

Useful Pharmacokinetic Equations

Symbols

D = dose

τ = dosing interval

CL = clearance

Vd = volume of distribution

k_e = elimination rate constant

k_a = absorption rate constant

F = fraction absorbed (bioavailability)

K_0 = infusion rate

T = duration of infusion

C = plasma concentration

General

Elimination rate constant

$$k_e = \frac{CL}{Vd} = \frac{\ln\left(\frac{C_1}{C_2}\right)}{(t_2 - t_1)} = \frac{\ln C_1 - \ln C_2}{(t_2 - t_1)}$$

Half-life

$$t_{1/2} = \frac{0.693 \cdot Vd}{CL} = \frac{\ln(2)}{k_e} = \frac{0.693}{k_e}$$

Intravenous bolus

Initial concentration

$$C_0 = \frac{D}{Vd}$$

Plasma concentration (single dose)

$$C = C_0 \cdot e^{-k_e \cdot t}$$

Plasma concentration (multiple dose)

$$C = \frac{C_0 \cdot e^{-k_e \cdot t}}{(1 - e^{-k_e \cdot \tau})}$$

Peak (multiple dose)

$$C_{\max} = \frac{C_0}{(1 - e^{-k_e \cdot \tau})}$$

Trough (multiple dose)

$$C_{\min} = \frac{C_0 \cdot e^{-k_e \cdot \tau}}{(1 - e^{-k_e \cdot \tau})}$$

Average concentration (steady state)

$$\bar{C}_{p_{ss}} = \frac{D}{CL \cdot \tau}$$

Oral administration

Plasma concentration (single dose)

$$C = \frac{F \cdot D \cdot k_a}{Vd(k_a - k_e)} \cdot (e^{-k_e \cdot t} - e^{-k_a \cdot t})$$

Time of maximum concentration (single dose)

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

Plasma concentration (multiple dose)

$$C = \frac{F \cdot D \cdot k_a}{Vd(k_a - k_e)} \cdot \left(\frac{e^{-k_e \cdot t}}{(1 - e^{-k_e \cdot \tau})} - \frac{e^{-k_a \cdot t}}{(1 - e^{-k_a \cdot \tau})} \right)$$

Time of maximum concentration (multiple dose)

$$t_{\max} = \frac{\ln\left(\frac{k_a \cdot (1 - e^{-k_e \cdot \tau})}{k_e \cdot (1 - e^{-k_a \cdot \tau})}\right)}{(k_a - k_e)}$$

Average concentration (steady state)

$$\bar{C} = \frac{F \cdot D}{CL \cdot \tau}$$

Clearance

$$Cl = \frac{Dose \cdot F}{AUC}$$

$$Cl = k_e \cdot V_d$$

Constant rate infusion

Plasma concentration (during infusion)

$$C = \frac{k_0}{CL} \cdot (1 - e^{-k_e \cdot t})$$

Plasma concentration (steady state)

$$C = \frac{k_0}{CL}$$

Calculated clearance (Chiou equation)

$$CL = \frac{2 \cdot k_0}{(C_1 + C_2)} + \frac{2 \cdot Vd \cdot (C_1 - C_2)}{(C_1 + C_2) \cdot (t_2 - t_1)}$$

Short-term infusion

Peak (single dose)

$$C_{\max(1)} = \frac{D}{CL \cdot T} \cdot (1 - e^{-k_e \cdot T})$$

Trough (single dose)

$$C_{\min(1)} = C_{\max(1)} \cdot e^{-k_e(\tau - T)}$$

Peak (multiple dose)

$$C_{\max} = \frac{D}{CL \cdot T} \cdot \frac{(1 - e^{-k_e \cdot T})}{(1 - e^{-k_e \cdot \tau})}$$

Trough (multiple dose)

$$C_{\min} = C_{\max} \cdot e^{-k_e(\tau - T)}$$

Calculated elimination rate constant

$$k_e = \frac{\ln\left(\frac{C_{\max}^*}{C_{\min}^*}\right)}{\Delta t}$$

with C_{\max}^* = measured peak and C_{\min}^* = measured trough,
measured over the time interval Δt

Calculated peak

$$C_{\max} = \frac{C_{\max}^*}{e^{-k_e \cdot t^*}}$$

with C_{\max}^* = measured peak, measured at time t^* after the end of the infusion

Calculated trough

$$C_{\min} = C_{\min}^* \cdot e^{-k_e \cdot t^*}$$

with C_{\min}^* = measured trough, measured at time t^* before the start of the next infusion

Calculated volume of distribution

$$Vd = \frac{D}{k_e \cdot T} \cdot \frac{(1 - e^{-k_e \cdot T})}{C_{\max} - C_{\min} \cdot e^{-k_e \cdot T}}$$

Calculated recommended dosing interval

$$\tau = \frac{\ln\left(\frac{C_{\max(\text{desired})}}{C_{\min(\text{desired})}}\right)}{k_e} + T$$

Calculated recommended dose

$$D = C_{\max(\text{desired})} \cdot k_e \cdot V \cdot T \cdot \frac{(1 - e^{-k_e \cdot \tau})}{(1 - e^{-k_e \cdot T})}$$

