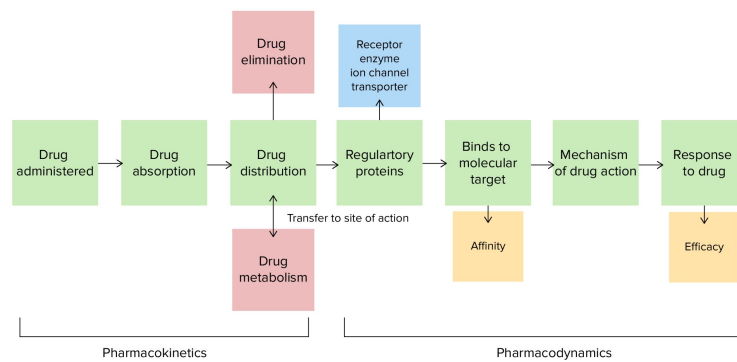


Basisbegrippen farmacologie

Apr. Dr. M. Van Thielen
Dienst Anesthesie
UZ Leuven

1

Lesinhoud

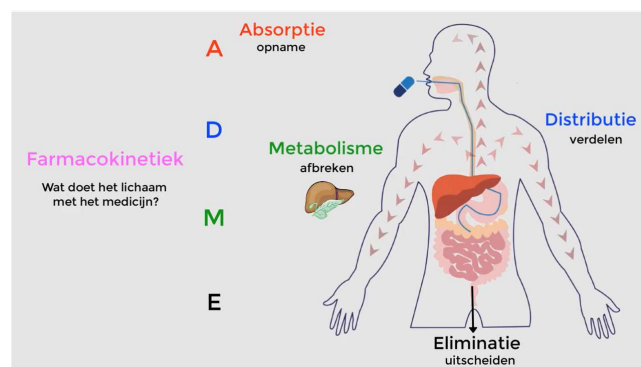


2

1. Farmacokinetiek

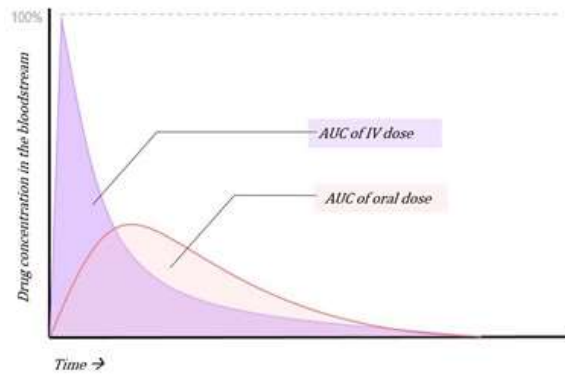
3

Farmacokinetiek



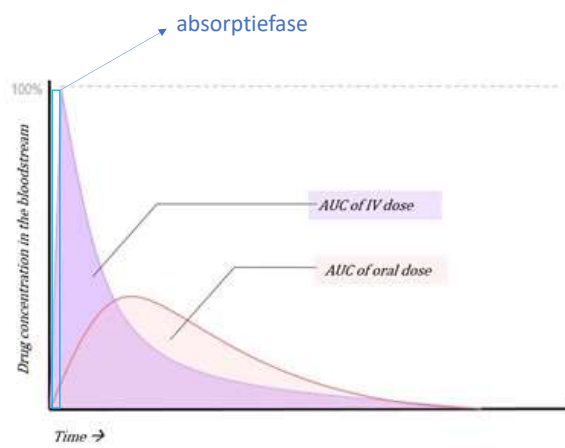
4

Farmacokinetiek



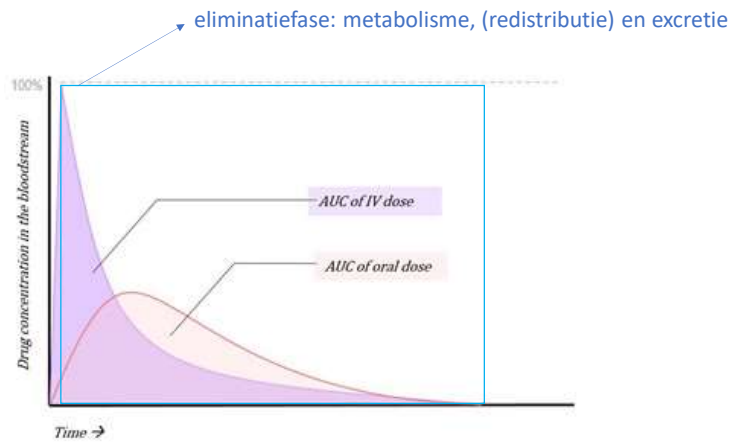
5

Farmacokinetiek



6

Farmacokinetiek



7

Farmacokinetiek

1. Absorptie

8

Farmacokinetiek

1. Absorptie: intraveneuze toegangsweg (IV)
→ biologische beschikbaarheid = 100%



9

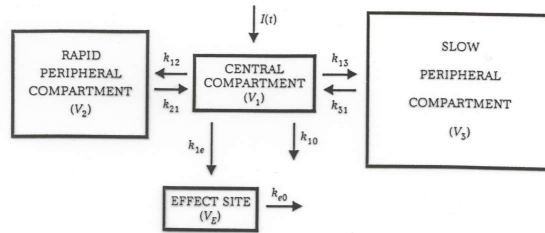
Farmacokinetiek

1. Absorptie
2. Distributie

10

Farmacokinetiek

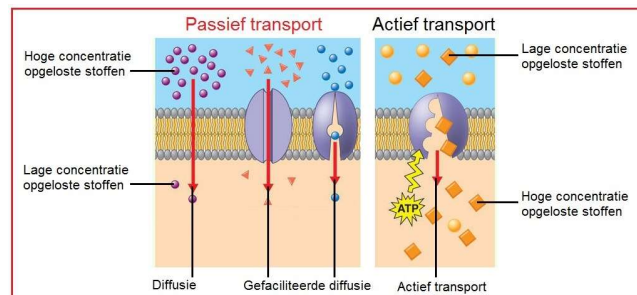
2. Distributie: verdeling over de weefsels



11

Farmacokinetiek

2. Distributie



12

Farmacokinetiek

2. Distributie

~ ionisatiegraad
~ proteïnebinding

Fick's Law of Diffusion

$$\text{Rate of Penetration} = \frac{\left[\text{Diffusion Coefficient} \right] \times \left[\text{Partition Coefficient} \right]}{\left[\text{Membrane Thickness} \right]} \times \left[\text{Surface Area} \right] \times \left[\text{Concentration Gradient} \right]$$

13

Farmacokinetiek

2. Distributie

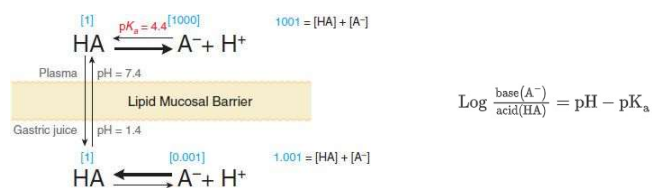
Ionisatie:

* meeste farmaca zijn zwakke zuren/basen

* Henderson-Hasselbach: $\text{pH} = \text{pKa} + \log \left(\frac{[\text{base}]}{[\text{zuur}]} \right)$

→ indien $\text{pH} = \text{pKa}$: $[\text{base}] = [\text{zuur}]$

→ ion trapping (pH partition theory):

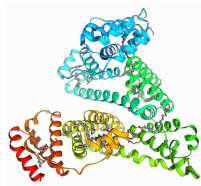


14

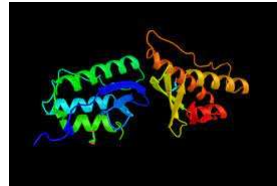
Farmacokinetiek

2. Distributie

Proteïnebinding:



albumine



α 1-glycoproteïne

15

Farmacokinetiek

2. Distributie

Distributievolume (V_d) = dosis / concentratie (L of L/kg LG)

V_d klein	V_d intermediair	V_d groot
sterke eiwitbinding/ionisatie/ weinig vetoplosbaar	lage proteïne-binding en slechte vetoplosbaarheid	weinig gebonden/lage ionisatie/sterk lipofiel; spec. bindingsplaatsen
enkel in plasma: V_d 60 mL/kg	in extracellulair water: V_d = 200 ml/kg	in total body water (ook intracellulair): V_d 600 mL/kg
warfarine, heparine, ICG	mannitol	EtOH

TABLE 3-2 Physical volumes (in L/kg body weight) of some body compartments into which drugs may be distributed.

Compartment and Volume	Examples of Drugs
Water	
Total body water (0.6 L/kg) ¹	Small water-soluble molecules: eg, ethanol
Extracellular water (0.2 L/kg)	Larger water-soluble molecules: eg, gentamicin
Blood (0.08 L/kg); plasma (0.04 L/kg)	Strongly plasma protein-bound molecules and very large molecules: eg, heparin
Fat (0.2-0.35 L/kg)	Highly lipid-soluble molecules: eg, DDT
Bone (0.07 L/kg)	Certain ions: eg, lead, fluoride

¹An average figure. Total body water in a young lean man might be 0.7 L/kg; in an obese woman, 0.5 L/kg.

