

Introduction to Pharmkin I

A Computer Simulation of Drug Levels in Patients

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PHARMKIN is a computer simulation of plasma drug levels in patients with different characteristics.

One goal is to help you determine the appropriate dose regimens of drugs in patients with different characteristics.

The other goal is to help you understand how to calculate the loading dose (LD), maintenance dose (MD) and plasma plateau level (C_{ss}) of drugs cleared by first-order (non-saturable clearance) and zero-order (saturable clearance) kinetics.

Introduction to Pharmkin II

First-Order

$$\text{LD} = (\text{Vd} \times \text{Cp})/\text{F}$$

$$\text{MD} = (\text{C}_{\text{ss}} \times \text{CL} \times \text{T})/\text{F}$$

$$\text{C}_{\text{ss}} = (\text{F} \times \text{D})/(\text{CL} \times \text{T})$$

Zero-Order

$$(\text{Vd} \times \text{Cp})/\text{F}$$

$$\text{DR} = (\text{C}_{\text{ss}} \times (\text{V}_{\text{m}} - \text{DR}))/\text{K}_{\text{m}}$$

$$(\text{K}_{\text{m}} \times \text{DR})/(\text{V}_{\text{m}} - \text{DR})$$

LD = Loading Dose; MD = Maintenance Dose; C_{ss} = Steady-Plasma Drug Level; V_d = Volume of Distribution; C_p = peak plasma level of drug; F = Bioavailability; T = Dose Interval; CL = drug's clearance; D = Drug Dose; DR = Dose Rate; V_m = V_{max}; K_m = drug dose that produces 50% V_{max}.

Plateau Principle [First-Order CL]

	Dosing interval														Plateau	
	1		2		3		4		5		6		7		A	B
	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B
1g [Body]	1	.5	1.5	.75	1.75	.88	1.88	.94	1.94	.97	1.97	.99	2	1		
2g [Body]	2	1	3	1.5	3.5	1.75	3.75	1.88	3.88	1.94	3.94	3.98	4	2		

$t_{1/2} = 4 \text{ h}$ Dose Interval = 4h A = level of drug immediately after dose.

B = level of drug just before dose is given and drug cleared in each $t_{1/2}$.

Drug accumulates until input = output ($7 t_{1/2}$) = plateau [all doses]

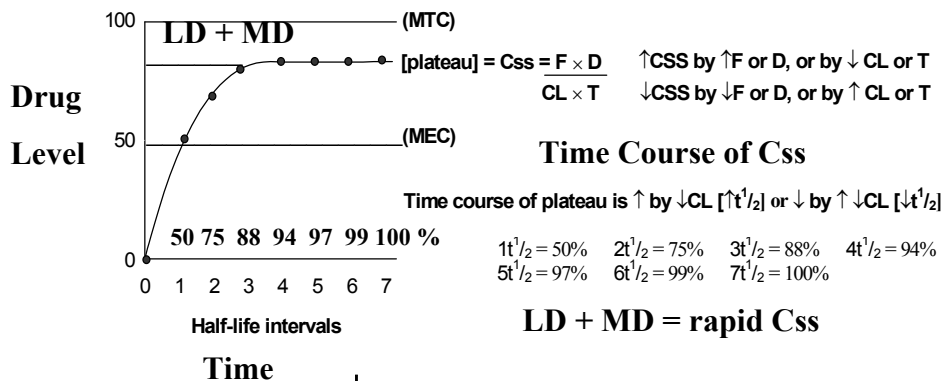
Time course of plateau is determined by drug's $t_{1/2}$.

Loading dose (2g or 4g) then 1/2 LD at $t_{1/2}$ intervals [Instant Plateau].

Plateau Principle of First-Order Cleared Drugs

Drug levels rise until input = output [C_{ss}]

Magnitude of C_{ss}



$$t_{1/2} = 0.693 \times Vd/CL$$

$$CL = Ke \times Vd$$

↓ CL: Liver, Heart, Kidney disease, Elderly, Infants, DM Inhibitors

↑ CL: DM inducers, smoking, drinking