CLINICAL PHARMACOKINETIC EQUATIONS AND CALCULATIONS

1- Intravenous Bolus Equation

$$C = (D/V)e^{-k_e t}$$

t =is the time after the intravenous bolus was given

C =is the concentration at time = t

V= is the volume of distribution

Ke= is the elimination rate constant

t1/2 = 0.693/ke

C_0= concentration at time = 0

$k_e = -(\ln C_1 - \ln C_2)/(t_1 - t_2)$

$V = D/C_0$

$C_0 = C/e^{-Ket}$

C_0= concentration at time = 0

2-Continuous and Intermittent Intravenous Infusion Equations

$C = (k_0/Cl)(1 - e^{-ket}) = [k_0/(keV)](1 - e^{-ket})$

k_0= the drug infusion rate (in amount per unit time, such as mg/h or µg/min).
Cl =is the drug clearance.

[Since Cl = keV, this substitution was made in the second version of the equation]
ke =is the eliminationrate constant
t =is the time that the infusion has been running.

*If the infusion is allowed to continue until steady state is achieved, the steady-state concentration (Css) can be calculated easily:
Css = k0 / Cl = k0/ (keV).

*If the infusion is stopped, post infusion serum concentrations (Cpostinfusion) can be computed

$C_{postinfusion} = C_{end}\, e^{-ke\, t}{}_{postinfusion}$

$ke = -(\ln C1 - \ln C2)/(t1 - t2)$
Where t1 and C1 are the first time/concentration pair and t2 and C2 are the second time/concentration pair;

$$V = \frac{k_0(1 - e^{-k_e t'})}{k_e[C_{max} - (C_{predose} e^{-k_e t'})]}$$

- where k0 is the infusion rate
- ke is the elimination rate constant
- t' = infusion time
- Cmax is the maximum concentration at the end of infusion
- Cpredose is the predose concentration.

3- Extravascular Equation

$C = \{(Fk_aD) / [V(k_a - k_e)]\}(e^{-ket} - e^{-kat})$

Where t is the time after the extravascular dose was given (t = 0 at the time the dose was administered)
C =is the concentration at time = t
F =is the bioavailability fraction

k_a =is the absorption rate constant

D =is the dose

V= is the volume of distribution

k_e= is the elimination rate constant.

* When only postabsorption, postdistribution serum concentrations are obtained for a drug that is administered extravascularly, the equation simplifies to:

$$C = [(FD)/V]e^{-k_e t}$$

Where C is the concentration at any postabsorption, postdistribution time
F =is the bioavailability fraction
D= is the dose
V= is the volume of distribution
Ke= is the elimination rate constant
t= is any postabsorption, postdistribution time.

$$k_e = -(\ln C_1 - \ln C_2)/(t_1 - t_2),$$
$$t_{1/2} = 0.693/k_e$$
$$C_0 = C/e^{-k_e t},$$
$$V/F = D/C_0$$

Where (V/F) volume of distribution/bioavailability constant

4- Multiple-Dose and Steady-State Equations

In order to change a single dose equation to the multiple dose versions, it is necessary to multiply each exponential term in the equation by the multiple dosing factors:

$(1 - e^{-nki\tau})/(1 - e^{-ki\tau})$
Where n is the number of doses administered
ki =is the rate constant found in the exponential of the single dose equation
τ =is the dosage interval.

$C = (D/V)[e^{-ket} / (1 - e^{-ke\tau})]$
Where C is the steady state concentration at any postdose time (t) after the dose (D) is given
V =is the volume of distribution
Ke= is the elimination rate constant
τ =is the dosage interval.