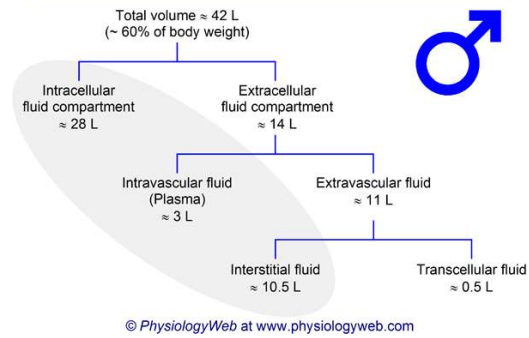
16

Farmacokinetiek

2. Distributie

Distributievolume (V_d)

Body Fluid Compartments of a 70-kg Adult Man



17

Farmacokinetiek

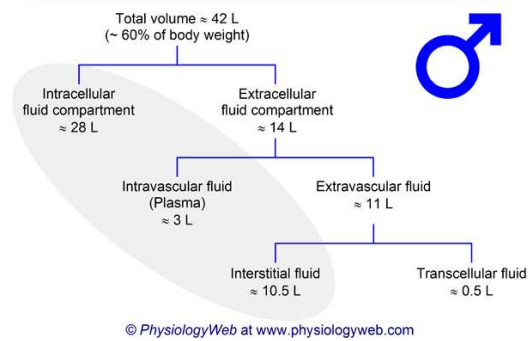
2. Distributie

Distributievolume (V_d)

Body Fluid Compartments of a 70-kg Adult Man



$V_d \leq 3L$



18

Farmacokinetiek

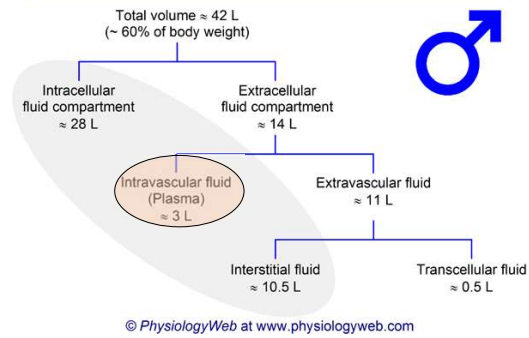
2. Distributie

Distributievolume (V_d)



$V_d \leq 3L$

Body Fluid Compartments of a 70-kg Adult Man



19

Farmacokinetiek

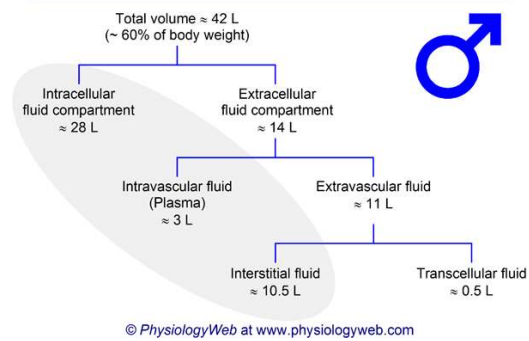
2. Distributie

Distributievolume (V_d)



$V_d \geq 42L$

Body Fluid Compartments of a 70-kg Adult Man

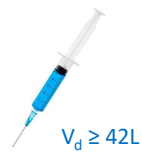


20

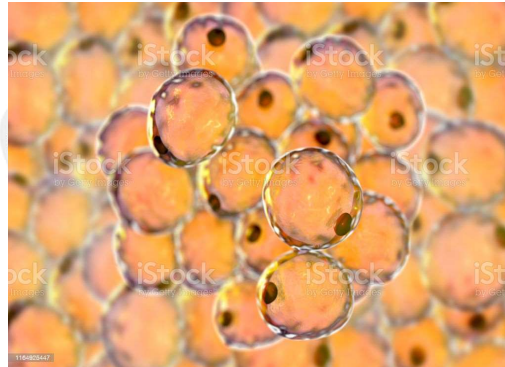
Farmacokinetiek

2. Distributie

Distributievolume (V_d)



$V_d \geq 42L$



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Farmacokinetiek

2. Distributie

Snelheid van distributie ~ bloedflow:

	% van lichaamsmassa	% van hartdebiet
Vaatrijk (hart, longen, lever, nieren, hersenen)	10	75
Spiere	50	19
Vetweefsel	20	5
Vaatarm (huid, been, ...)	20	< 1

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Farmacokinetiek

1. Absorptie
2. Distributie
3. Metabolisme (biotransformatie)

23

Farmacokinetiek

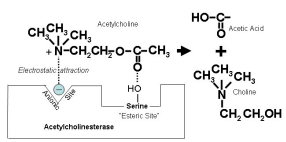
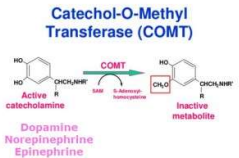
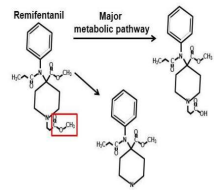
3. Metabolisme: doel = geneesmiddel wateroplosbaar te maken

fase	0	I	II	III
orgaan	lever e.a.	lever e.a.	lever e.a.	bacteriën
reacties		oxidatie; reductie; hydrolyse; dealkylering; deaminering	conjugatie: glucuronidering sulfatering glutathionconjug. glycineconjug. acetylering e.a.	deconjugatie: deglucuronidering desulfatering etc.
product	moedermolekuul	fase I metaboliet	conjugatie- metaboliet	moedermolekuul
enzym		cytochroom P450: CYP2C9; CYP2C8	glucuronyl- transferase etc.	β -glucuronidase sulfatase etc.
reactiviteit	(meestal) actief	inactivatie (soms) activatie	(meestal) inactivatie	reactivatie
wateroplosbaarheid	lipofiel	hydrofiel	meer hydrofiel	lipofiel
polariteit	apolair	polair	meer polair	apolair

