Biopharmaceutical Classification System

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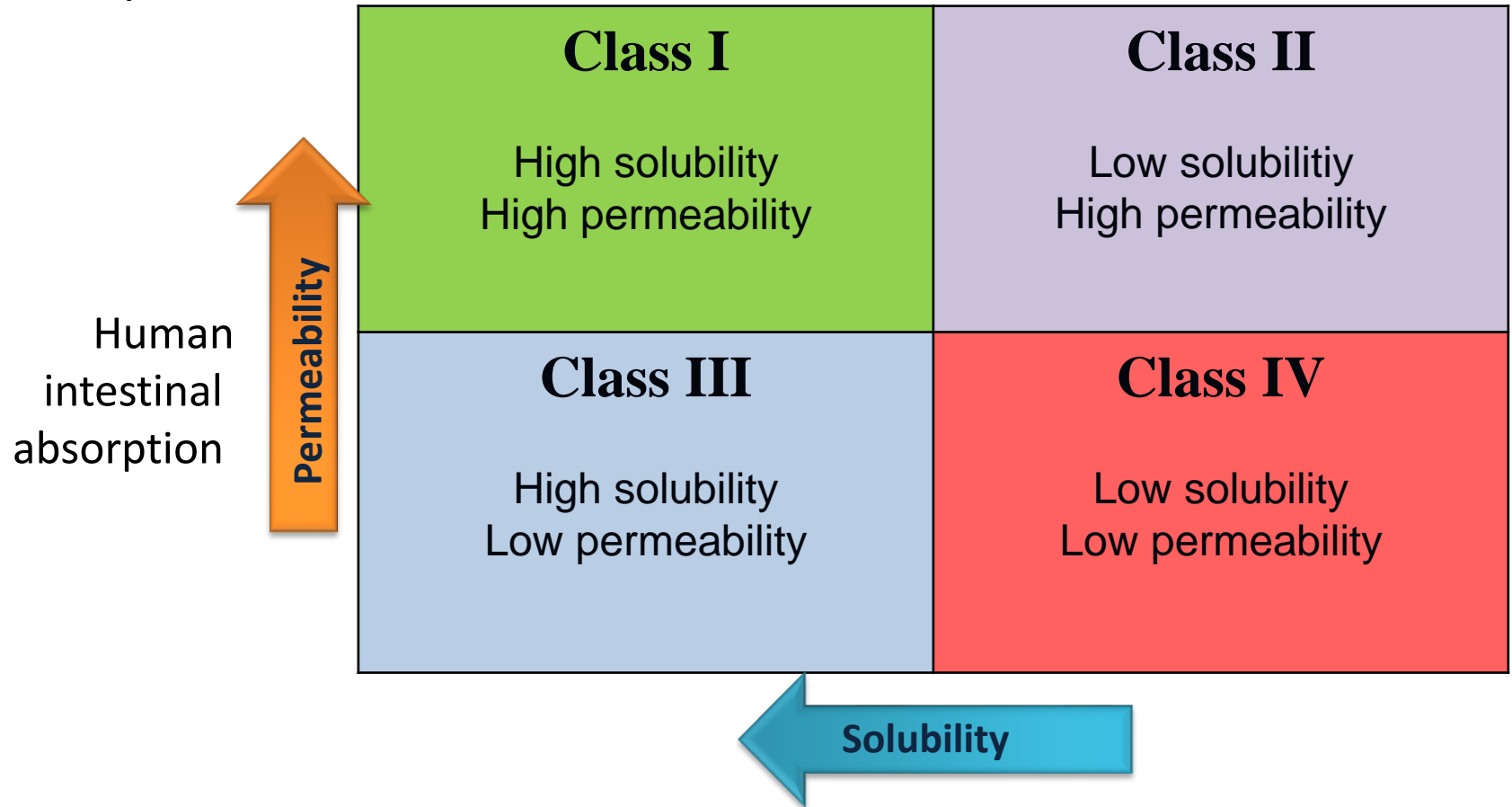

Gordon L. Amidon,

Amidon et al. published the importance of **Biopharmaceutical Clasification System (BCS)** in 1995, which is an important characteristic of the preparation's bioavailability.

According to their suggestion APIs can be categorized into four groups regarding the gastrointestinal absorption by their solubility and permeability characters.

Biopharmaceutical Classification System

APIs can be categorized into four groups according to their solubility and permeability:

Class I High solubility High permeability	**Class II** Low solubilitiy High permeability
Class III High solubility Low permeability	**Class IV** Low solubility Low permeability

Human intestinal absorption

Permeability ↑

Solubility ←

Volume of water required to dissolve the highest dose streght across the physilogical pH range (1.2 ; 4.5; 6.8)
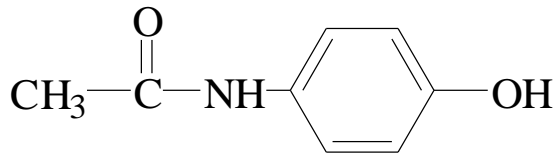
BCS Class I

APIs with high solubility and high permeability

API absorbs well (though the metabolism can decrease the bioavailability), the rate controlling step will be the dissolution.
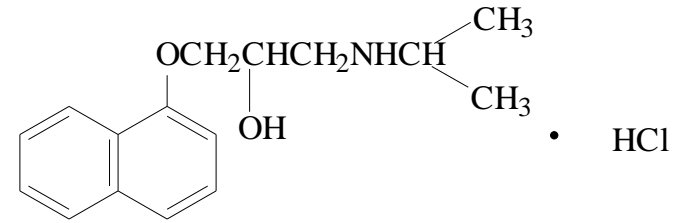
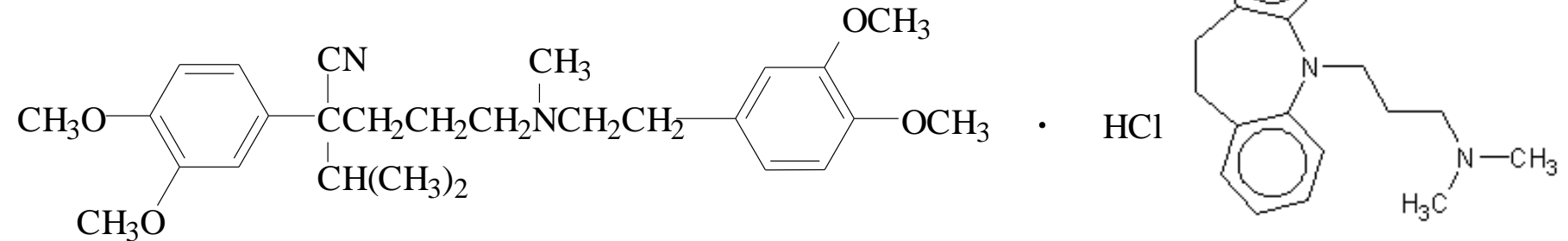$$k_{diss} << k_{abs}$$

