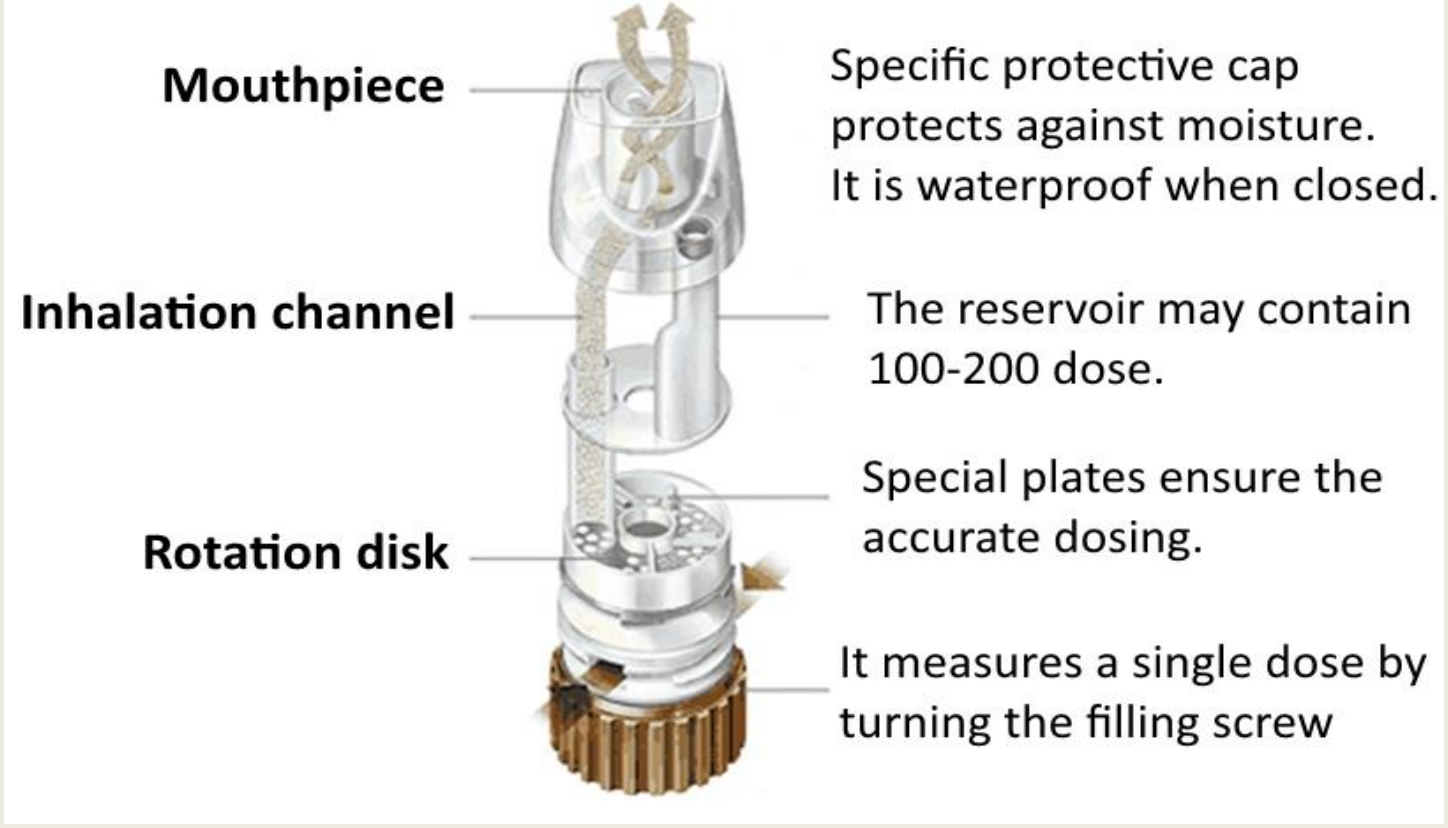
Solid preparations

Powders for inhalation - Turbuhaler



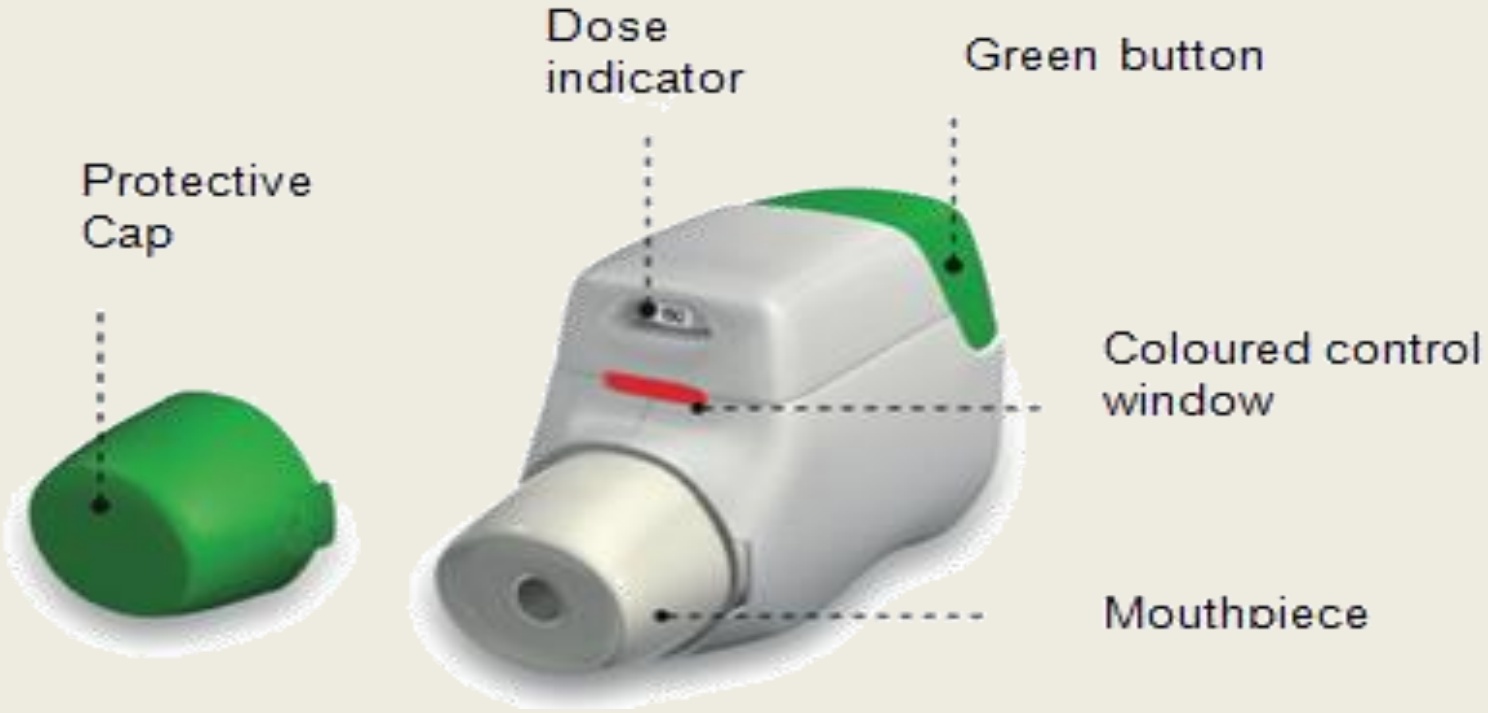