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Farmacokinetiek

3. Metabolisme



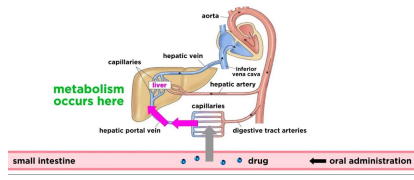
CYP1	CYP1A, CYP1A1, CYP1A2	Drug and steroid (especially estrogen) metabolism, benzodiazepine reformation
CYP1B	CYP1B1	
CYP1D	CYP1D1	
CYP2	CYP2A, CYP2A6, CYP2A7, CYP2A13, CYP2A14, CYP2A17, CYP2A19	Drug and steroid metabolism
CYP2B	CYP2B6, CYP2B7	
CYP2C	CYP2C8, CYP2C9, CYP2C18, CYP2C19, CYP2C23, CYP2C24, CYP2C37, CYP2C49, CYP2C50	
CYP2D	CYP2D6, CYP2D7, CYP2D8	
CYP2E	CYP2E1	
CYP2F	CYP2F1, CYP2F2	
CYP3	CYP3A, CYP3A4, CYP3A5, CYP3A7, CYP3A4A, CYP3A42, CYP3A43, CYP3A45, CYP3A52, CYP3A57	Drug and steroid (including testosterone) metabolism
CYP4	CYP4A, CYP4A1, CYP4A2, CYP4A3, CYP4A4, CYP4A9, CYP4A10, CYP4A11, CYP4A12, CYP4A13, CYP4A14, CYP4A15, CYP4A16, CYP4A17, CYP4A18, CYP4A19, CYP4A20, CYP4A21, CYP4A22, CYP4A23, CYP4A24, CYP4A25, CYP4A26, CYP4A27, CYP4A28, CYP4A29, CYP4A30, CYP4A31, CYP4A32, CYP4A33, CYP4A34, CYP4A35, CYP4A36, CYP4A37, CYP4A38, CYP4A39, CYP4A40, CYP4A41, CYP4A42, CYP4A43, CYP4A44, CYP4A45, CYP4A46, CYP4A47, CYP4A48, CYP4A49, CYP4A50, CYP4A51, CYP4A52, CYP4A53, CYP4A54, CYP4A55, CYP4A56, CYP4A57, CYP4A58, CYP4A59, CYP4A60, CYP4A61, CYP4A62, CYP4A63, CYP4A64, CYP4A65, CYP4A66, CYP4A67, CYP4A68, CYP4A69, CYP4A70, CYP4A71, CYP4A72, CYP4A73, CYP4A74, CYP4A75, CYP4A76, CYP4A77, CYP4A78, CYP4A79, CYP4A80, CYP4A81, CYP4A82, CYP4A83, CYP4A84, CYP4A85, CYP4A86, CYP4A87, CYP4A88, CYP4A89, CYP4A90, CYP4A91, CYP4A92, CYP4A93, CYP4A94, CYP4A95, CYP4A96, CYP4A97, CYP4A98, CYP4A99, CYP4A100	Acetylcholinic acid or fatty acid metabolism
CYP4F	CYP4F2, CYP4F3, CYP4F8, CYP4F9, CYP4F10, CYP4F11, CYP4F12, CYP4F13, CYP4F14, CYP4F15, CYP4F16, CYP4F17, CYP4F18, CYP4F19, CYP4F20, CYP4F21, CYP4F22, CYP4F23, CYP4F24, CYP4F25, CYP4F26, CYP4F27, CYP4F28, CYP4F29, CYP4F30, CYP4F31, CYP4F32, CYP4F33, CYP4F34, CYP4F35, CYP4F36, CYP4F37, CYP4F38, CYP4F39, CYP4F40, CYP4F41, CYP4F42, CYP4F43, CYP4F44, CYP4F45, CYP4F46, CYP4F47, CYP4F48, CYP4F49, CYP4F50, CYP4F51, CYP4F52, CYP4F53, CYP4F54, CYP4F55, CYP4F56, CYP4F57, CYP4F58, CYP4F59, CYP4F60, CYP4F61, CYP4F62, CYP4F63, CYP4F64, CYP4F65, CYP4F66, CYP4F67, CYP4F68, CYP4F69, CYP4F70, CYP4F71, CYP4F72, CYP4F73, CYP4F74, CYP4F75, CYP4F76, CYP4F77, CYP4F78, CYP4F79, CYP4F80, CYP4F81, CYP4F82, CYP4F83, CYP4F84, CYP4F85, CYP4F86, CYP4F87, CYP4F88, CYP4F89, CYP4F90, CYP4F91, CYP4F92, CYP4F93, CYP4F94, CYP4F95, CYP4F96, CYP4F97, CYP4F98, CYP4F99, CYP4F100	
CYP5	CYP5A, CYP5A1	Thromboxane A2 synthase
CYP7	CYP7A, CYP7A1	Bile acid biosynthesis, 7-alpha hydroxylase of steroid nucleus
CYP8	CYP8A, CYP8A1	Varied (bile acid biosynthesis, prostacyclin synthase)
CYP9	CYP9A, CYP9A1	
CYP10	CYP10A, CYP10A1	
CYP11	CYP11A, CYP11A1	
CYP12	CYP12A, CYP12A1	
CYP13	CYP13A, CYP13A1	
CYP14	CYP14A, CYP14A1	
CYP15	CYP15A, CYP15A1	
CYP16	CYP16A, CYP16A1	
CYP17	CYP17A, CYP17A1	
CYP18	CYP18A, CYP18A1	
CYP19	CYP19A, CYP19A1	
CYP20	CYP20A, CYP20A1	
CYP21	CYP21A, CYP21A1	
CYP22	CYP22A, CYP22A1	
CYP23	CYP23A, CYP23A1	
CYP24	CYP24A, CYP24A1	
CYP25	CYP25A, CYP25A1	
CYP26	CYP26A, CYP26A1	
CYP27	CYP27A, CYP27A1	
CYP28	CYP28A, CYP28A1	
CYP29	CYP29A, CYP29A1	
CYP30	CYP30A, CYP30A1	
CYP31	CYP31A, CYP31A1	
CYP32	CYP32A, CYP32A1	
CYP33	CYP33A, CYP33A1	
CYP34	CYP34A, CYP34A1	
CYP35	CYP35A, CYP35A1	
CYP36	CYP36A, CYP36A1	
CYP37	CYP37A, CYP37A1	
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CYP39	CYP39A, CYP39A1	
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CYP49	CYP49A, CYP49A1	
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CYP63	CYP63A, CYP63A1	
CYP64	CYP64A, CYP64A1	
CYP65	CYP65A, CYP65A1	
CYP66	CYP66A, CYP66A1	
CYP67	CYP67A, CYP67A1	
CYP68	CYP68A, CYP68A1	
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CYP70	CYP70A, CYP70A1	
CYP71	CYP71A, CYP71A1	
CYP72	CYP72A, CYP72A1	
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CYP75	CYP75A, CYP75A1	
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CYP77	CYP77A, CYP77A1	
CYP78	CYP78A, CYP78A1	
CYP79	CYP79A, CYP79A1	
CYP80	CYP80A, CYP80A1	
CYP81	CYP81A, CYP81A1	
CYP82	CYP82A, CYP82A1	
CYP83	CYP83A, CYP83A1	
CYP84	CYP84A, CYP84A1	
CYP85	CYP85A, CYP85A1	
CYP86	CYP86A, CYP86A1	
CYP87	CYP87A, CYP87A1	
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CYP97	CYP97A, CYP97A1	
CYP98	CYP98A, CYP98A1	
CYP99	CYP99A, CYP99A1	
CYP100	CYP100A, CYP100A1	

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Farmacokinetiek

3. Metabolisme

Hepatische klaring:



$$Cl_H = Q_H \times \frac{fu \times Cl_{int}}{Q_H + fu \times Cl_{int}}$$

Labels for the equation:

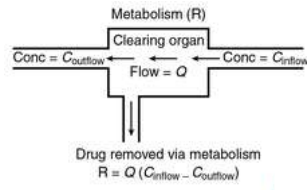
- Hepatic clearance (points to Cl_H)
- Hepatic blood flow (points to Q_H)
- Fraction of drug unbound in plasma (points to fu)
- Intrinsic clearance (points to Cl_{int})
- extractie ratio (E_H) (points to the entire fraction)

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Farmacokinetiek

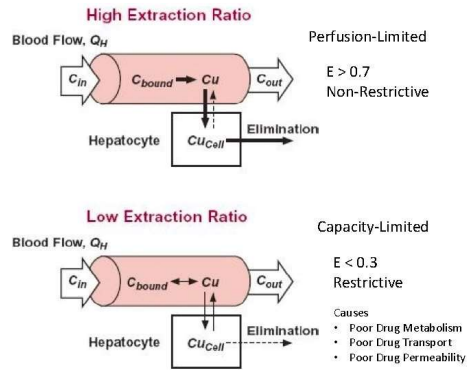
3. Metabolisme

Hepatische klaring:



$$ER = \frac{C_{inflow} - C_{outflow}}{C_{inflow}}$$

$$= \frac{Cl_{intrinsic}}{(Cl_{intrinsic} + Q_{hepatic})}$$

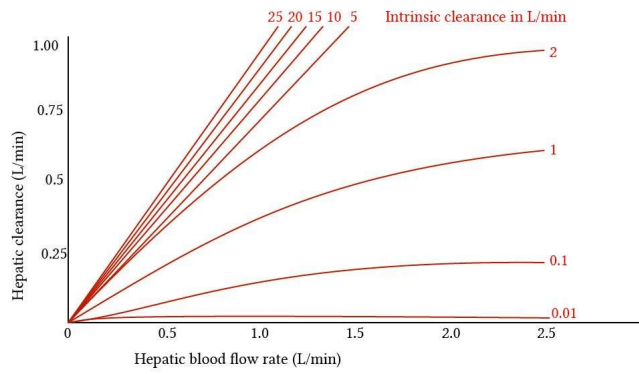


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Farmacokinetiek

3. Metabolisme

Hepatische klaring:



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Farmacokinetiek

3. Metabolisme

Hepatische klaring:

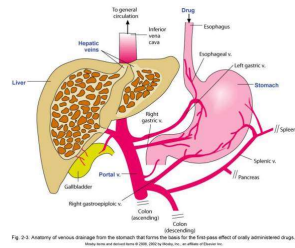
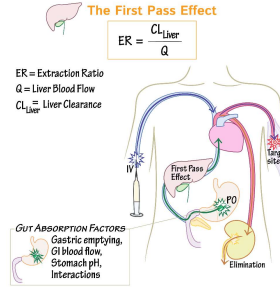


Fig. 2-3 Anatomy of various drainage from the stomach that forms the basis for the first pass effect of orally administered drugs. How the extraction ratio (ER), hepatic v. or portal clearance.



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Farmacokinetiek

3. Metabolisme

Hepatische klaring:

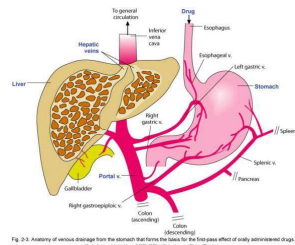
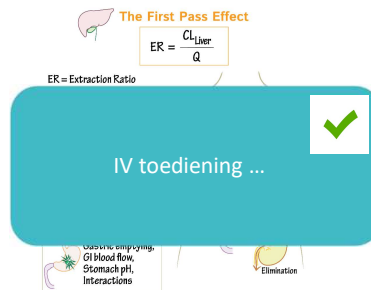


Fig. 2-3 Anatomy of various drainage from the stomach that forms the basis for the first pass effect of orally administered drugs. How the extraction ratio (ER), hepatic v. or portal clearance.



