Name of Unit	Pharmacokinetics
Course/Subject Name	Biopharmaceutics and Pharmacokinetics
Course/Subject Code	BP604T
Class: B. Pharm. Semester	6th
Faculty:	Gurminder Kaur
Email id	gurminderbanwait91@gmail.com
Mobile No.	6283849096

Learning Outcome of Unit-3

LO	Learning Outcome(LO)	Course Outcome
LO1	Students will learn about the various aspects of compartment and non- compartment modeling.	BP604.4
LO2	Students will learn about the calculation and significance of different pharmacokinetic parameters.	BP604.4

CONTENT OF MODULE

Topic
Pharmacokinetics Definition and introduction to Pharmacokinetics. Compartment models. Non compartment models , Physiological models. One compartment open model, Intravenous Injection (Bolus) Intravenous infusion, Extra vascular administrations **Pharmacokinetic Parameters** KE t1/2 Vd AUC Ka, Clt and CLR- definitions methods of eliminations understanding of their significance and application

PHARMACOKINETICS

Definition and introduction to Pharmacokinetics:

Dosage regimen: The frequency of administration of a drug in a particular dose is called as dosage regimen.

Therapeutic window: The therapeutic and the toxic effects, depend upon the concentration of drug at the site of action which is difficult to measure. However, it corresponds to a specific concentration of drug in plasma which can be measured with accuracy. The drug fails to elicit a therapeutic response when the concentration is below the effective level and precipitates adverse reactions when above the toxic level. The plasma drug concentration between these two limits is called as the therapeutic concentration range or therapeutic window (the ratio of maximum safe concentration to minimum effective concentration of the drug is called as the therapeutic index).

Pharmacokinetics: Pharmacokinetics is defined as the kinetics of drug absorption, distribution, metabolism and excretion (KADME) and their relationship with the pharmacological, therapeutic or toxicological response in man and animals.

Plasma Drug Concentration-Time Profile: A direct relationship exists between the concentration of drug at the biophase (site of action) and the concentration of drug in plasma. Two categories of parameters can be evaluated from a plasma concentration time profile –

1. Pharmacokinetic parameters, and
2. Pharmacodynamic parameters.

A typical plasma drug concentration-time curve obtained after a single oral dose of a drug and showing various pharmacokinetic and pharmacodynamic parameters is depicted in Fig. given below. Such a profile can be obtained by measuring the concentration of drug in plasma samples taken at various intervals of time after administration of a dosage form and plotting the concentration of drug in plasma (*Y*-axis) versus the corresponding time at which the plasma sample was collected (*X*-axis).

Pharmacokinetic Parameters

The three important **pharmacokinetic parameters** that describe the plasma level-time curve and useful in assessing the bioavailability of a drug from its formulation are –