TABLE 2-1 Single-Dose, Multiple-Dose, and Steady-State One-Compartment Model Equations

ROUTE OF ADMINISTRATION	SINGLE DOSE	MULTIPLE DOSE	STEADY STATE
Intravenous bolus	$C = (D/V)e^{-k_e t}$	$C = (D/V)e^{-k_e t}[(1 - e^{-nk_e\tau})/(1 - e^{-k_e\tau})]$	$C = (D/V)[e^{-k_e t}/(1 - e^{-k_e\tau})]$
Continuous intravenous infusion	$C = [k_0/(k_e V)](1 - e^{-k_e t})$	N/A	$Css = k_0/Cl = k_0/(k_e V)$
Intermittent intravenous infusion	$C = [k_0/(k_e V)](1 - e^{-k_e t'})$	$C = [k_0/(k_e V)](1 - e^{-k_e t'})[(1 - e^{-nk_e\tau})/(1 - e^{-k_e\tau})]$	$C = [k_0/(k_e V)][(1 - e^{-k_e t'})/(1 - e^{-k_e\tau})]$
Extravascular (postabsorption, postdistribution)	$C = [(FD)/V]e^{-k_e t}$	$C = [(FD)/V]e^{-k_e t}[(1 - e^{-nk_e\tau})/(1 - e^{-k_e\tau})]$	$C = (FD/V)[e^{-k_e t}/(1 - e^{-k_e\tau})]$
Average steady-state concentration (any route of administration)	N/A	N/A	$Css = [F(D/\tau)]/Cl$

Symbol key: C is drug serum concentration at time = t, D is dose, V is volume of distribution, k_e is the elimination rate constant, n is the number of administered doses, τ is the dosage interval, k_0 is the infusion rate, Cl is clearance, t′ is infusion time, N/A is not applicable.

TABLE 2-2 Single-Dose, Multiple-Dose, and Steady-State Pharmacokinetic Constant Computations Utilizing a One Compartment Model

ROUTE OF ADMINISTRATION	SINGLE DOSE	MULTIPLE DOSE	STEADY STATE
Intravenous bolus	$k_e = -(\ln C_1 - \ln C_2)/(t_1 - t_2)$ $t_{1/2} = 0.693/k_e$ $V = D/C_0$ $Cl = k_e V$	$k_e = -(\ln C_1 - \ln C_2)/(t_1 - t_2)$ $t_{1/2} = 0.693/k_e$ $V = D/(C_0 - C_{predose})$ $Cl = k_e V$	$k_e = -(\ln C_1 - \ln C_2)/(t_1 - t_2)$ $t_{1/2} = 0.693/k_e$ $V = D/(C_0 - C_{predose})$ $Cl = k_e V$
Continuous intravenous infusion	N/A	N/A	$Cl = k_0/Css$
Intermittent intravenous infusion	$k_e = -(\ln C_1 - \ln C_2)/(t_1 - t_2)$ $t_{1/2} = 0.693/k_e$ $V = [k_0(1 - e^{-k_e t'})]/\{k_e[C_{max} - (C_{predose}e^{-k_e t'})]\}$ $Cl = k_e V$	$k_e = -(\ln C_1 - \ln C_2)/(t_1 - t_2)$ $t_{1/2} = 0.693/k_e$ $V = [k_0(1 - e^{-k_e t'})]/\{k_e[C_{max} - (C_{predose}e^{-k_e t'})]\}$ $Cl = k_e V$	$k_e = -(\ln C_1 - \ln C_2)/(t_1 - t_2)$ $t_{1/2} = 0.693/k_e$ $V = [k_0(1 - e^{-k_e t'})]/\{k_e[C_{max} - (C_{predose}e^{-k_e t'})]\}$ $Cl = k_e V$
Extravascular (postabsorption, postdistribution)	$k_e = -(\ln C_1 - \ln C_2)/(t_1 - t_2)$ $t_{1/2} = 0.693/k_e$ $V/F = D/C_0$ $Cl/F = k_e(V/F)$	$k_e = -(\ln C_1 - \ln C_2)/(t_1 - t_2)$ $t_{1/2} = 0.693/k_e$ $V/F = D/(C_0 - C_{predose})$ $Cl/F = k_e(V/F)$	$k_e = -(\ln C_1 - \ln C_2)/(t_1 - t_2)$ $t_{1/2} = 0.693/k_e$ $V/F = D/(C_0 - C_{predose})$ $Cl/F = k_e(V/F)$
Average steady-state concentration (any route of administration)	N/A	N/A	$Cl/F = (D/\tau)/Css$