BCS Class I
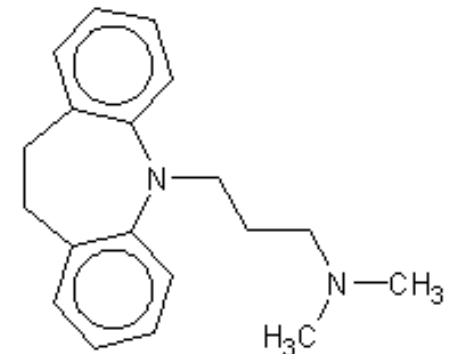
APIs with high solubility and high permeability

acetaminophen, paracetamol

propranolol

verapamil

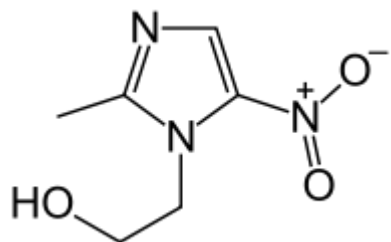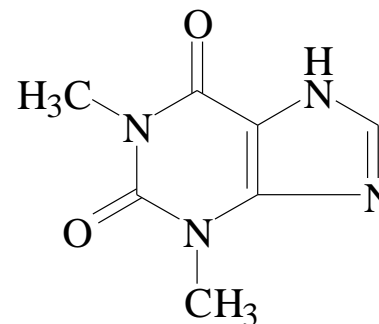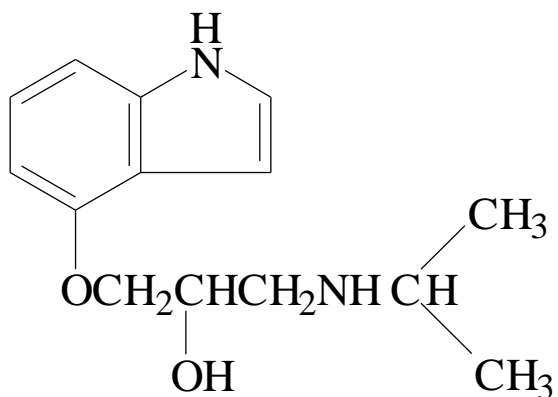imipramine

BCS Class I

APIs with high solubility and high permeability

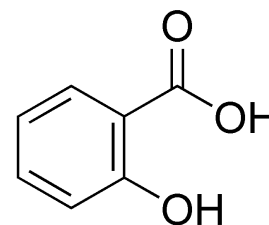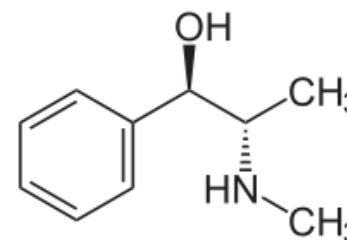metronidazole

theophylline

pindolol

salicylic acid

ephedrine

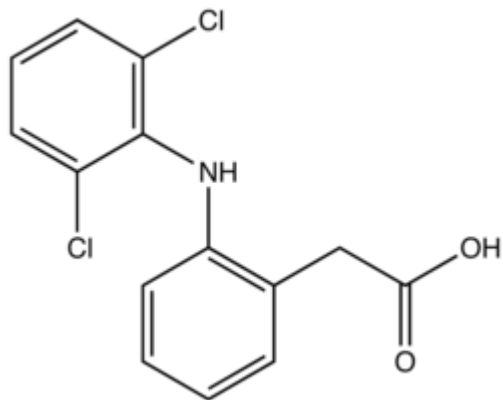### APIs with low solubility and high permeability

API's absorption is restricted by the dissolution's speed and amount.

Because of the low solubility the absorption occurs at the GI tract's longer regions, the dissolution lasts for a longer period of time and it influences the concentration at the place of absoprtion.
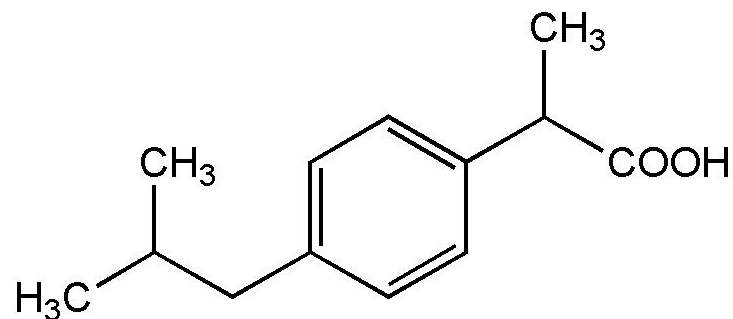
$$k_{diss} \leq k_{abs}$$
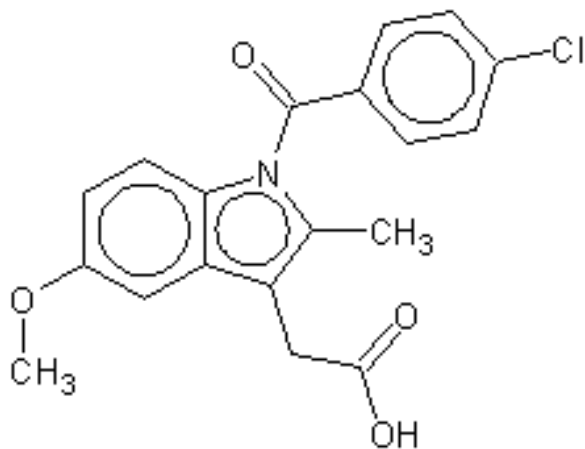
BCS Class II