30

Farmacokinetiek

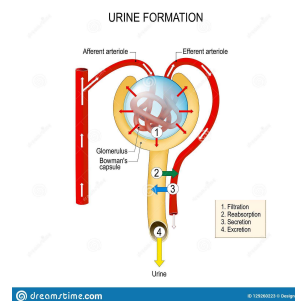
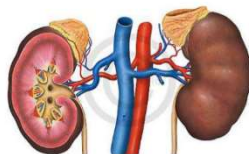
1. Absorptie
2. Distributie
3. Metabolisme
4. Excretie

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Farmacokinetiek

4. Excretie

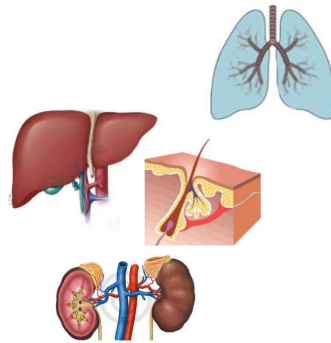
Renale klaring:



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Farmacokinetiek

4. Excretie



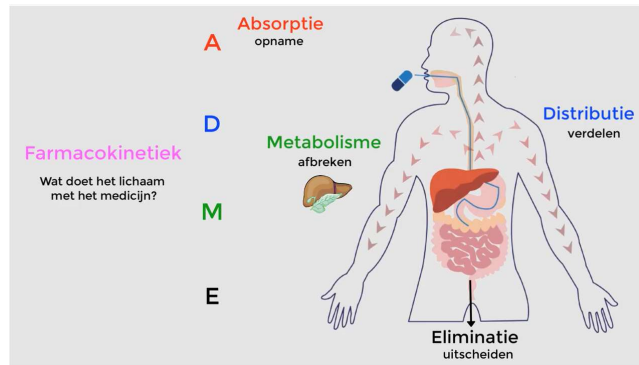
33

Farmacokinetiek

1. Absorptie
 2. Distributie
 3. Metabolisme
 4. Excretie
- } eliminatie

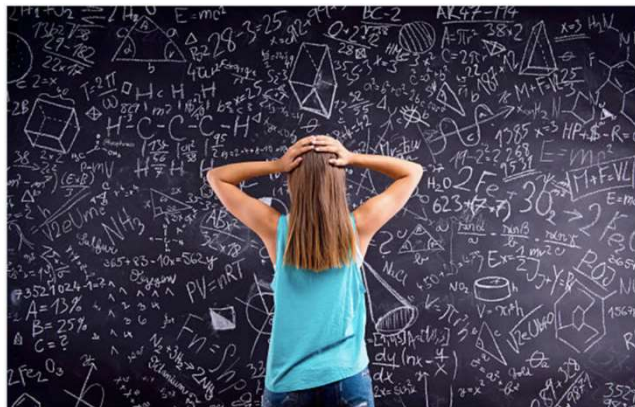
34

Farmacokinetiek



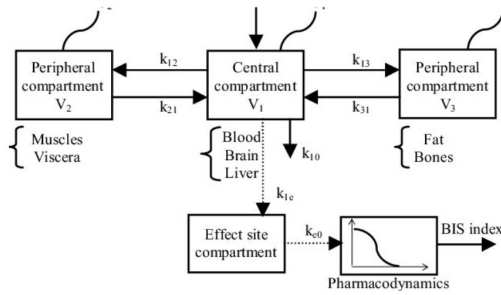
35

Farmacokinetiek: wiskunde



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Farmacokinetiek: wiskunde



Figure

Caption

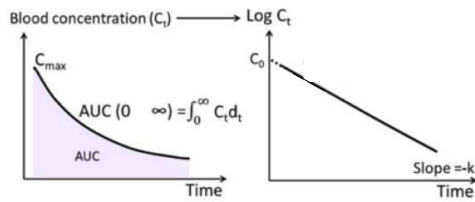
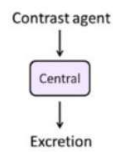
Figure 1. Pharmacokinetics-pharmacodynamic compartmental model with the effect site [5].

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Farmacokinetiek: wiskunde

One-compartment model:
 $C_t = C_0 e^{-kt}$



$$dC/dt = -k \cdot C^n$$

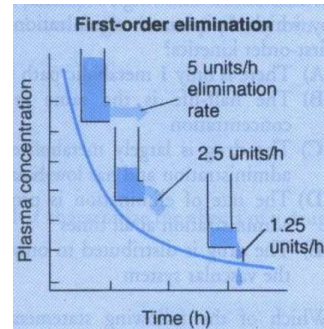
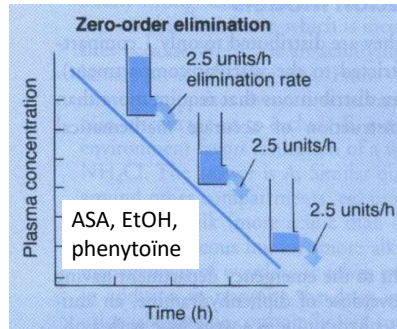
dC/dt = snelheid waarmee concentratie (C) verandert

k = snelheidsconstante

$n = 0$ (0^{de} orde kinetiek) of $n = 1$ (1^{ste} orde kinetiek)

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Farmacokinetiek: wiskunde



✳ **Michaelis-Menten elimination**

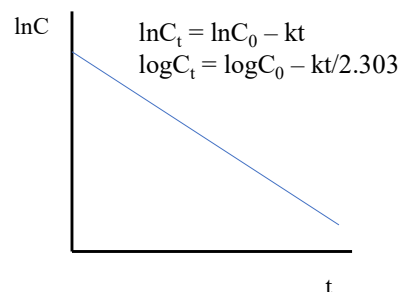
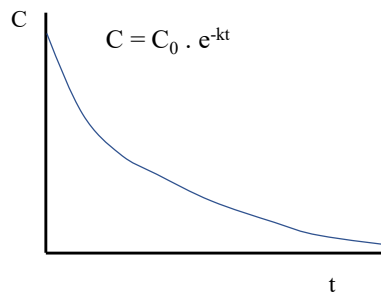
$$\text{Rate of elimination} = \frac{V_{\max} \times C}{K_m + C}$$

K_m = Michaëlis-Menten cst: de concentratie substraat waarbij de reactie verloopt aan ½ max snelheid

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Farmacokinetiek: wiskunde

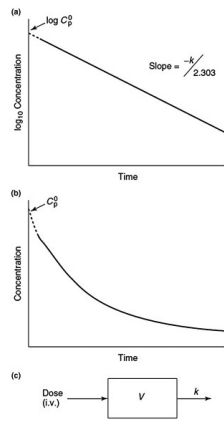
1^{ste} orde kinetiek:



k = eerste orde eliminatieconstante die aangeeft met welke proportie concentratie daalt

40

Farmacokinetiek: wiskunde

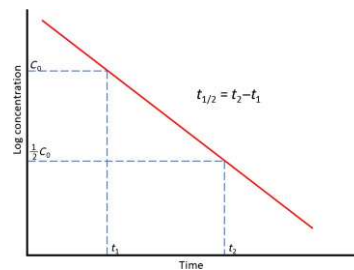
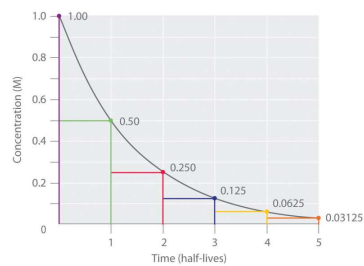


- Eliminatie snelheidsconstante, k_{eo} : fractie van GM dat wordt geëlimineerd uit het lichaam over een bepaalde tijdsperiode
- Beïnvloed door (distributie), metabolisme en excretie
- Meestal 1^{ste} orde snelheidsconstante

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Farmacokinetiek: wiskunde

1^{ste} orde kinetiek: halfwaardetijd:



$$t_{1/2,elim} = \frac{\ln(2)}{k} \approx \frac{0.693}{k}$$

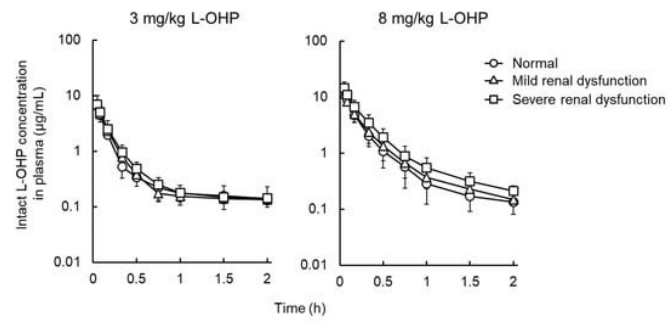
$$k = \frac{\ln(2)}{t_{1/2,elim}} \approx \frac{0.693}{t_{1/2,elim}}$$

$$T_{1/2} = 0.693 \times V_d / Cl$$

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Farmacokinetiek: wiskunde

1^{ste} orde kinetiek: renale klaring:

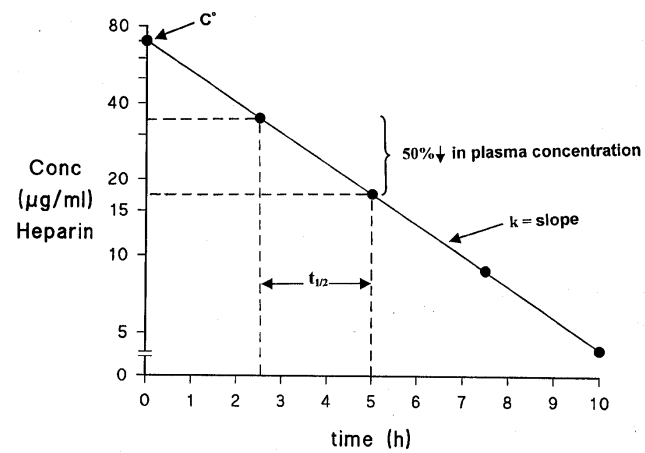


$$CL = \frac{F \cdot Dose}{AUC} = K_{10} \cdot Vd$$

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Farmacokinetiek: wiskunde

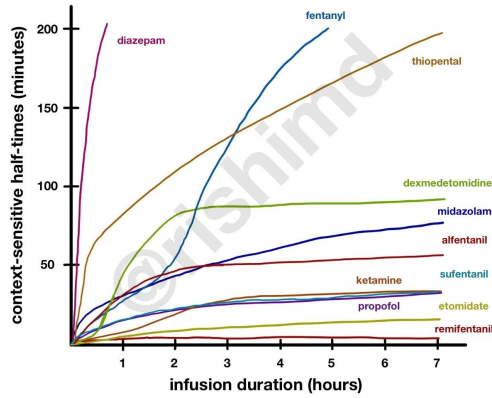
heparine



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Farmacokinetiek: wiskunde

CONTEXT-SENSITIVE HALF-TIMES

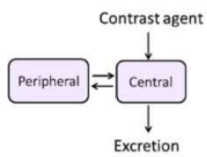


45

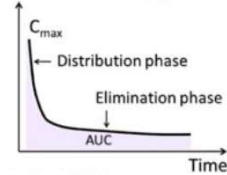
Farmacokinetiek: wiskunde

Two-compartment model:

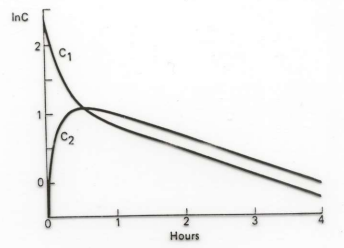
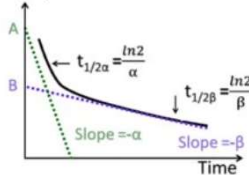
$$C_t = Ae^{-\alpha t} + Be^{-\beta t}$$



Blood concentration (C_t)



Log C_t



$$C = A.e^{-\alpha t} + B.e^{-\beta t}$$

met α en β hybride snelheidsconstanten

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Farmacokinetiek: wiskunde

Drie compartimenteel model

$$C = A \cdot e^{-\alpha t} + B \cdot e^{-\beta t} + C \cdot e^{-\gamma t}$$

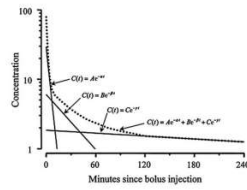
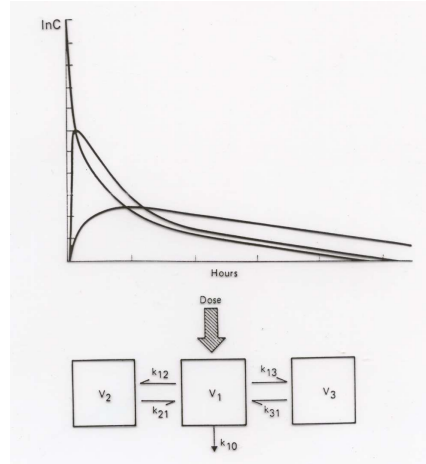


Fig 1 Plasma concentration vs time curve demonstrating tri-exponential decline after a bolus injection. In conventional pharmacokinetic terminology, these are phases I-III. The plasma concentration at time t(C) may be derived from $C(t) = Ae^{-\alpha t} + Be^{-\beta t} + Ce^{-\gamma t}$, where t is time since i.v. bolus, C, concentration after a bolus dose. A-C represent the phase coefficients which sum to the plasma concentration after an i.v. bolus. α , β and γ represent phase rate constants. e, natural logarithm.

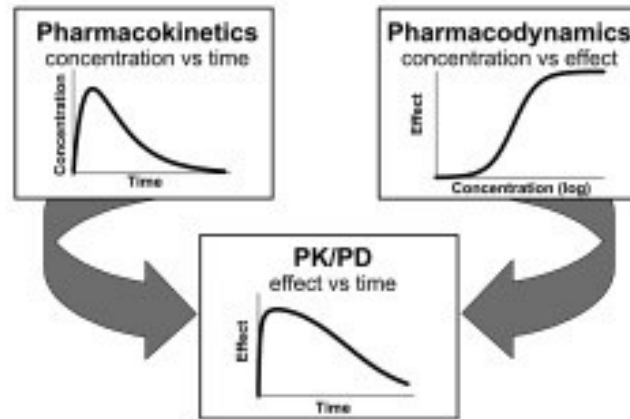


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PK/PD



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PK/PD

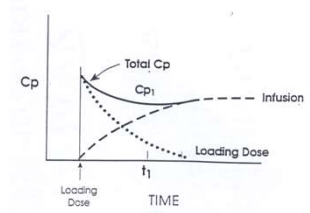
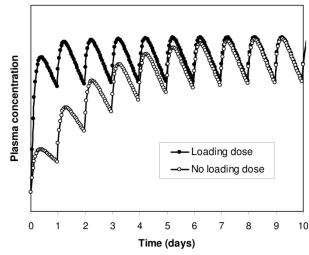
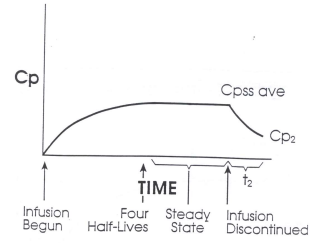
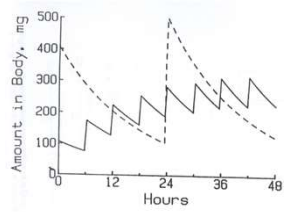
- Studie populatie: jonge, gezonde, niet-obese ptn
- Meestal $\Delta < 25\%$ tussen geschatte en gemeten concentratie
- Totaal lichaamsgewicht? Gecorrigeerd lichaamsgewicht?

=> vb. EEG monitor

PK model	Relevant groups
Marsh (adult)	Adults, elderly
Marsh (children)	Children
Schneider	Adults, obese, elderly
Kataria	Children
Kataria (no covariates)	Children
Cortinez	Adults, obese, elderly
Coppens	Children
Wietasch	Adults, elderly
Paedfusor	Children
Short	Children
Knibbe	Children, adults, elderly
Rigby-Jones	Young children, children
Rigby-Jones (multicenter)	Young children, children
Schuttler	Children, adults, elderly
ShangGuan	Children
VanKralingen (obese)	Obese
VanKralingen (obese and lean)	Obese, adults
Dyck	Adults, elderly
Tackley	Adults, elderly
White	Adults, elderly
Wang	Children, adults, elderly

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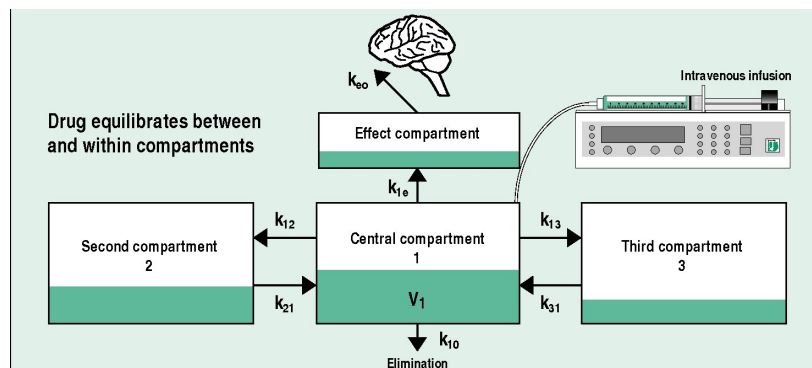
PK/PD