Solid preparations

Powders for inhalation - Turbuhaler



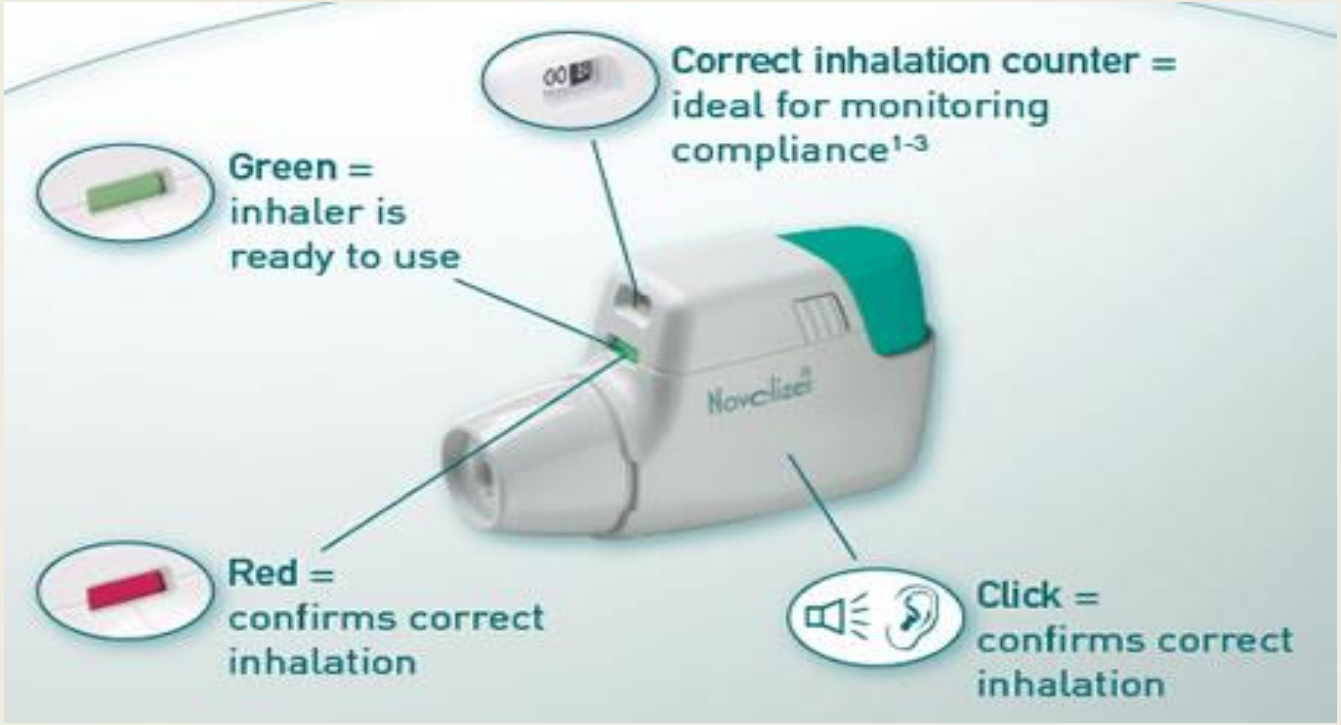
Solid preparations

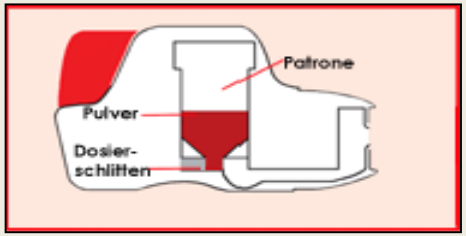