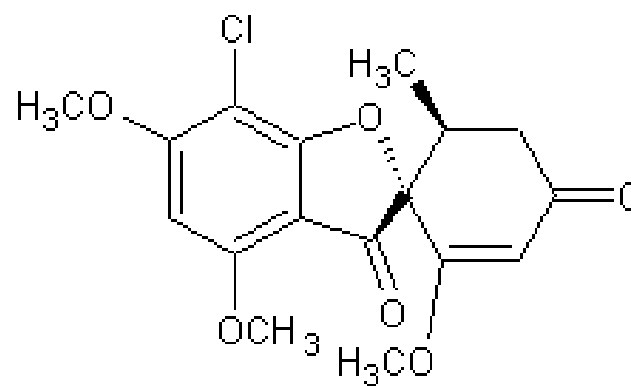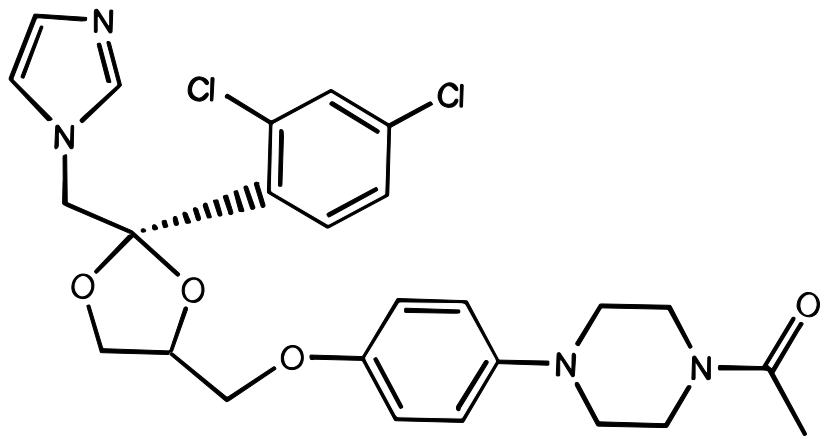## APIs with low solubility and high permeability
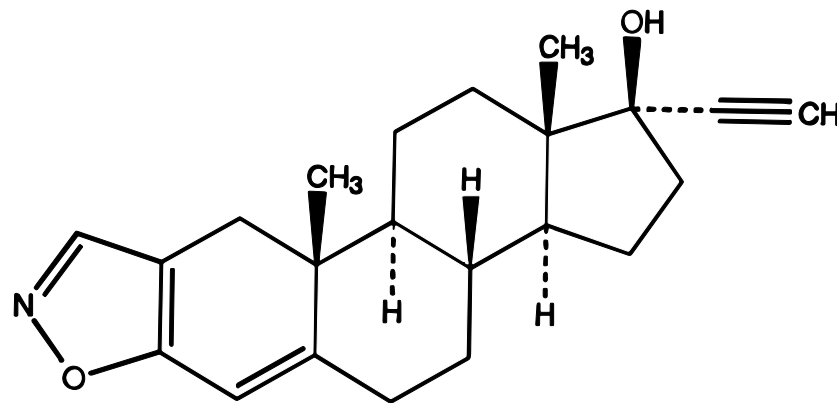

diclofenac
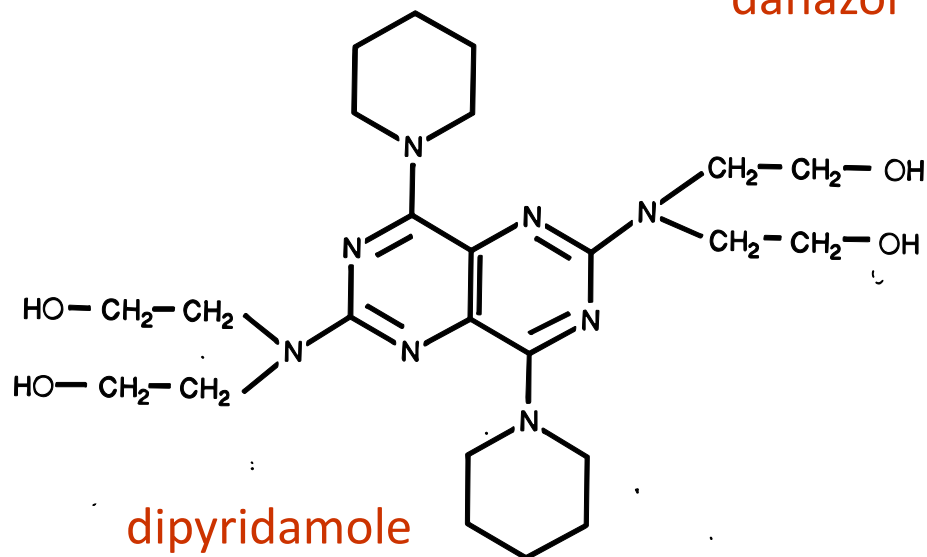

ibuprofen

indometacin

griseofulvine

BCS Class II

APIs with low solubility and high permeability

ketoconazole

danazol

dipyridamole

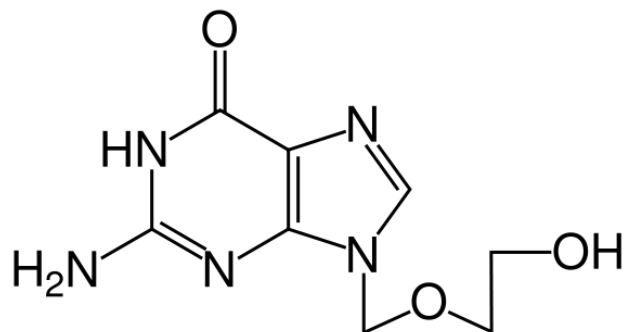## APIs with high solubility and low permeability

The transfer speed through the membranes is very important in this case.