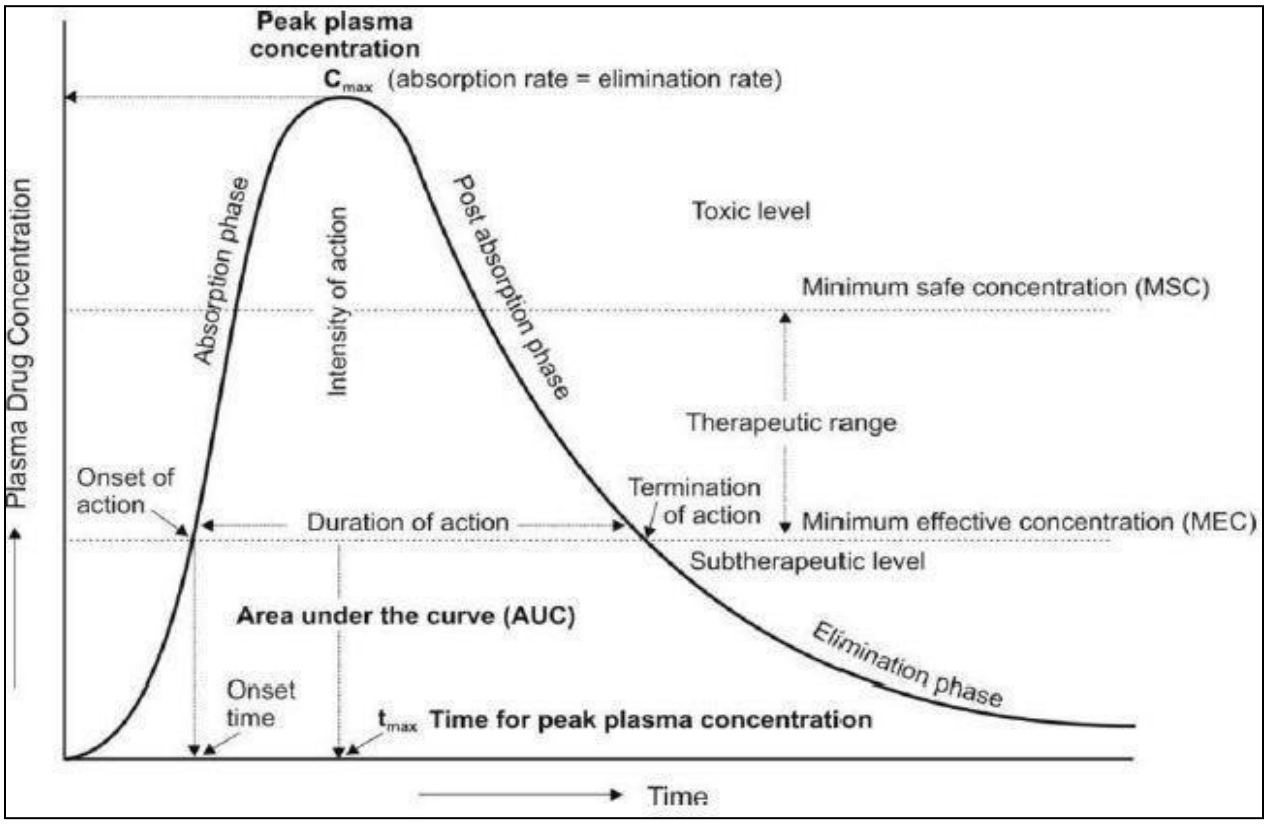


Fig. *A typical plasma concentration-time profile showing pharmacokinetic and pharmacodynamic parameters, obtained after oral administration of single dose of a drug.*

1. Peak Plasma Concentration (Cmax)

The point of maximum concentration of drug in plasma is called as the **peak** and the concentration of drug at peak is known as ***peak plasma concentration***. It is also called as ***peak height concentration*** *and* ***maximum drug concentration***. Cmax is expressed in mcg/ml. The peak plasma level depends upon –

(a)The administered dose

(b)Rate of absorption, and

(c)Rate of elimination.

The peak represents the point of time when absorption rate equals elimination rate of drug. The portion of curve to the left of peak represents **absorption phase** i.e. when the rate of absorption is greater than the rate of elimination. The section of curve to the right of peak generally represents **elimination phase** i.e. when the rate of elimination exceeds rate of absorption. Peak

concentration is often related to the intensity of pharmacological response and should ideally be above minimum effective concentration (MEC) but less than the maximum safe concentration (MSC).

2. **Time of Peak Concentration (tmax)**

The time for drug to reach peak concentration in plasma (after extravascular administration) is called as the **time of peak concentration**. It is expressed in hours and is useful in estimating the rate of absorption. Onset time and onset of action are dependent upon tmax. This parameter is of particular importance in assessing the efficacy of drugs used to treat acute conditions like pain and insomnia which can be treated by a single dose.

3. Area Under the Curve (AUC)

It represents the total integrated area under the plasma level-time profile and expresses the total amount of drug that comes into the systemic circulation after its administration. AUC is expressed in mcg/ml X hours. It is the most important parameter in evaluating the bioavailability of a drug from its dosage form as it represents the extent of absorption. AUC is also important for drugs that are administered repetitively for the treatment of chronic conditions like asthma or epilepsy.

Pharmacodynamic Parameters

The various pharmacodynamic parameters are –

Minimum Effective Concentration (MEC)

It is defined as the minimum concentration of drug in plasma required to produce the therapeutic effect. It reflects the minimum concentration of drug at the receptor site to elicit the desired pharmacological response. The concentration of drug below MEC is said to be in the **sub-therapeutic level**.

In case of antibiotics, the term **minimum inhibitory concentration** (MIC) is used. It describes the minimum concentration of antibiotic in plasma required to kill or inhibit the growth of microorganisms.

