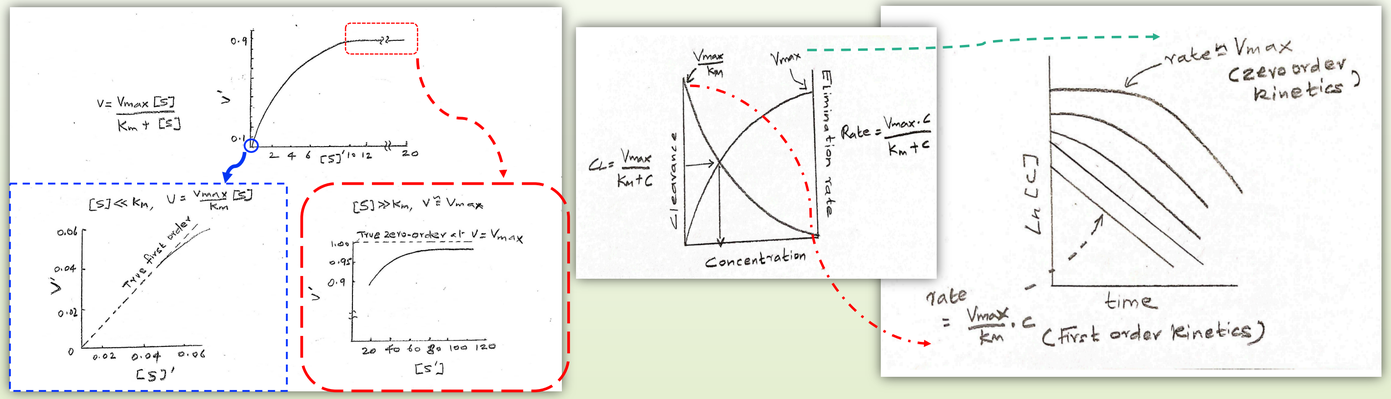
Enzyme Kinetics and Pharmacokinetics

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Enzyme Kinetics	Pharmacokinetics
Enzymes catalyze biochemical reactions-characterized in vitro	Drug metabolizing enzymes and transporters catalyze drug elimination by metabolism or transport
-dS/dt = rate of enzyme reaction converting substrate to product	-dC/dt = rate of drug elimination from organ/tissue/body
V= velocity of reaction, Measure of decrease in substrate concentration or increasing product concentration per unit time	V = velocity of drug metabolism or transporter reaction Clearance [CL} - Measure of drug elimination from body per unit time related to V
$k = V_{max}/K_M$ = first order rate constant Constant fraction of Substrate converted to product per unit time	K_e = first order drug elimination rate constant Constant fraction of drug concentration eliminated per unit time
Michaelis-Menten (MM) equation $V = \frac{V_{max}[S]}{K_M+[S]}$ [S] = substrate concentration	Elimination (Clearance-CL) described in terms of MM equation $dc/dt = K_e C = [CL/V_d]C$ $K_e = CL/V_d$ $V_d * dc/dt = \frac{V_{max}}{K_M+[C]} * [C]$ $CL = \frac{V_{max}}{K_M+[C]}$ [C] = drug concentration in plasma; V_d = Volume of distribution
First order kinetics = [S] <<K_M • V decreases with decreasing [S] • $V = \frac{V_{max}}{K_M}[S]$ • V increases linearly with [S] with k constant • Half-life= $T_{1/2} = 0.693/k$ • {S] v time curves linear on log-linear plots	First order Kinetics = [C] << K_M • V(rate of elimination) decreases with decreasing C • $V = k_e.[C]$; $k_e = CL/V_d$; $CL = \frac{V_{max}}{K_M}$ • Elimination increases with [C] with CL constant • Elimination half life = $t_{1/2} = 0.693/k_e$ • [C] v time curves linear on log-linear plots • AUC increases in dose proportional manner
Zero order kinetics = [S] >> K_M • V independent of [S] • $V = V_{max}$ • V increases linearly with [S] with k constant • $T_{1/2}$ dependent on [S] • [S] v time curves non-linear on log-linear plot	Zero order Kinetics = [C] >> K_M • V(rate of elimination) independent of [C] • $V = V_{max}$ • CL independent of drug concentration - decreases with increasing [C] • Elimination half life $t_{1/2}$ function of [C] • [C] v time curves non-linear on log-linear plots • AUC increases more than dose proportionally with increasing dose

References:
1. Irwin H. Segel . Biochemical calculations. 2nd edition.1975.
2. Gabrielsson J, Weiner, D. Pharmacokinetic and Pharmacodynamic Data Analysis: concepts & applications. 3rd edition. 2000

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Linear plot

Log-Linear plot