Long contact time with the mucus is required to increase the absorption (mucoadhesive systems).
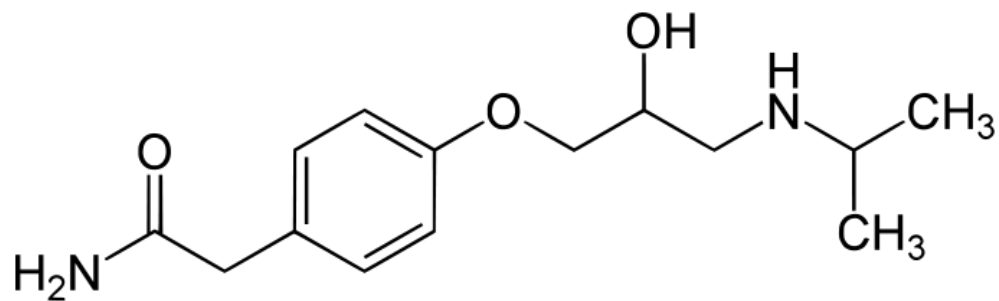
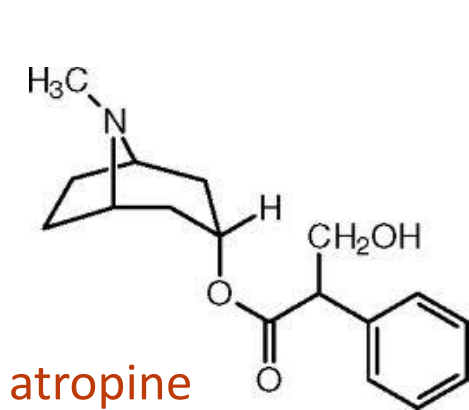$$k_{diss} >> k_{abs}$$

BCS Class III

APIs with high solubility and low permeability

acyclovir

atenolol

atropine
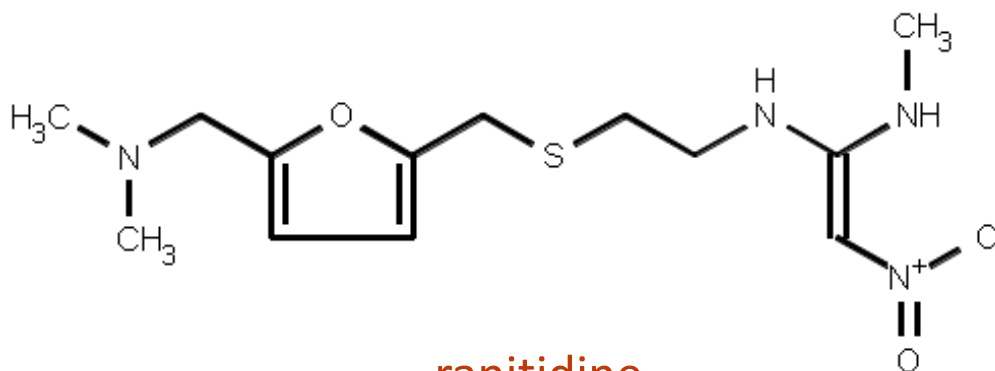
ranitidine

BCS Class III

APIs with high solubility and low permeability
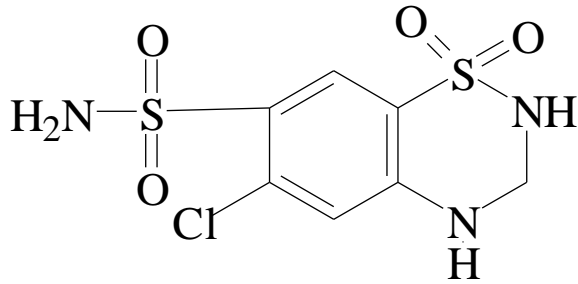
hydrochlorothiazide
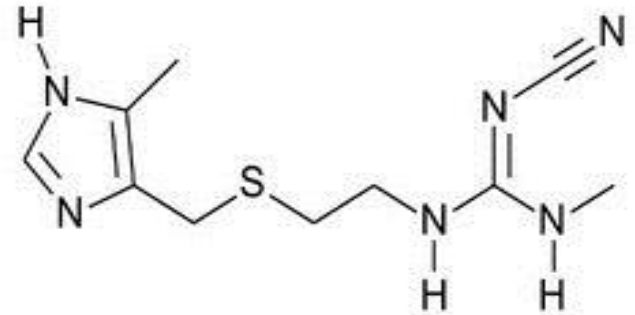
cimetidine
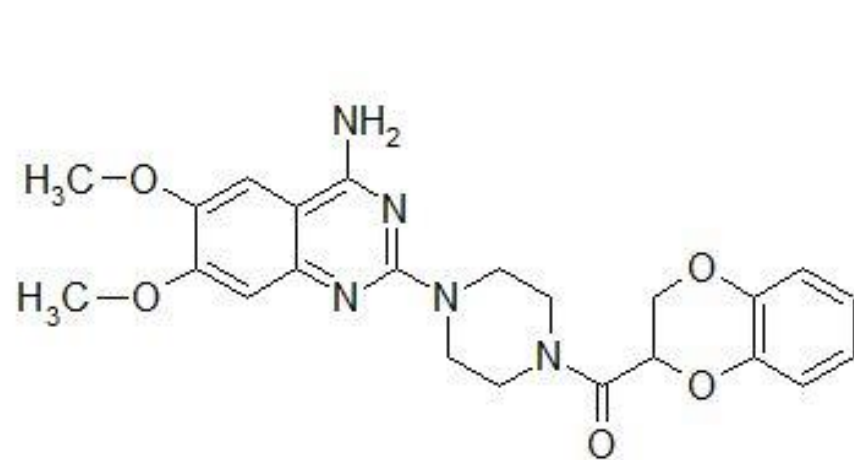
doxazosin
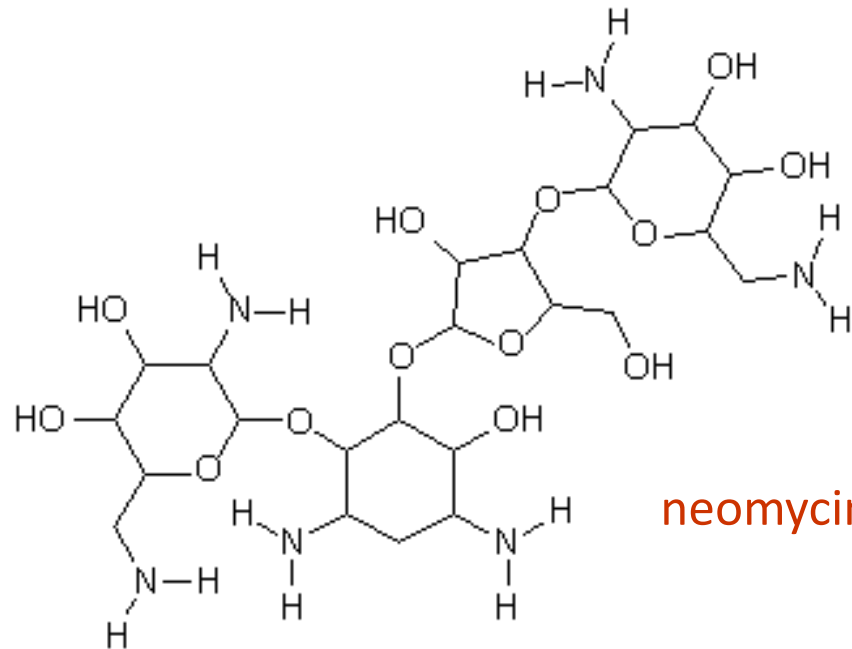
neomycin