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PK/PD

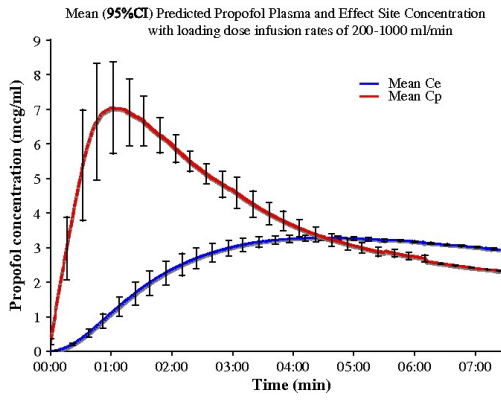
Effect site



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PK/PD

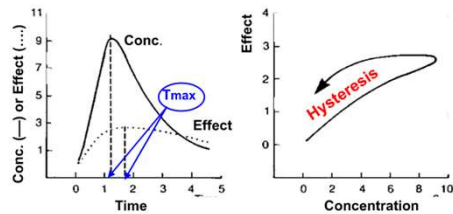
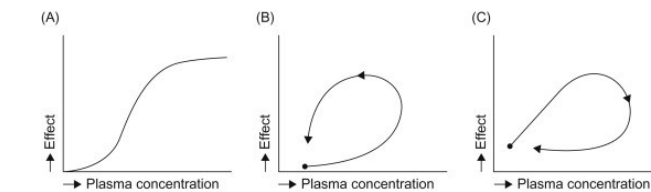
Hysteresis



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PK/PD

Hysteresis:

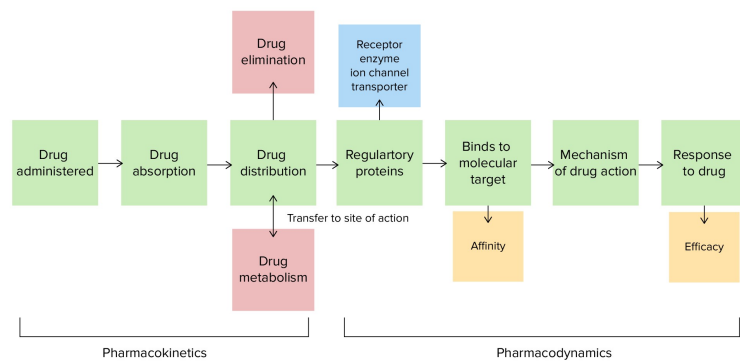


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2. Farmacodynamiek

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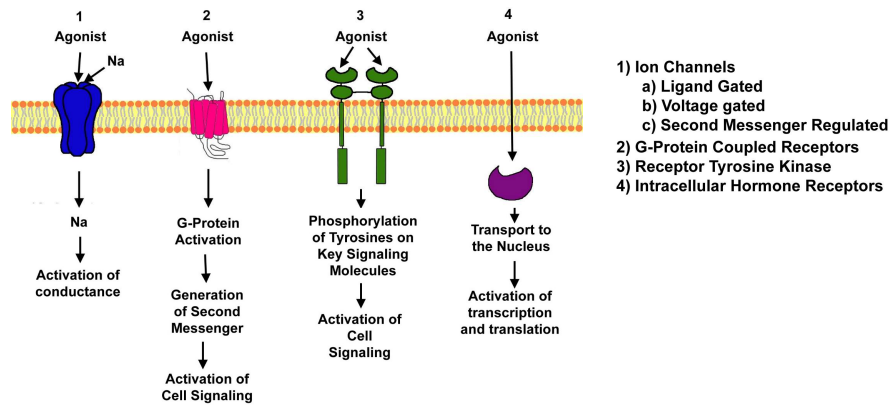
Farmacodynamiek



= wat doet het farmacon met het lichaam?

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Farmacodynamiek



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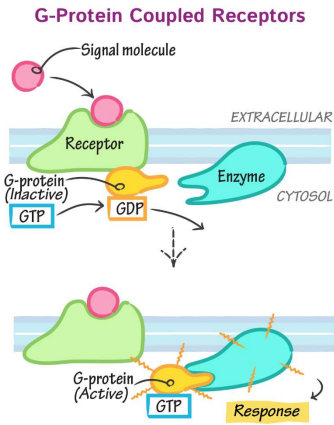
Farmacodynamiek

Membraanverankerde receptoren:

- Catecholamine receptor: α , β_1 , β_2 , dopamine...
- Serotonine receptor
- Histamine receptor: H1, H2
- Acetylcholine receptor: muscarine en nicotine
- GABA receptor
- N-methyl-D-Aspartaat (NMDA) receptor
- Opiaatreceptor: μ_1 , μ_2 , κ , σ , δ ...

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Farmacodynamiek



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Farmacodynamiek

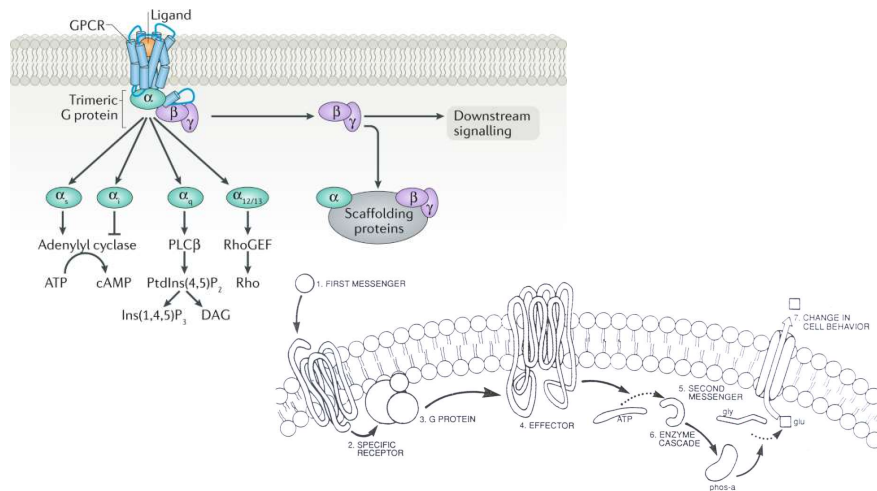
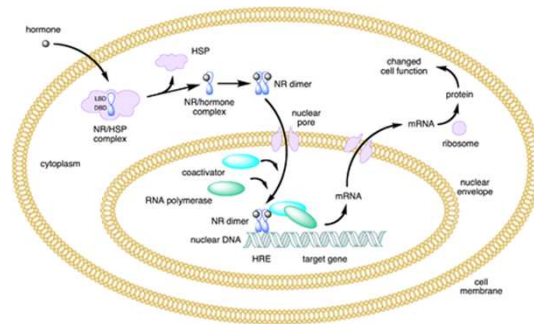


Fig. 16-16. Epinephrine-stimulated glycogenolysis in a liver cell demonstrates the role of G proteins in cellular function. The first messenger (epinephrine) binds to its specific receptor, stimulating the G protein (in this case G $_s$) to activate the effector, adenylyl cyclase. This enzyme converts adenosine triphosphate (ATP) to cyclic adenosine monophosphate (cAMP), the second messenger, which then triggers a cascade of enzymatic reactions that stimulates the enzyme phosphorylase (phos-a) to convert glycogen into glucose, which the cell finally extrudes. (From Linder and Gilman,⁷⁸ with permission.)

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Farmacodynamiek

Cytoplasmatische/nucleaire receptoren:



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Farmacodynamiek

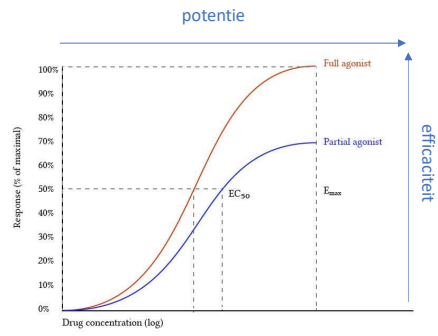
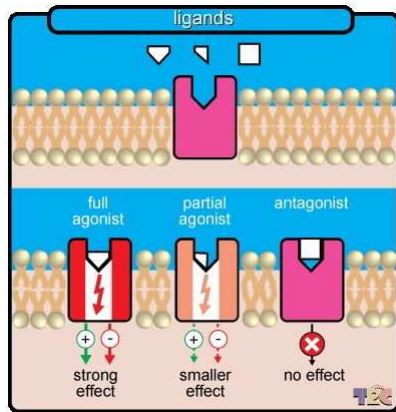
Agonist-receptor: sleutel-slot principe



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Farmacodynamiek

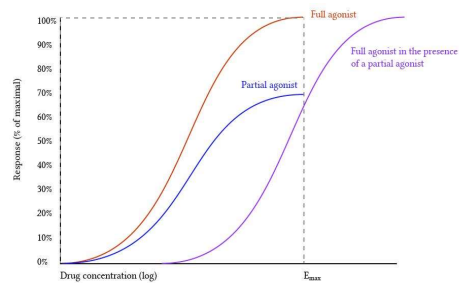
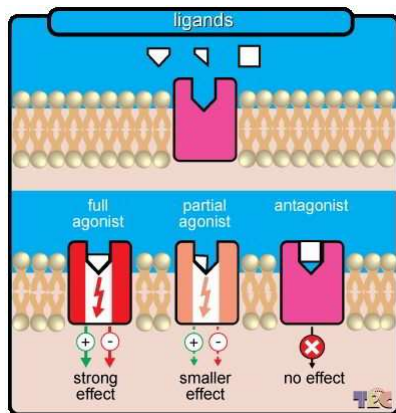
Intrinsieke activiteit van geneesmiddel:



65

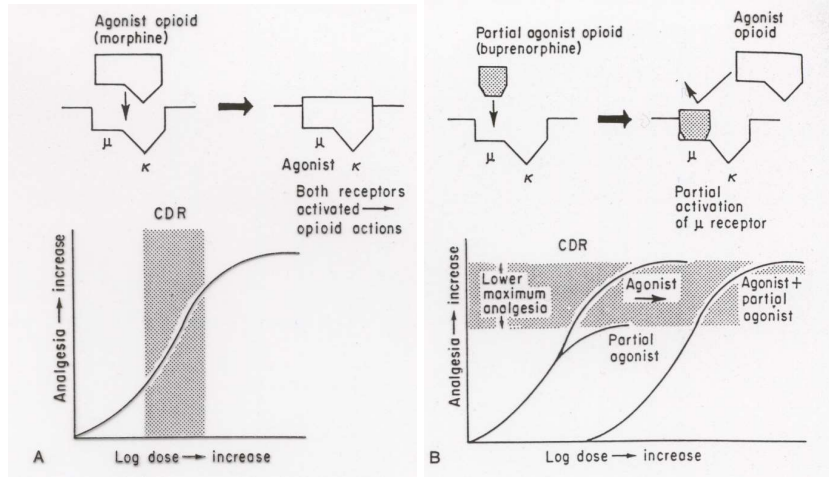
Farmacodynamiek

Intrinsieke activiteit van geneesmiddel:



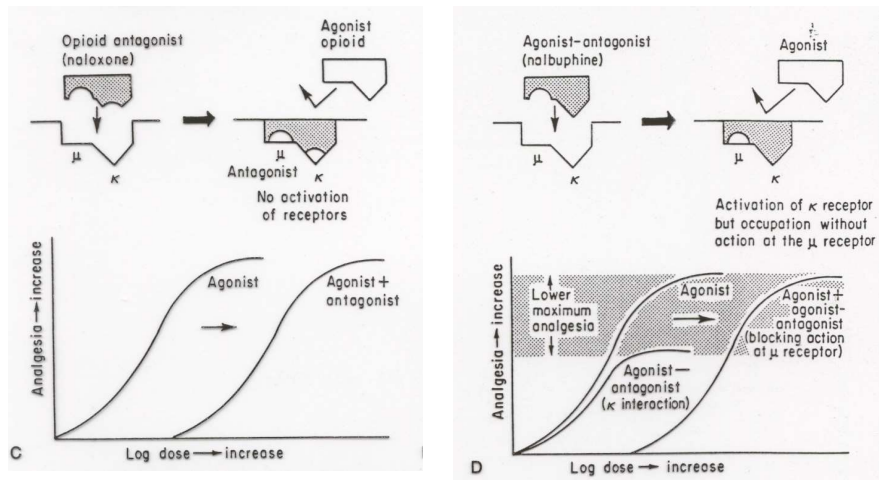
66

Farmacodynamiek



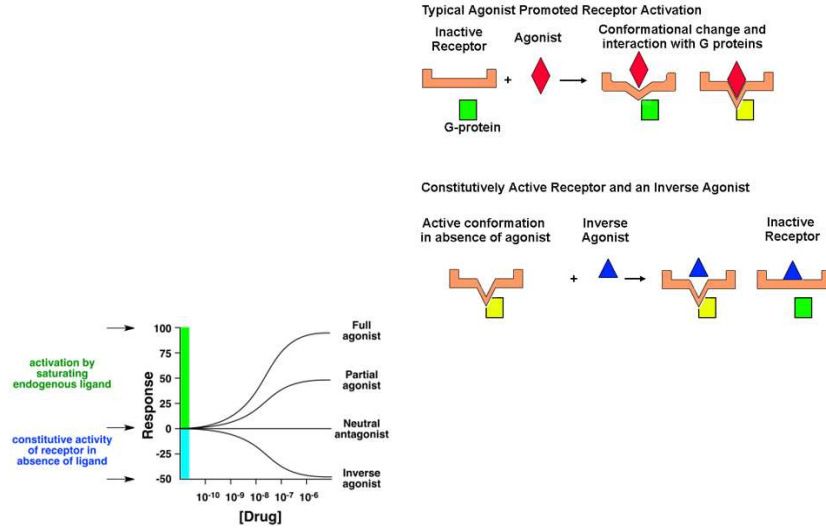
67

Farmacodynamiek



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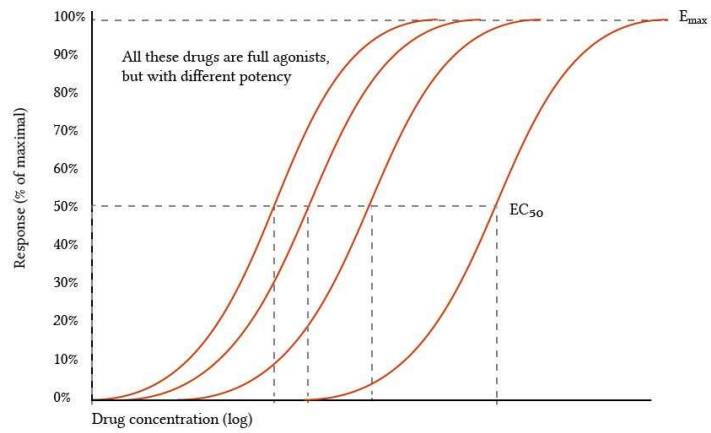
Farmacodynamiek



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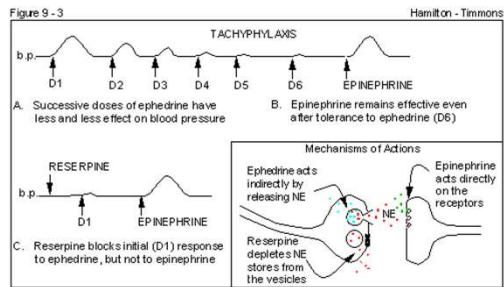
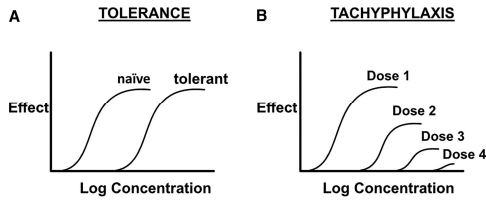
Farmacodynamiek

Intrinsieke activiteit van geneesmiddel:



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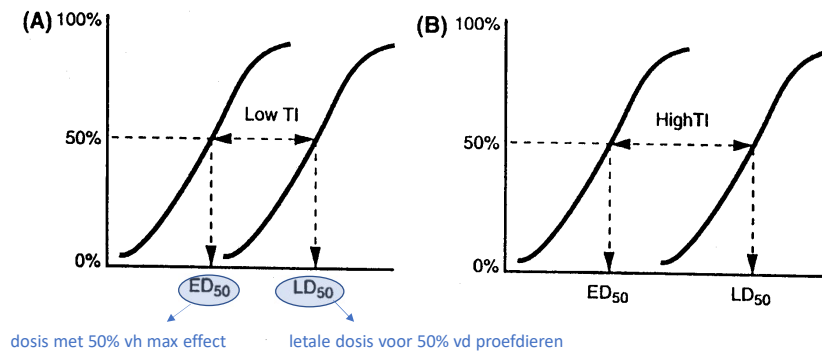
Farmacodynamiek



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Farmacodynamiek

LD50/ED50: therapeutische index

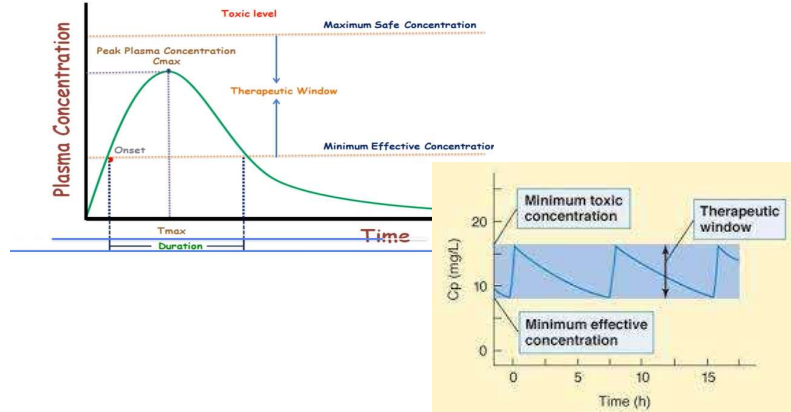


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Farmacodynamiek

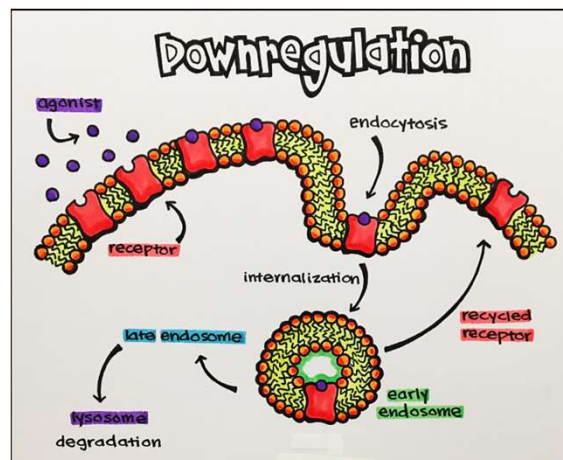
therapeutisch concentratievenster:

Plasma Concentration-Time Curve

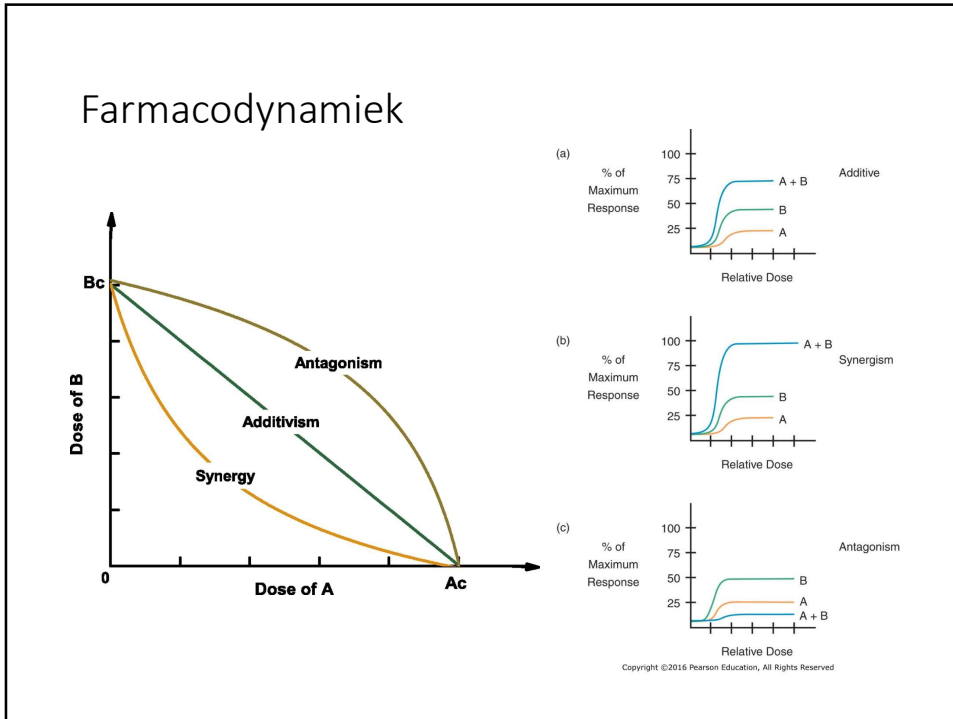


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Farmacodynamiek



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Referenties

Referenties

Lesinhoud:

<https://www.lecturio.com/concepts/pharmacokinetics-and-pharmacodynamics/>

Slide 4: ADME:
<https://accesspharmacy.mhmedical.com/content.aspx?bookid=513§ionid=41488024>

Slide 14: distributie:
<https://basicmedicalky.com/pharmacokinetics-the-dynamics-of-drug-absorption-distribution-metabolism-and-elimination/>

<https://slideplayer.com/slide/10834345/>

Slide 16: distributie:
https://www.brainkart.com/article/Clearance---Pharmacokinetics_24423/

Slide 24: metabolisme:
http://www.groengezondheid.nl/content.php?title=biotransformatie_bloed_naar_uitscheidingsorganen

Slide 25: metabolisme:
https://www.researchgate.net/figure/Classification-of-CYP450-Family-Subfamily-Genes-Pseudogenes-Function_tbl1_283521791/download

<https://www.atsdr.cdc.gov/csem/cholinesterase-inhibitors/inhibitors.html>

<https://www.gatewaypsychiatric.com/same-s-adenosyl-methionine/>

Slide 26: metabolisme:
<https://derangedphysiology.com/main/cicm-primary-exam/required-reading/pharmacokinetics/Chapter%203336/hepatic-clearance>

<https://www.youtube.com/watch?v=1LW0q1E0f4>

Slide 27: metabolisme:
<https://clinicalgate.com/mechanisms-of-hepatic-drug-metabolism-and-excretion/>

Slide 28: metabolisme:
<https://derangedphysiology.com/main/cicm-primary-exam/required-reading/pharmacokinetics/Chapter%203336/hepatic-clearance>

Slide 29: metabolisme:
<https://derangedphysiology.com/main/cicm-primary-exam/required-reading/pharmacokinetics/Chapter%203336/hepatic-clearance>

https://media.lanecc.edu/users/driscollin/RT127/Softchalk/Pharmacology_SF7CHLX_Lesson/Pharmacology_lesson8.html

Slide 37: farmacokinetiek: wiskunde

https://www.researchgate.net/publication/224316494_Generalized_Predictive_Control_of_Depth_of_Anesthesia_by_Using_a_Pharmacokinetic-Pharmacodynamic_Model_of_the_Patient/figures?on=1

Slide 39: farmacokinetiek: wiskunde

<https://www.slideshare.net/UsmanKhalid135/drug-elimination>

Slide 41: farmacokinetiek: wiskunde

<https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/elimination-rate-constant>

Slide 42: farmacokinetiek: wiskunde

<https://www.slidesserve.com/gasha/dosage-regimen>

Slide 43: farmacokinetiek: wiskunde

<https://www.mdpi.com/2072-6694/13/24/6382/htm>

Slide 46: farmacokinetiek: wiskunde

(helling: 2.303)

Slide 47: farmacokinetiek: wiskunde

<https://basicmedicalky.com/pharmacokinetics-of-an-intravenous-bolus-injection-in-a-one-compartment-model/>

Slide 49: PK/PD

https://www.researchgate.net/publication/11776107_Current_concepts_in_pharmacokinetics_and_their_implications_for_clinical_medicine/figures?on=1&utm_source=google&utm_medium=organic

Slide 50: PK/PD

<https://pubmed.ncbi.nlm.nih.gov/24722258/>

Slide 53: PK/PD

<https://slideplayer.com/slide/9564082/>

Slide 55: PK/PD

<https://www.cambridgechemconsulting.com/resources/ADME/distribution.html>

Slide 56: PK/PD

<https://www.sciencedirect.com/topics/medicine-and-dentistry/drug-effect>

Slide 59: farmacodynamiek

<http://www.uky.edu/~mta/pha824mp/PHA824mp.html>

Slide 61: farmacodynamiek

<https://dravittoknowit.com/course/cell-biology/glossary/cellular-anatomy-physiology/g-coupled-receptor>

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Referenties

Slide 62: farmacodynamiek

<https://www.nature.com/articles/s41569-019-0220-3>

Slide 63: farmacodynamiek

<https://www.usgnet.be/ge/nl/boekomstige-studenten/infodagen/geneskunde/cel-iv-moleculaire-biologie-en-genetica.pdf>

https://en.wikipedia.org/wiki/Nuclear_receptor

Slide 65: farmacodynamiek

<https://www.cannify.us/education/cannabis-and-the-body/cannabinoid-clinical-pharmacology/pharmacodynamics/ligand-binding-to-receptors/>

<https://derangedphysiology.com/main/cicm-primary-exam/required-reading/pharmacodynamics/Chapter%20417/Full-agonists-partial-agonists-and-inverse-agonists>

Slide 69: farmacodynamiek

https://en.wikipedia.org/wiki/Inverse_agonist/media/File:Inverse_agonist_3.svg

<https://www.sciencedirect.com/topics/neuroscience/inverse-agonist>

<http://www.uky.edu/~mta/pha824mp/PHA824mp.html>

Slide 70: farmacodynamiek

<https://derangedphysiology.com/main/cicm-primary-exam/required-reading/pharmacodynamics/Chapter%20417/Full-agonists-partial-agonists-and-inverse-agonists>

Slide 71: farmacodynamiek

<https://pet.aspetjournals.org/content/38/1/22>

<https://users.drew.edu/ctimmons/drugs/ch09-03.htm>

Slide 73: farmacodynamiek

<https://docplayer.nl/67454075-Voeding-prof-dr-non-h-j-mathijssen-interim-oncolog-klinisch-farmacoloog.html>

<https://www.facebook.com/DrCaitiaTubo-1142955890687/videos/biopharmaceutics-2-plasma-concentration-time-curve/28489499713253/>

Slide 74: farmacodynamiek

<https://open.lib.umn.edu/pharmacology/chapter/receptor-regulation/>

Slide 75: farmacodynamiek

<https://biology-forums.com/index.php?action=gallery;sa=view;id=28366>

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