Powders for inhalation - Novolizer

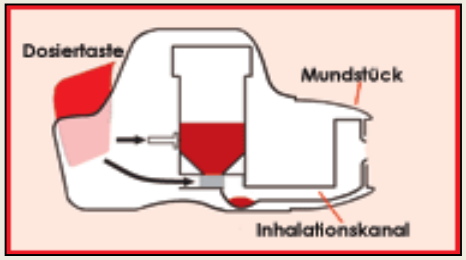


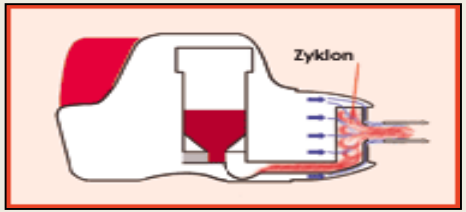
Solid preparations

Powders for inhalation - Novolizer



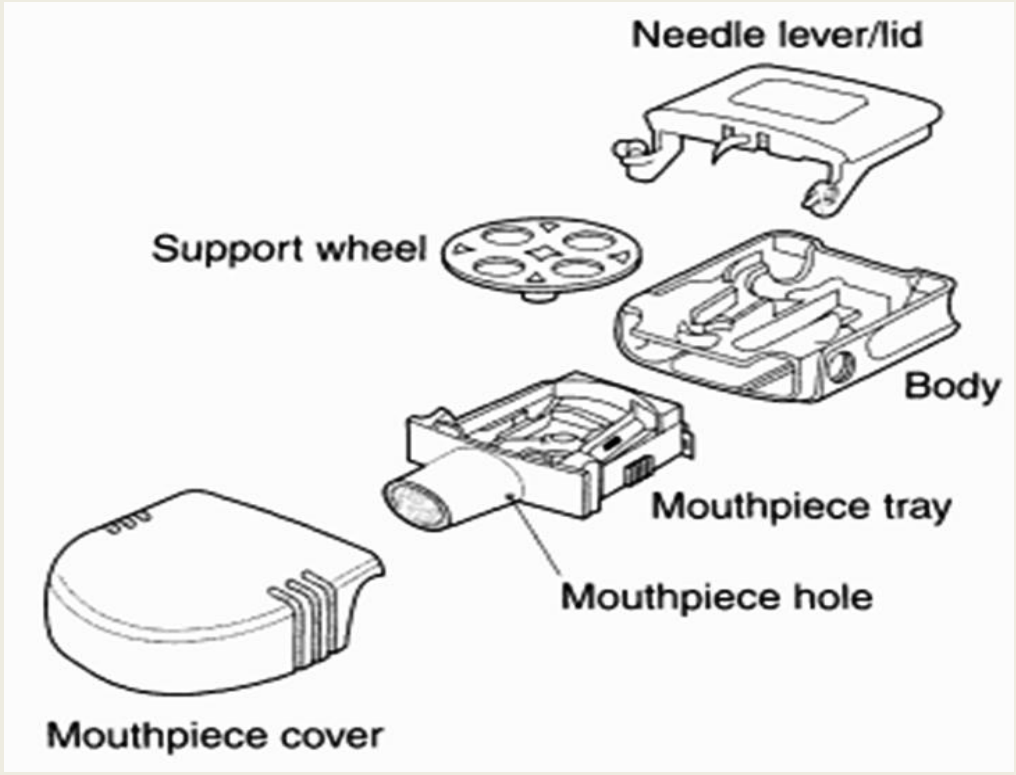






Solid preparations

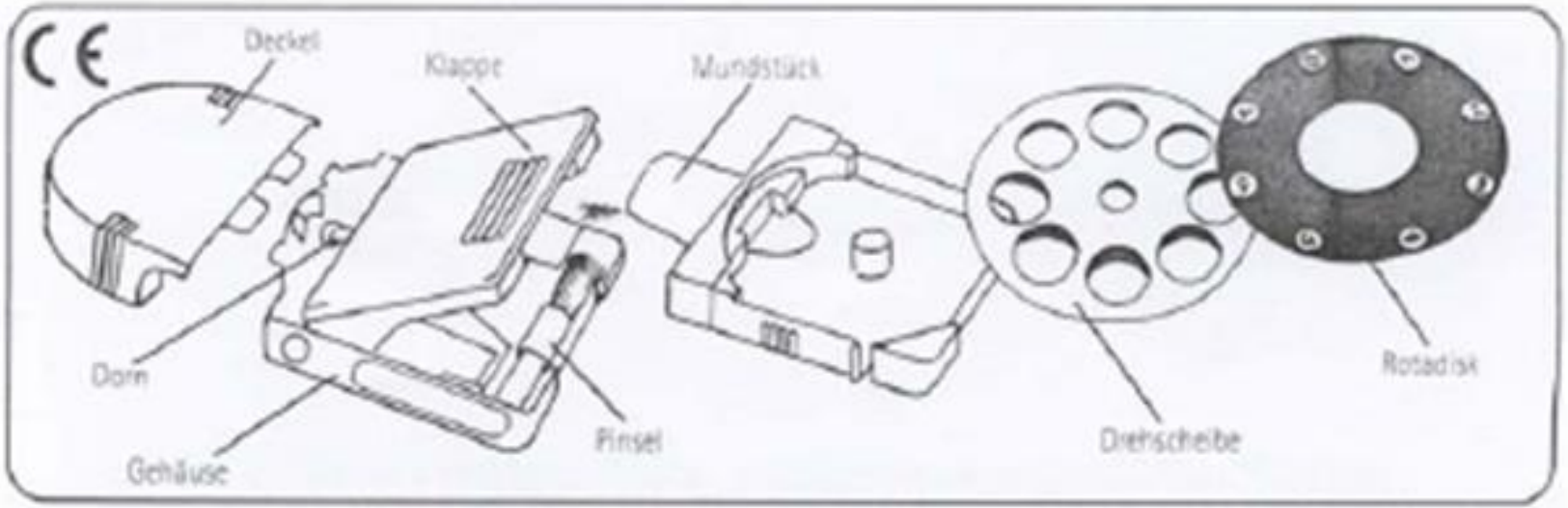