BCS Class III

APIs with high solubility and low permeability
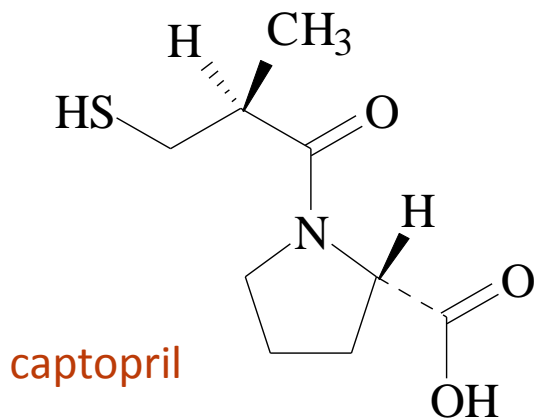
captopril
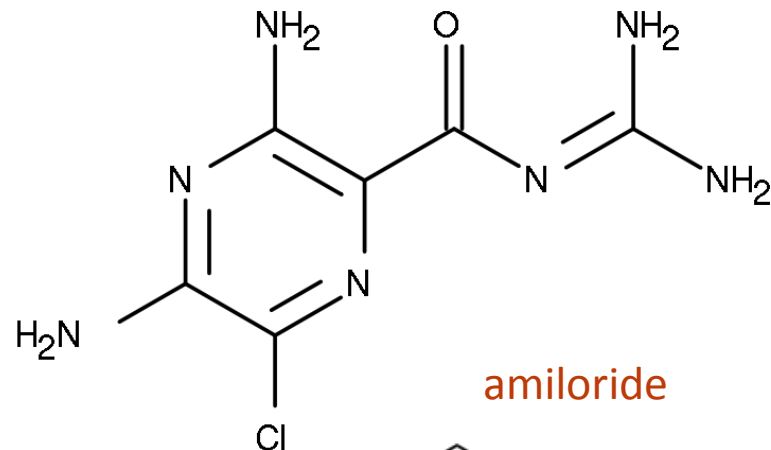
amiloride
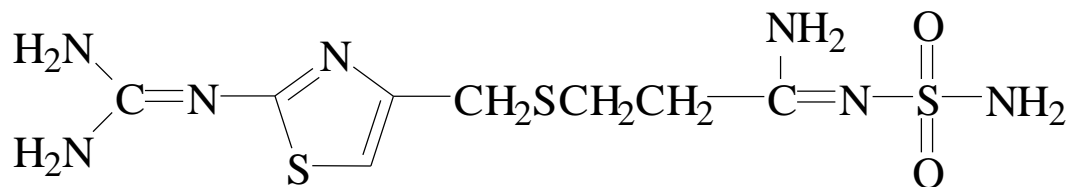
famotidine
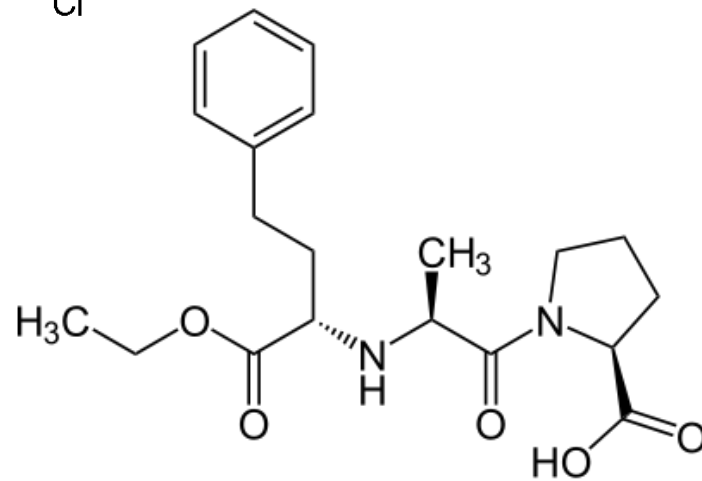
enalapril

APIs with low solubility and low permeability

Absoprtion of APIs belongign into this group is low, thus peroral administration is doubtful.

Technologies increasing the solubility should be applied: molecular dispersion, solubilisation.

