PHARMACOKINETIC EQUATIONS Dr. Hisham

A. INTRAVENOUS BOLUS DOSE:

$$A = A_o.e^{-k_d t}$$

$$C = C_o.e^{-k_d t}$$

$$\ln A = \ln A_o - k_d t$$

$$\log A = \log A_o - \frac{k_d}{2.303}.t$$

$$t½ = \frac{0.693}{k_d}$$

$$CL = k_d.V_d$$

$$V_d = \frac{D}{C_o}$$

$$AUC\Big|_0^\infty = \frac{D}{CL}$$

$$f_r = (0.5)^n$$

B. Constant-Rate I.V. Infusion:

$$A = \frac{R_o}{k_d}(1 - e^{-k_d t})$$

$$C = \frac{R_o}{CL}(1 - e^{-k_d t})$$

$$A = A_{ss}(1 - e^{-k_d t})$$

$$C = C_{ss}(1 - e^{-k_d t})$$

$$C_{ss} = \frac{R_o}{k_d.V_d}$$

$$C_{ss} = \frac{1.44\,R_o\,t½}{V_d}$$

$$f_{ss\%} = 1 - (0.5)^n$$

C: RENAL EXCRETION OF DRUGS

$$\frac{\Delta A_e}{\Delta t} = CL_R.C_{t_{mid}}$$

$$[\Delta A_e]_o^t = CL_R\,[AUC]_o^t$$

$$CL_R = \frac{A_{e\infty}}{AUC}$$

$$\ln\left[\frac{\Delta A_e}{\Delta t}\right] = \ln(k_e A_o) - k_d t_{mid}$$

$$\log\left[\frac{\Delta A_e}{\Delta t}\right] = \log(k_e A_o) - \frac{k_d}{2.303} t_{mid}$$

$$A_e = \frac{k_e A_o}{k_d}\left(1 - e^{-k_d t}\right)$$

$$A_{e\infty} = \frac{k_e A_o}{k_d}$$

$$\ln(A_{e\infty} - A_e) = \ln A_{e\infty} - k_d t$$

$$\log(A_{e\infty} - A_e) = \log A_{e\infty} - \frac{k_d}{2.303} t$$

$$f_e = \frac{CL_R}{CL} = \frac{k_e}{k_d} = \frac{A_{e\infty}}{D}$$

A. Oral absorption and bioavailability:

$$Cp = \frac{FDk_a}{V_d(k_a - k_d)}\left(e^{-k_d t} - e^{-k_a t}\right)$$

$$F_{A/B} = \frac{D_B.AUC_A}{D_A.AUC_B}$$

$$CL = k_d.V_d \qquad AUC\Big|_0^\infty = \frac{FD}{CL}$$

$$t_{max} = \frac{\ln\left(k_a / k_d\right)}{k_a - k_d}$$

$$F = \frac{D_{iv}.AUC_{po}}{D_{po}.AUC_{iv}}$$

B. Multiple dosing and dosage regimen:

$$C^{ss}_{max} = \frac{FD}{Vd(1 - e^{-kd\tau})}$$

$$C^{ss}_{min} = C^{ss}_{max}.e^{-kd\tau}$$

$$FD = A^{max}_{ss} - A^{min}_{ss}$$

(continued on next page)

$$C_{ss}^{min} = C_{ss}^{max}.e^{-k_d.\tau}$$

$$C_N^{max} = \frac{FD\left(1-e^{-Nk_d\tau}\right)}{V_d\left(1-e^{-k_d\tau}\right)}$$

$$A_N^{max} = \frac{FD\left(1-e^{-Nk_d\tau}\right)}{\left(1-e^{-k_d\tau}\right)}$$

$$C_{ss}^{max} = \frac{FD}{V_d\left(1-e^{-k_d\tau}\right)}$$

$$\overline{C}_{ss} = \frac{1.44t½FD}{V_d\tau}$$

$$\overline{A}_{ss} = \frac{FD}{k_d\tau}$$

$$R_{Acc} = \frac{1.44t½}{\tau} \quad \overline{C}_{ss} = \frac{AUC}{\tau}$$

C. **Nonlinear Kinetics**:

$$\frac{FD}{\tau} = \frac{V_{max}\ \overline{C}_{ss}}{K_m + \overline{C}_{ss}} \qquad K_m = \frac{R_2 - R_1}{\dfrac{R_1}{C_1} - \dfrac{R_2}{C_2}}$$

$$V_{max} = \frac{R}{C}\left(K_m + C\right) \qquad t½ = \frac{0.693\ V_d}{CL}$$

$$\frac{FD}{\tau} = CL.\overline{C}_{ss} \qquad \overline{C}_{ss} = \frac{\left(FD/\tau\right)K_m}{V_{max} - \left(FD/\tau\right)}$$

$$CL = \frac{V_{max}}{K_m + \overline{C}_{ss}}$$

D. **Disease States:**

$$Q = \left[f_e\left(KF-1\right)+1\right]$$

$$KF = \frac{GFR_{(u)}}{GFR_{(n)}} = \frac{CL_{Cr(u)}}{CL_{Cr(n)}}$$

$$f_e = \frac{k_e}{k_d} = \frac{CL_R}{CL} = \frac{A_{e(\infty)}}{D}$$

$$D_{(u)} = D_{(n)}.Q$$

$$\tau_{(u)} = \frac{\tau_{(n)}}{Q}$$

$$\left(\frac{D}{\tau}\right)_u = \left(\frac{D}{\tau}\right)_n.Q$$

$$f_e = \frac{t½_{anephric} - t½_{normal}}{t½_{anephric}}$$

$$CL_{cr}(males) = \frac{98 - 0.8(Age - 20)}{S_{cr}}$$

$$CL_{cr}(males) = \frac{[140 - Age]W}{72S_{cr}}$$

Two-compartment model:

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

$$A = \frac{D\left(\alpha - k_{21}\right)}{V_d\left(\alpha-\beta\right)}$$

$$B = \frac{D\left(k_{21} - \beta\right)}{V_d\left(\alpha-\beta\right)}$$

$$\alpha + \beta = k_{12} + k_{21} + k_{10}$$

$$\alpha\beta = k_{21}k_{10}$$

$$C_o = A + B$$

$$AUC = \frac{A}{\alpha} + \frac{B}{\beta}$$

$$k_{10} = \frac{C_o}{AUC}$$

$$k_{21} = \frac{\alpha\beta}{k_{10}}$$

$$k_{12} = \left(\alpha+\beta\right) - \left(k_{21} + k_{10}\right)$$

$$V_c = \frac{D}{C_o}$$

$$CL = k_{10}V_c$$

$$V_{ss} = V_c\left(1 + \frac{k_{12}}{k_{21}}\right)$$

$$V_\beta = V_{area} = \frac{D}{\beta.AUC}$$

$$V_{extrap} = \frac{D}{B}$$