Powders for inhalation - Dischaler



Solid preparations

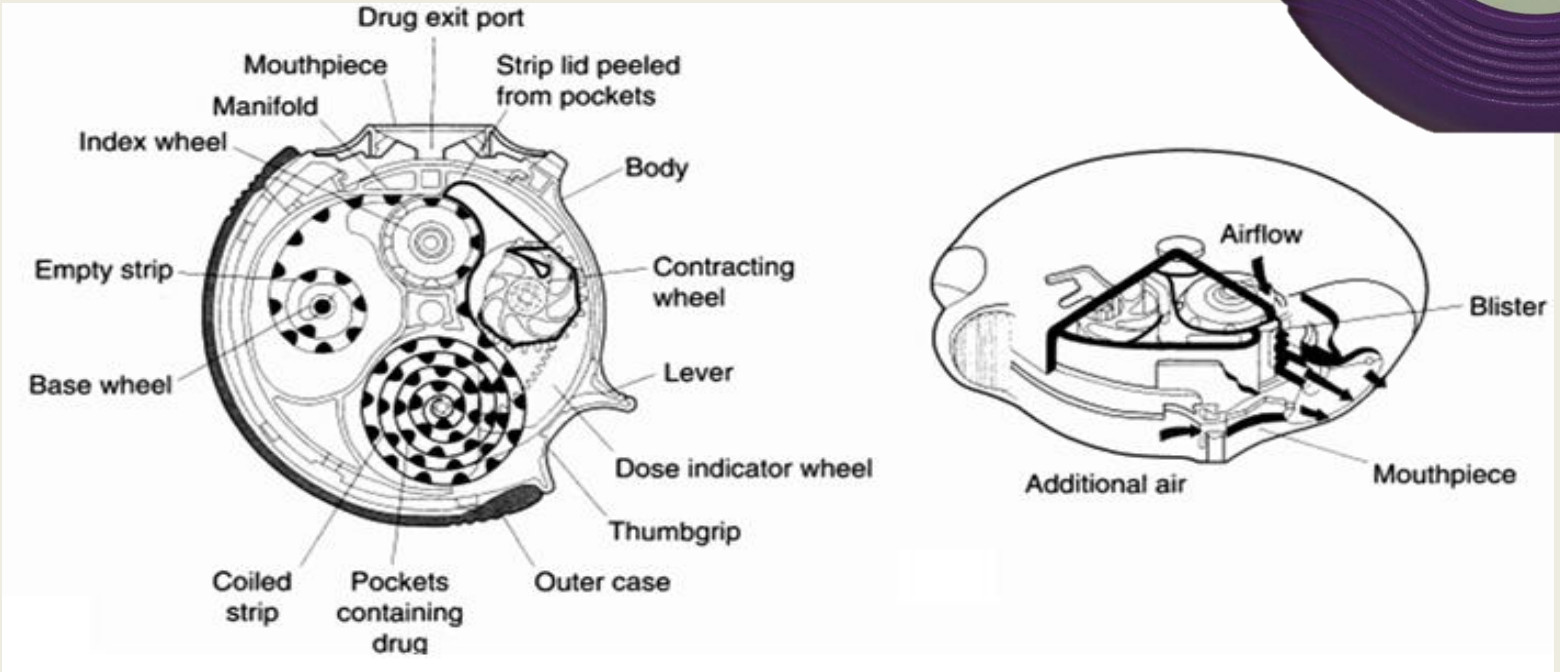
Powders for inhalation - Diskhaler

Diskhaler® (Rotadisk)