APIs with low solubility and low permeability

amphotericin B
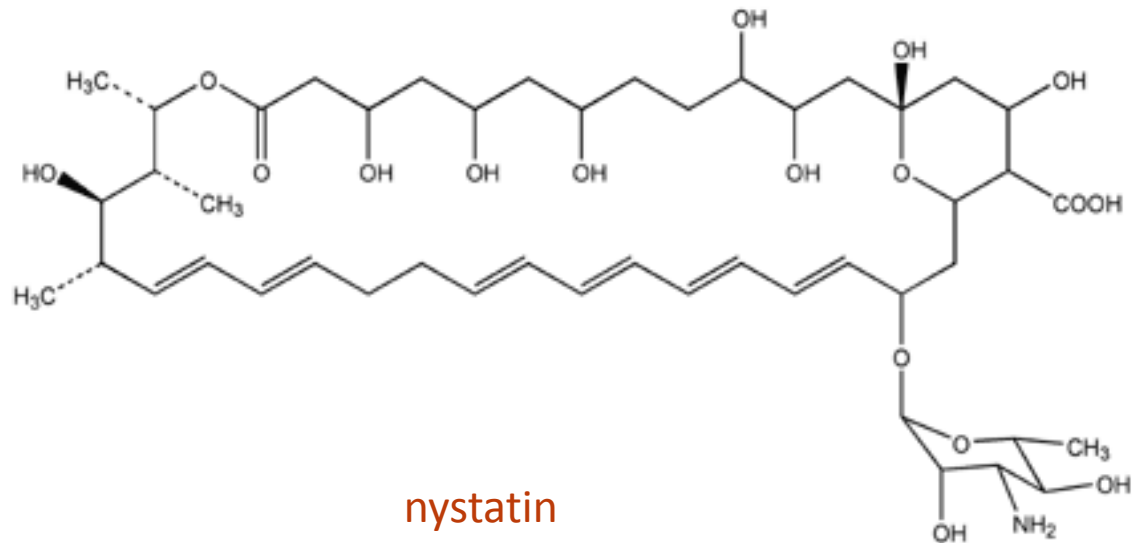
nystatin

BCS Class IV

APIs with low solubility and low permeability
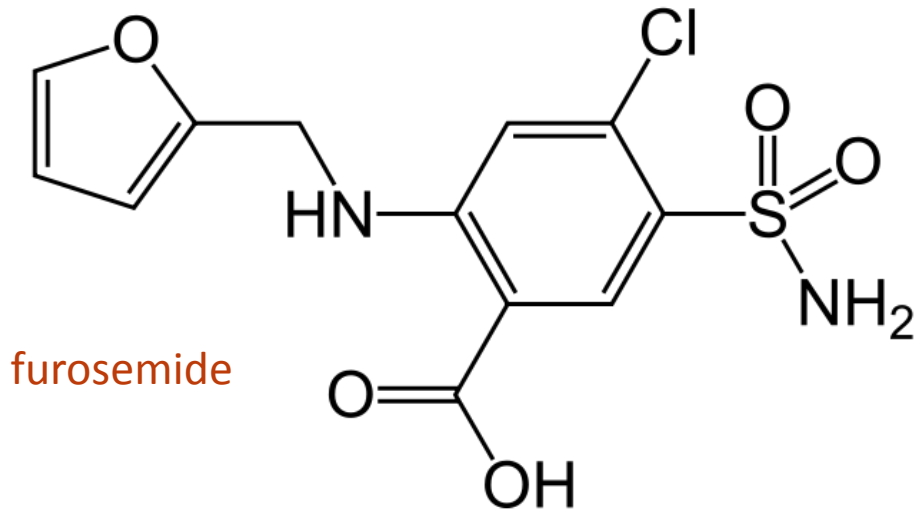
furosemide
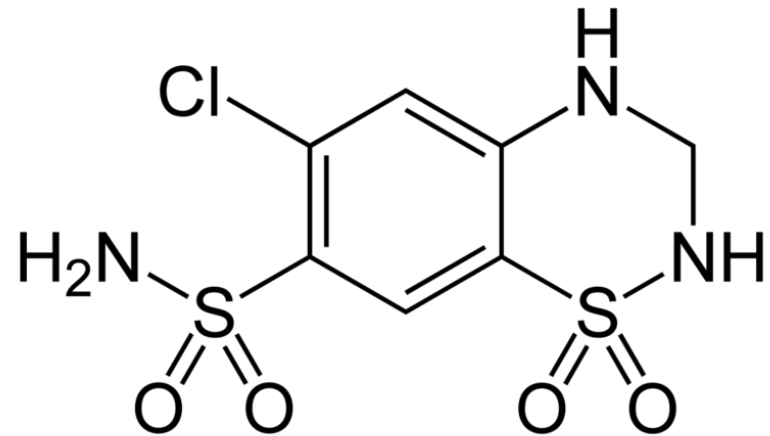
hidrochlorotiazide