Symbol key: C_1 is drug serum concentration at time = t_1, C_2 is drug serum concentration at time = t_2, k_e is the elimination rate constant, $t_{1/2}$ is the half-life, V is the volume of distribution, k_0 is the continuous infusion rate, t′ is the infusion time, V/F is the hybrid constant volume of distribution/bioavailability fraction, D is dose, C_0 is the concentration at time = 0, Cl is drug clearance, Cl/F is the hybrid constant clearance/bioavailability fraction, $C_{predose}$ is the predose concentration, Css is the steady-state concentration, N/A is not applicable.

5- Average Steady-State Concentration Equation

$Css = [F(D/\tau)]/Cl$

Where F is the bioavailability fraction
D =is the dose
τ =is the dosage interval
Cl= is the drug clearance

$Cl/F = (D/\tau)/Css$
Where D is dose and τ is the dosage interval

6- DESIGNING INDIVIDUALIZED DOSAGE REGIMENS USING ONE COMPARTMENT MODEL EQUATIONS

TABLE 2-3 Equations to Compute Individualized Dosage Regimens for Various Routes of Administration

ROUTE OF ADMINISTRATION	DOSAGE INTERVAL (τ), MAINTENANCE DOSE (D OR k_0), AND LOADING DOSE (LD) EQUATIONS
Intravenous bolus	$\tau = (\ln Css_{max} - \ln Css_{min})/k_e$ $D = Css_{max}\, V(1 - e^{-k_e\tau})$ $LD = Css_{max}\, V$
Continuous intravenous infusion	$k_0 = Css\ Cl = Css\ k_e V$ $LD = CssV$
Intermittent intravenous infusion	$\tau = [(\ln Css_{max} - \ln Css_{min})/k_e] + t'$ $k_0 = Css_{max} k_e V[(1 - e^{-k_e\tau})/(1 - e^{-k_e t'})]$ $LD = k_0/(1 - e^{-k_e\tau})$
Extravascular (postabsorption, postdistribution)	$\tau = [(\ln Css_{max} - \ln Css_{min})/k_e] + T_{max}$ $D = [(Css_{max} V)/F][(1 - e^{-k_e\tau})/e^{-k_e T_{max}}]$ $LD = (Css_{max} V)/F$
Average steady-state concentration (any route of administration)	$D = (Css\ Cl\ \tau)/F = (Css\ k_e V\tau)/F$ $LD = (CssV)/F$

Symbol key: Css_{max} and Css_{min} are the maximum and minimum steady-state concentrations, k_e is the elimination rate constant, V is the volume of distribution, Css is the steady-state concentration, k_0 is the continuous infusion rate, t' is the infusion time, T_{max} is the time that Css_{max} occurs, F is the bioavailability fraction.

7- MULTICOMPARTMENT MODELS

The equation that describes a two compartment model after an intravenous bolus is:

$[V1(\alpha - \beta)]\}e^{-\alpha t} + \{[D(k21 - \beta)] / [V1(\alpha - \beta)]\}e^{-\beta t}$

Where C is the drug serum concentration,
D is the intravenous bolus dose
k21 is the rate constant that describes the transfer of drug from compartment 2 to compartment 1
α is the distribution rate constant
β is the elimination rate constant
V1 is the volume of distribution for compartment 1
t is the time after the dose was administered.

8-MICHAELIS-MENTEN EQUATIONS FOR SATURABLE PHARMACOKINETICS

D = (Vmax . Css) / (Km + Css)
Where D is the dose
C=ss is the steady-state drug concentration
V=max is the maximum rate of drug metabolism
Km= is the concentration where the rate of metabolism equals Vmax/2.
D = Vmax − [Km(D/Css)]

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