Maximum Safe Concentration (MSC): Also called as **minimum toxic concentration (MTC)**, it is the concentration of drug in plasma above which adverse or unwanted effects are precipitated. Concentration of drug above MSC is said to be in the **toxic level**.

Onset of Action

The beginning of pharmacological response is called as **onset of action**. It occurs when the plasma drug concentration just exceeds the required MEC.

Onset Time

It is the time required for the drug to start producing pharmacological response. It corresponds to the time for the plasma concentration to reach MEC after administration of drug.

Duration of Action

The time period for which the plasma concentration of drug remains above the MEC level is called as **duration of drug action**. It is also defined as the difference between onset time and time for the drug to decline back to MEC.

Intensity of Action

It is the maximum pharmacological response produced by the peak plasma concentration of drug. It is also called as **peak response**.

Therapeutic Range

The drug concentration between MEC and MSC represents the **therapeutic range**. It is also known as **therapeutic window**.

Therapeutic Index

The ratio of MSC to MEC is called as **therapeutic index**. It is also defined as the ratio of dose required to produce toxic or lethal effects to dose required to produce therapeutic effect.

COMPARTMENT MODELS:

Model: Model is a hypothesis using mathematical terms to describe quantitative relationships concisely.

The key parameters in a process are commonly estimated by fitting the model to the experimental data, known as *variables*. A *pharmacokinetic parameter* is a constant for the drug that is estimated from the experimental data. For example, estimated pharmacokinetic parameters such as *k* depend on the method of tissue sampling, the timing of the sample, drug analysis, and the predictive model selected.

Such mathematical models can be devised to simulate the rate processes of drug absorption, distribution, and elimination to describe and *predict* drug concentrations in the body as a function of time. Pharmacokinetic models are used to:

2. Predict plasma, tissue, and urine drug levels with any dosage regimen.

3. Calculate the optimum dosage regimen for each patient individually.
4. Estimate the possible accumulation of drugs and/or metabolites.
5. Correlate drug concentrations with pharmacologic or toxicologic activity.
6. Evaluate differences in the rate or extent of availability between formulations (bioequivalence).
7. Describe how changes in physiology or disease affect the absorption, distribution, or elimina- tion of the drug.
8. Explain drug interactions.

A very simple and useful tool in pharmacokinetics is *compartmentally based models*. For example, assume a drug is given by intravenous injection and that the drug dissolves (distributes) rapidly in the body fluids. One pharmacokinetic model that can describe this situation is a tank containing a volume of fluid that is rapidly equilibrated with the drug. The concentration of the drug in the tank after a given dose is governed by two parameters:

(1) The fluid volume of the tank that will dilute the drug, and

(2) The elimination rate of drug per unit of time.

Though this model is perhaps an overly simplistic view of drug disposition in the human body, a drug's pharmacokinetic properties can frequently be described using a fluid-filled tank model called the *one-compartment open model* . In both the tank and the one-compartment body model, a fraction of the drug would be continually eliminated as a function of time. In pharmacokinetics, these parameters are assumed to be constant for a given drug. If drug concentrations in the tank are determined at various time intervals following administration of a known dose, then the volume of fluid in the tank or compartment (Vd, volume of distribution) and the rate of drug elimination can be estimated.

Because a model is based on a hypothesis and simplifying assumptions, a certain degree of caution is necessary when relying totally on the pharmacokinetic model to predict drug action. For some drugs, plasma drug concentrations are not useful in predicting drug activity. For other drugs, an individual's genetic differences, disease state, and the compensatory response of the body may modify the response to the drug. If a simple model does not fit all the experimental observations accurately, a new, more elaborate model may be proposed and subsequently tested.

Depending upon whether the compartments are arranged parallel or in a series, compartment models are divided into two categories —

(a)Mammillary model (b)Catenary model.

Mammillary Model

This model is the most common compartment model used in pharmacokinetics. It consists of one or more peripheral compartments connected to the central compartment in a manner similar to connection of satellites to a planet (i.e. they are joined parallel to the central compartment). The **central compartment** (or **compartment 1**) comprises of plasma and highly perfused tissues such as lungs, liver, kidneys, etc. which rapidly equilibrate with the drug. The drug is directly absorbed into this compartment (i.e. blood). Elimination too occurs from this compartment since the chief organs involved in drug elimination are liver and kidneys, the highly perfused tissues and therefore presumed to be rapidly accessible to drug in the systemic circulation. The **peripheral compartments** or **tissue compartments** are those with low vascularity and poor perfusion.