BCS Class Membership of Selected Model Drugs

Class I

Verapamil
Propranolol
Metoprolol

Class II

Ketoprofen
Naproxen
Carbamezapine

Class III

Ranitidine
Cimetidine
Atenolol

Class IV

Hydrochlorothiazide
Furosemide

Jejunal Permeability, Peff (x10^{-4}) cm/sec
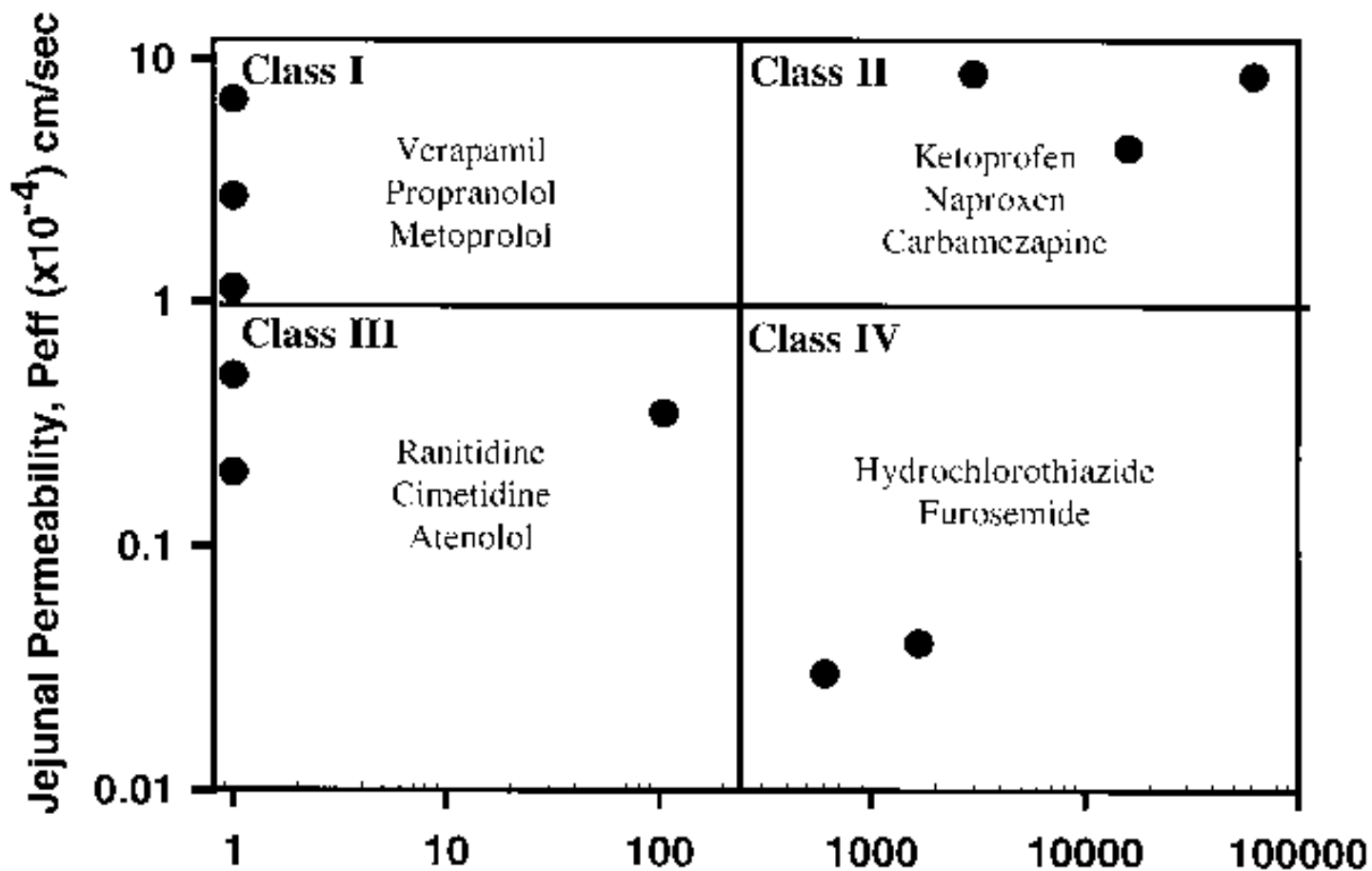
Volume (ml) of required to dissolve the highest dose strength
at the lowest solubility in pH 1-8 range (Note: 1 ml set as low value)

Three type of rates can be introduced according to the BCS that help researchers to develop preparations:

- absorption rate (A_n)
- dose rate (D_o)
- dissolution rate (D_n)

<u>Absorption rate</u>(A_n) – ration of residence time in the small intestine and the time needed for absorption:

$$A_n = \frac{t_{res}}{t_{abs}}$$

t_{res} residence time

t_{abs} time needed for absorption

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Dose ratio *(D$_o$)* – can be calculated by the solubility, dose and tha amount (volume) of water used for the administration:

$$D_o = \frac{D}{V_o C_s}$$

D dose,
V_o volume of water used at the administration,
C_s solubility.

Dissolution ratio *(D$_n$)* – is the ratio of API's residence time in the GI tract and the time of dissolution:

$$D_n = \frac{t_{res}}{t_{diss}}$$

t_{res} residence time,
t_{diss} dissolution time,

Biopharmaceutical Classification System

Literature shows that there is an increasing number of poorly soluble compounds in the drug discovery pipeline – including 70 per cent BCS Class II compounds – although only about 30 per cent are BCS Class II in the existing top 200 market

New chemical entities

IV. 20%   I. 1,5%

III. 5%

II. 70%
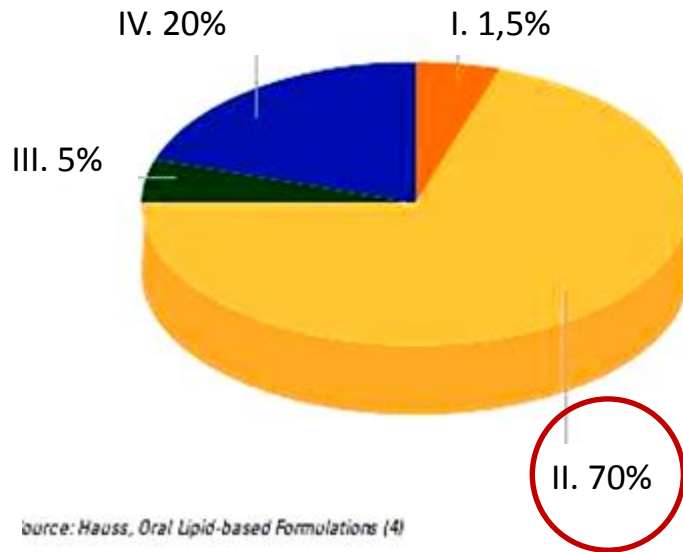
Top 200 marketed drugs in USA

Unclassified 10%

IV. 6%   I. 31%

III. 23%

II. 30%

Biopharmaceutical Classification System

Sources of pharmaceutical technology to increase the bioavailability of drug delivery systems accourding to the BCS

