Non-Compartmental Pharmaco-kinetics

Sym: Non-compt. Analysis, Model-Independent-method. i.e.,

→ It does not require the assumption of specific compt. model.

Assumption: Based on the assumption that the drugs or metabolites follow linear-kinetics, and on this basis, this technique can be applied to any compartment model.

⇒ The non-compartmental approach, based on the 'Statistical-moment theory':

→ Theory Involves collection of experimental data following a single dose of drug.

→ Theory provides a unique way to study time-related changes in macroscopic events. A macroscopic event is considered as the overall event brought about by the constitutive elements involved.

→ Time course of drug concentration in plasma as a statistical distribution curve, then (Drug conc $\xrightarrow{\text{Time}}$ plasma)

$$MRT = \frac{AUMC}{AUC}$$

MRT → mean residence time

AUMC → area under first-moment curve

AUC → " " Zero " "

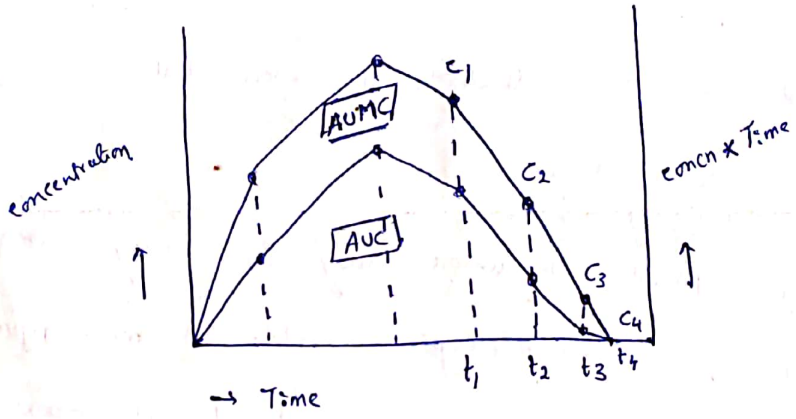
→ AUMC is obtained by from a plot of product of plasma drug concentration and time (i.e. C.t) versus time t from zero to infinity.

$$AUMC = \int_0^\infty Ct \cdot dt.$$

→ AUC is obtained from a plot of plasma drug concentration versus time from zero to infinity,

$$AUC = \int_0^\infty C \cdot dt.$$

→ AUMC & AUC can be calculated by the Trapezoidal rule.



∴ Trapezoidal rule, $AUC = \frac{(t_2 - t_1)(C_1 + C_2)}{2}$

MRT :- MRT is defined as the average amount of time spent by the drug in the body before being eliminated.

→ It is the statistical moment analogy of half-life ($t_{1/2}$).

App :-

Non-compt Analysis :

1) used to estimate the important pharmacokinetic parameters like bio availability, clearance and apparent volume of distribution.

2) Determination of $t_{1/2}$, rate of absorption (~~K~~, first order absorption rate constant of the drug.

Adv:-

1. Ease of derivation of pharmacokinetic parameters by simple algebraic Equations.
2. The same mathematical treatment can be applied to almost any drug or metabolite provided they follow 1st-order kinetics.
3. A detailed description of drug disposition characteristics is not required.

Dis. Adv:-

1) Provides limited information regarding the plasma drug conc. time profile (death & Averaging)
2) This method does not adequately treat non-linear cases.

⇒ MRT For various compartmental models:

$$MRT_{(\text{for any route of Admn})} = \frac{AUMC}{AUC}$$

i) $$MRT_{I.V} = \frac{1}{Kd}$$

$$= \frac{1}{\lambda}$$ $\lambda \rightarrow$ Elimination rate const.

$$t_{1/2} = 0.693 \times MRT_{I.V.}$$

MRT = time for 63.2% of I.V. dose to be eliminated.

= time required for concentration to fall to $\frac{1}{e}$ of original.

(i.e. 36.8% remaining).

→ $MRT_{oral} > MRT_{I.V}$

(or)

$MRT_{Non\text{-}I.V.\ Admn} > MRT_{I.V.\ Admn.}$

ii) I.V. infusion:

$$MRT_{inf} = MRT_{I.V} + \frac{\tau}{2}.$$

iii) Oral dose:

$$MRT_{oral} = MRT_{I.V} + \frac{1}{Ka}$$

$$= MRT_{I.V} + MAT$$

$$= \frac{1}{\lambda} + \frac{1}{Ka}.$$

∵ MAT = mean Absorption time

$$MAT = \frac{1}{Ka}.$$

∴

$$MRT_{oral} = MRT_{I.V} + MAT$$

$$MAT = MRT_{oral} - MRT_{I.V.}$$

$MRT_{oral\ (or)\ Nm\ I.V}$ = nm Intravenous mean residence time.

$$t_{1/2\ abs} = 0.693 \times MAT.$$

→ Apparent volume of distribution at steady-state:

i) For I.V. bolus:

$$MRT = \frac{V_{ss}}{Cl.}$$

$$V_{ss} = Cl. \cdot MRT$$

$$Cl = \frac{D_{I.V}}{AUC}$$

$$V_{ss} = \frac{D_{I.V}}{AUC} \cdot \frac{AUMC}{AUC}$$

$$V_{ss} = \frac{D_{I.V.} \cdot AUMC}{(AUC)^2}$$

ii) For I.V. Infusion

$$V_{ss} = \frac{R_0 \cdot \tau \cdot AUMC}{(AUC)^2} - \frac{R_0 \cdot \tau^2}{2\,AUC}$$

$$= \frac{(\text{Infused dose})\, AUMC}{(AUC)^2} - \frac{(\text{infused dose})\,\tau}{2\,AUC}$$

$R_0 \cdot \tau$ = (infused dose) ; τ = infusion time.

iii) For oral:

$$V_{ss} = \frac{F.D. AUMC}{(AUC)^2} - \frac{F.D}{Ka. AUC}$$

iv) I.V. bolus + I.V. Infusion:

$$V_{ss} = \frac{(R_0 \cdot \tau + D_{I.V}) AUMC}{(AUC)^2} - \frac{R_0 \cdot \tau^2}{2\,AUC.}$$