Catenary Model

In pharmacokinetics, the mammillary model must be distinguished from another type of compartmental model called the catenary model. The catenary model consists of compartments joined to one another like the compartments of a train. In contrast, the mammillary model consists of one or more compartments around a central compartment like satellites. Because the catenary model does not apply to the way most functional organs in the body are directly connected to the plasma, it is not used as often as the mammillary model.

Physiologic Pharmacokinetic Model (Flow Model)

Physiologic pharmacokinetic models, also known as blood flow or perfusion models, are pharmacokinetic models based on known anatomic and physiologic data. The models describe the data kinetically, with the consideration that blood flow is responsible for distributing drug to various parts of the body. Uptake of drug into organs is determined by the binding of drug in these tissues. In contrast to an estimated tissue volume of distribution, the actual tissue volume is used. Because there are many tissue organs in the body, each tissue volume must be obtained and its drug concentration described. The model would potentially predict realistic tissue drug concentrations, which the two-compartment model fails to do. Unfortunately, much of the information required for adequately describing a physiologic pharmacokinetic model is

experimentally difficult to obtain. In spite of this limitation, the physiologic pharmacokinetic model does provide much better insight into how physiologic factors may change drug distribution from one animal species to another.

NON COMPARTMENTAL ANALYSIS:

The **non compartmental analysis**, also called as the **model-independent method**, does not require the assumption of specific compartment model. This method is, however, 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 moments theory**, involves collection of experimental data following a single dose of drug. If one considers the time course of drug concentration in plasma as a statistical distribution curve, then:

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

Where MRT = mean residence time

AUMC = area under the first-moment curve AUC = area under the zero-moment curve

AUMC is obtained from a plot of product of plasma drug concentration and time (i.e. C.t) versus time t from zero to infinity . Mathematically, it is expressed by equation:

$$AUMC = \int_0^\infty C\,t\,dt$$

AUC is obtained from a plot of plasma drug concentration versus time from zero to infinity. Mathematically, it is expressed by equation:

$$AUC = \int_0^\infty C\,dt$$

Practically, the AUMC and AUC can be calculated from the respective graphs by the **trapezoidal rule** (the method involves dividing the curve by a series of vertical lines into a

number of trapezoids, calculating separately the area of each trapezoid and adding them together