Class I

Cass II

micronisation, nanoparticles, solubilisation, solid dispersion, salt forming, self emulsifying systems, complexes, buffers, surfactants, liquid-filled capsules
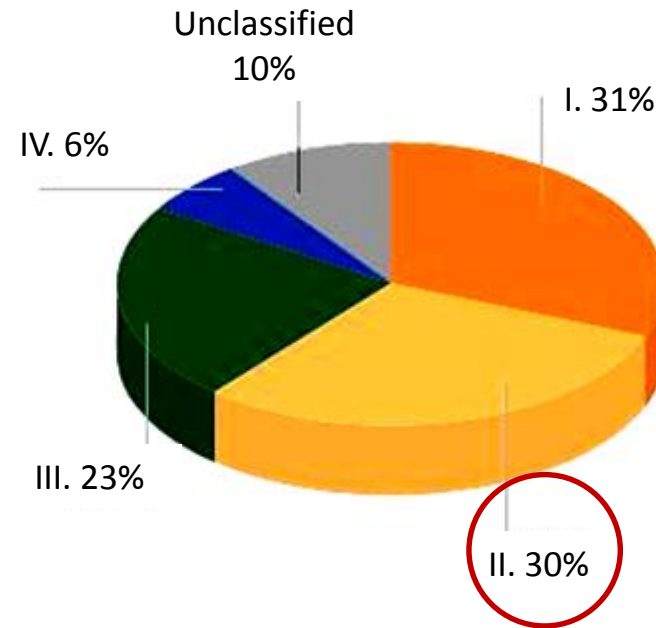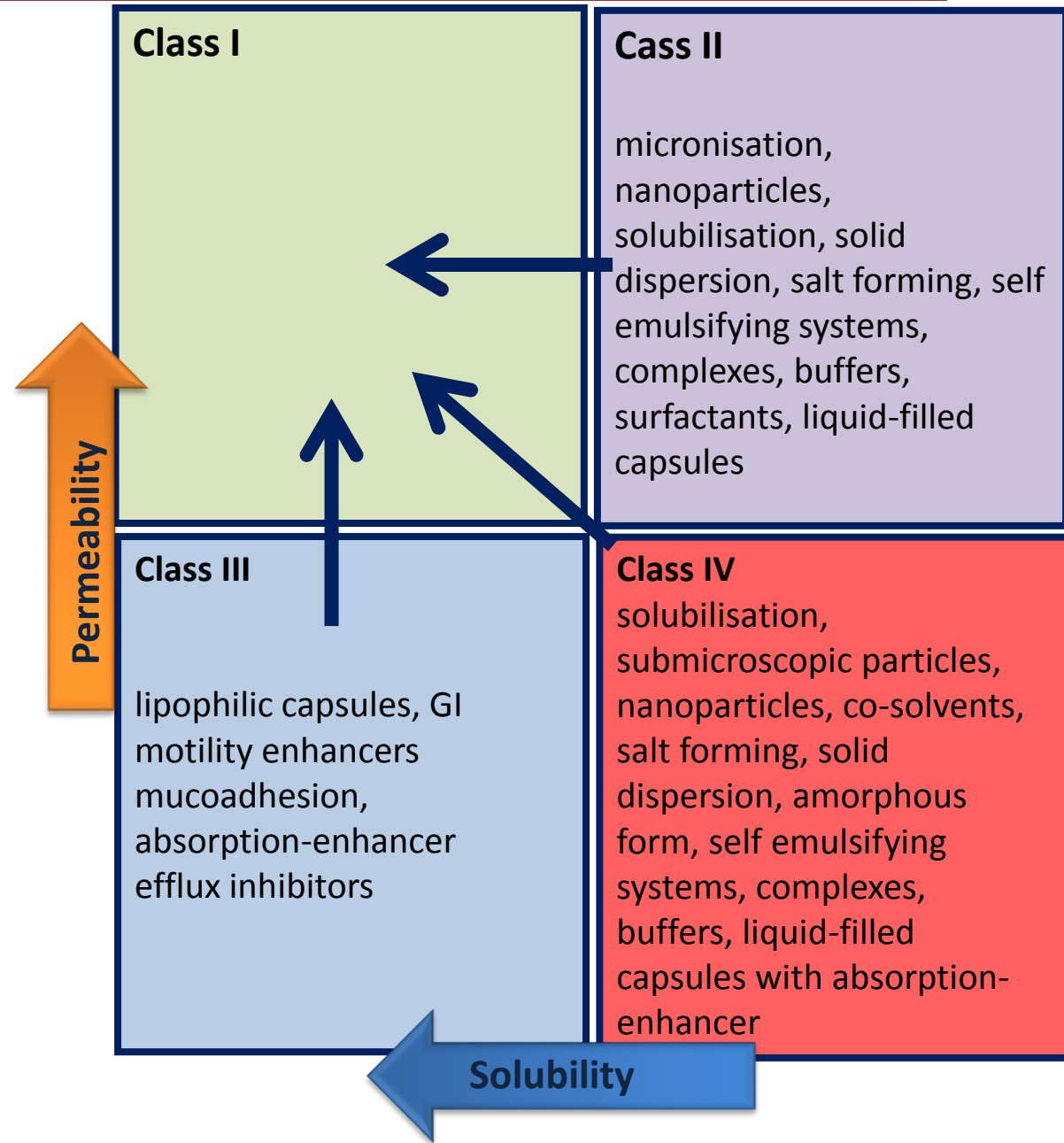
Class III

lipophilic capsules, GI motility enhancers mucoadhesion, absorption-enhancer efflux inhibitors

Class IV

solubilisation, submicroscopic particles, nanoparticles, co-solvents, salt forming, solid dispersion, amorphous form, self emulsifying systems, complexes, buffers, liquid-filled capsules with absorption-enhancer

Permeability

Solubility

Many THANKS for Your Attention

Dziękuję Ďakujem dhanya-waad Дякую

bedankt ありがとう go raibh maith agat

tesekkürle Спасибо شكراً Thank you

谢谢 Merci köszi tack så mycket

Thank you faleminderit

Shukriyâ Danke hvala díky kiitos

takk Obrigada Mulţumesc nandri

Ευχαριστώ Grazie anugurihiitosumi תודה

Muchas gracias dhanya-waad köszönöm

너를 감사하십시요 ačiû Terima Kasih tack

aitäh děkuji vam mange tak salamat