Solid preparations

Powders for inhalation - Accuhaler



Solid preparations

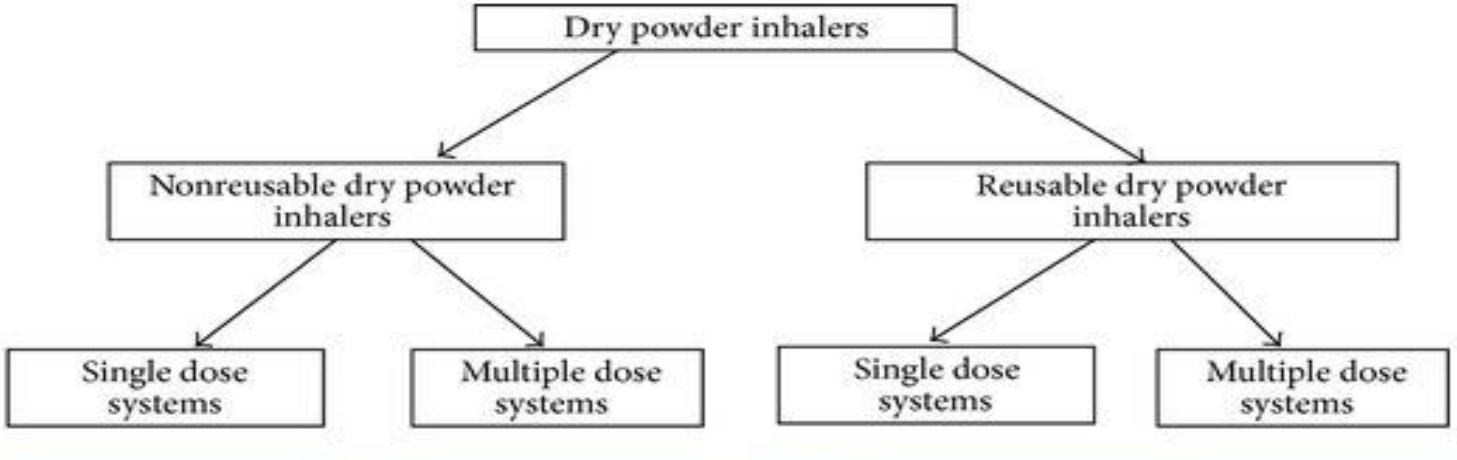
Powders for inhalation - NEXThaler

Solid preparations

FORADIL 12 µg
SPIRIVA 18 µg
MIFLONIDE 200 µg
RELENZA 5 mg
SEEBRI BREEZHALER 44 µg
ONBREZ BREEZHALER 150 µg
lBUVENTOL Easyhaler 200 µg
FLIXOTIDE DISKUS 100 µg
BUDESONID EASYHALER 100 µg
FORMOTEROL EASYHALER 12 µg
RHINOCORT Turbuhaler 100 µg

BRICANYL TURBUHALER 0,5 mg
OXIS TURBUHALER 4,5 µg
SEREVENT Diskus 50 µg
THOREUS Diskus 50/100 µg
SERETIDE Diskus 50/100 µg
DIMENIO 50 µg/250 µg
PULMICORT TURBUHALER 100 µg
SYMBICORT Turbuhaler 4,5 µg/160 µg
SYMBICORT forte Turbuhaler 9 µg/320 µg
SYMBICORT mite Turbuhaler 4,5 µg/80 µg

Comparison of dry powder inhalers



Diskus	Turbuhaler	Easyhaler	Aerolizer	Rotadisk	Novolizer
Useable for					
60 SD	200 SD	200 SD	50 SD	3 months	1 year

SD: single dose

Advantages and disadvantages of inhalers

Device	Advantage	Disadvantage
pMDI	• Compact • Portable • Multidose • Metered dose • Familiarity by patient	• Co-ordination required • High plume speed • High deposition in mouth and pharynx • 'Cold Freon' effect • Dose counter not always available • Contains propellants that are greenhouse gases
pMDI + spacer	• No co-ordination necessary • Holds aerosol for short period prior to inhalation • Slows down aerosol plume • Reduces deposition in mouth and pharynx • Can improve lung deposition	• Bulky to carry around • Some dose lost in spacer • Static charge may be a problem • Requires regular cleaning • Contains propellants
Breath-actuated pMDI	• No co-ordination required • Compact • Portable • Breath-actuated	• 'Cold Freon' effect • Minimum required flow to trigger • Contains propellants
DPI	• Breath-actuated • Does not require propellants • Multiple dose devices available • Compact • Portable • Reproducible dose delivered	• Multiple designs (may be confusing to patients) • Requires patient to achieve a minimum inspiratory threshold to generate dose • Moisture-sensitive • May be complicated to load • Single capsule devices require loading each time
Nebulisers	• Can be used to dispense drugs not available as pMDI or DPI • Can deliver high doses of drug • Delivery by tidal breathing • Vibrating mesh devices are portable • Intelligent nebulisers allow more efficient delivery	• Jet and ultrasonic nebulisers require external energy source • Older designs are very inefficient at delivery • Long treatment times • Newer devices are expensive
Soft mist inhaler	• Portable • Multidose • Slow mist generated over 1.5 seconds • Fine aerosol droplets • Easy to use	• Only one device currently available • Some co-ordination necessary

Application problem... OMG!!!

Thank you
for your attention!