Two-Compartment-Body Model

$$C = a \cdot e^{-\alpha t} + b \cdot e^{-\beta t}$$

$$AUC_{\infty} = a / \alpha + b / \beta$$

$$Vd_{\text{area}} > Vd_{\text{ss}} > Vc$$

Creatinine Clearance

$$CL_{\text{creat}} (\text{male}) = \frac{(140 - \text{age}) \cdot \text{weight}}{72 \cdot Cp_{\text{creat}}}$$

$$CL_{\text{creat}} (\text{female}) = \frac{(140 - \text{age}) \cdot \text{weight}}{85 \cdot Cp_{\text{creat}}}$$

With weight in kg, age in years, creatinine plasma conc. in mg/dl and CL_{creat} in ml/min

K_e for aminoglycosides

$$K_e = 0.00293(\text{CrCL}) + 0.014$$

Metabolic and Renal Clearance

$$E_H = \frac{Cl_{int} \cdot fu_b}{Q_H + Cl_{int} \cdot fu_b}$$

$$Cl_H = E_H \cdot Q_H = \frac{Q_H \cdot Cl_{int} \cdot fu_b}{Q_H + Cl_{int} \cdot fu_b}$$

$$F_H = \frac{Q_H}{Q_H + Cl_{int} \cdot fu_b}$$

$$Cl_{ren} = \text{RBF} \cdot E = \text{GFR} \cdot \frac{C_{in} - C_{out}}{C_{in}}$$

$$Cl_{ren} = \frac{\text{rate of excretion}}{\text{plasma concentration}}$$

$$Cl_{ren} = fu \cdot \text{GFR} + \left[\frac{\text{Rate of secretion} - \text{Rate of reabsorption}}{\text{Plasma concentration}} \right]$$

$$Cl_{ren} = \frac{\text{Urine flow} \cdot \text{urine concentration}}{\text{Plasma concentration}}$$

Ideal Body Weight

Male

IBW = 50 kg + 2.3 kg for each inch over 5ft in height

Female

IBW = 45.5 kg + 2.3 kg for each inch over 5ft in height

Obese

ABW = IBW + 0.4*(TBW-IBW)

Volume of Distribution

$$V = V_p + V_T \cdot K_p$$

$$V = V_p + V_T \cdot \frac{fu}{fu_T}$$

Clearance

$$Cl = \frac{\text{Dose}}{\text{AUC}}$$

$$Cl = k_e \cdot V_d$$

For One Compartment Body Model

<p>If the dosing involves the use of I.V. bolus administration:</p>	<p>For a single I.V. bolus administration:</p> $C_0 = \frac{D}{V}$ $C = C_0 \cdot e^{-k_e t}$	<p>For multiple I.V. bolus administration:</p> $Cn(t) = \frac{D}{V} \cdot \frac{(1 - e^{-nk_e \tau})}{(1 - e^{-k_e \tau})} \cdot e^{-k_e t}$ <p>at peak: $t = 0$; at steady state $n \rightarrow \infty$</p> <p>at trough: $t = \tau$</p> $C_{\max ss} = \frac{D}{V} \cdot \frac{1}{(1 - e^{-k_e \tau})}$ $C_{\min ss} = C_{\max ss} \cdot e^{-k_e \tau}$
<p>If the dosing involves the use of I.V. infusion:</p>	<p>For a single short-term I.V. infusion:</p> <p>Since $\tau = t$ for C_{\max}</p> $C_{\max} = \frac{D}{Vk_e T} \cdot (1 - e^{-k_e T})$ $C_{\min} = C_{\max} \cdot e^{-k_e (\tau - T)}$	<p>For multiple short-term I.V. infusion at steady state:</p> $C_{\max} = \frac{D}{Vk_e T} \cdot \frac{(1 - e^{-k_e T})}{(1 - e^{-k_e \tau})}$ $C_{\min} = C_{\max} \cdot e^{-k_e (\tau - T)}$
<p>If the dosing involves a I.V. infusion (more equations):</p>	$C_t = \frac{D}{Vk_e T} \cdot (e^{k_e T} - 1) \cdot e^{-k_e t}$ (most general eq.) during infusion $t = T$ so, $C_t = \frac{D}{Vk_e T} \cdot (1 - e^{-k_e t})$ (during infusion) $C_{pss} = \frac{D}{Vk_e T} = \frac{k_0}{Vk_e} = \frac{k_0}{CL}$ (steady state)	<p>at steady state $t \rightarrow \infty$, $e^{-k_e t}$, $t \rightarrow 0$ so, remembering $k_0 = \frac{D}{T}$ and $CL = V \cdot k_e$</p>
<p>If the dosing involves oral administration:</p>	<p>For a single oral dose:</p> $C = \frac{F \cdot D \cdot k_a}{V(k_a - k_e)} \cdot (e^{-k_e t} - e^{-k_a t})$ $t_{\max} = \ln \left[\frac{k_a}{k_e} \right] \cdot \frac{1}{(k_a - k_e)}$	<p>For multiple oral doses:</p> $C = \frac{F \cdot D \cdot k_a}{V(k_a - k_e)} \cdot \left[\frac{e^{-k_e t}}{(1 - e^{-k_e \tau})} - \frac{e^{-k_a t}}{(1 - e^{-k_a \tau})} \right]$ $t_{\max} = \ln \left[\frac{k_a \cdot (1 - e^{-k_e \tau})}{k_e \cdot (1 - e^{-k_a \tau})} \right] \cdot \frac{1}{(k_a - k_e)}$