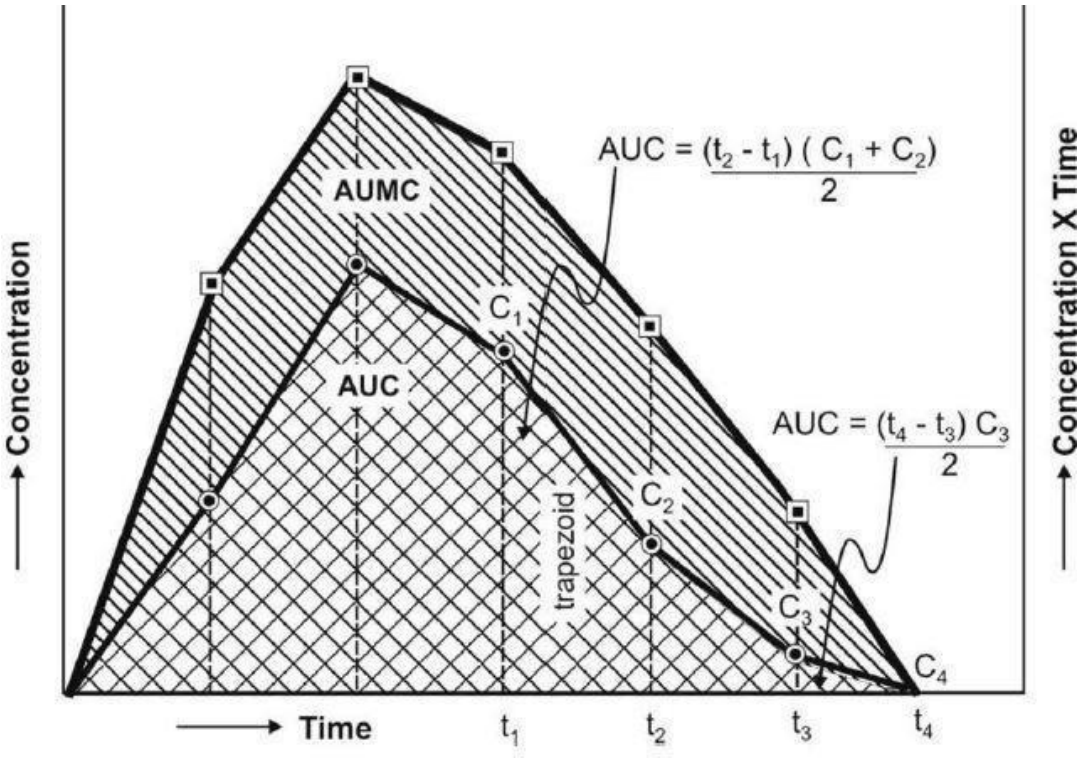


Fig. AUC and AUMC plots

MRT (mean residence time) is defined as the average amount of time spent by the drug in the body before being eliminated. In this sense, it is the statistical moment analogy of half-life, t½. In effect, MRT represents the time for 63.2% of the intravenous bolus dose to be eliminated. The values will always be greater when the drug is administered in a fashion other than i.v. bolus.

Applications of noncompartmental technique includes –

1. It is widely used to estimate the important pharmacokinetic parameters like bioavailability, clearance and apparent volume of distribution.
2. The method is also useful in determining half-life, rate of absorption and first-order absorption rate constant of the drug.

Advantages of noncompartmental method include —

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 first-order kinetics.
3. A detailed description of drug disposition characteristics is not required.

Disadvantages of this method include –

1. It provides limited information regarding the plasma drug concentration-time profile. More often, it deals with averages.
2. The method does not adequately treat non-linear cases.

ONE-COMPARTMENT OPEN MODEL:

The one-compartment open model is the simplest model. Owing to its simplicity, it is based on following assumptions –

1. The body is considered as a single, kinetically homogeneous unit that has no barriers to the movement of drug.
2. Final distribution equilibrium between the drug in plasma and other body fluids (i.e. mixing) is attained instantaneously and maintained at all times. This model thus applies only to those drugs that distribute rapidly throughout the body.
3. Drugs move dynamically, in (absorption) and out (elimination) of this compartment.
4. Elimination is a first-order (monoexponential) process with first-order rate constant.
5. Rate of input (absorption) > rate of output (elimination).
6. The anatomical **reference compartment** is plasma and concentration of drug in plasma is representative of drug concentration in all body tissues i.e. any change in plasma drug concentration reflects a proportional change in drug concentration throughout the body.

However, the model does not assume that the drug concentration in plasma is equal to that in other body tissues. The term **open** indicates that the input (availability) and output (elimination) are unidirectional and that the drug can be eliminated from the body.

Depending upon the rate of input, several one-compartment open models can be defined:

- One-compartment open model, i.v. bolus administration.
- One-compartment open model, continuous i.v. infusion.
- One-compartment open model, e.v. administration, zero-order absorption.
- One-compartment open model, e.v. administration, first-order absorption.

One-compartment open model, i.v. bolus administration:

While the oral route of drug administration is the most convenient, intravenous (IV) administration is the most desirable for critical care when reaching desirable drug concentrations

quickly is needed. Examples of when IV administration is desirable include antibiotic administration during septic infections or administration of antiarrhythmic drugs during a myocardial infarction. Because pharmacokinetics is the science of the kinetics of drug absorption, distribution, and elimination, IV administration is desirable in understanding these processes since it simplifies drug absorption, essentially making it complete and instantaneous. When a drug that distributes rapidly in the body is given in the form of a rapid intravenous injection (i.e. i.v. bolus or slug), it takes about one to three minutes for complete circulation and therefore the rate of absorption is neglected in calculations. The model can be depicted as follows:

The general expression for **rate of drug presentation** to the body is:

$$\frac{dX}{dt} = \text{Rate in (availability)} - \text{Rate out (elimination)}$$

Since **rate in** or absorption is absent, the equation becomes:

$$\frac{dX}{dt} = -\text{Rate out}$$

If the **rate out** or elimination follows first-order kinetics, then:

$$\frac{dX}{dt} = -K_E X$$

where, KE = first-order elimination rate constant, and

X = amount of drug in the body at any time t remaining to be eliminated. Negative sign indicates that the drug is being lost from the body.

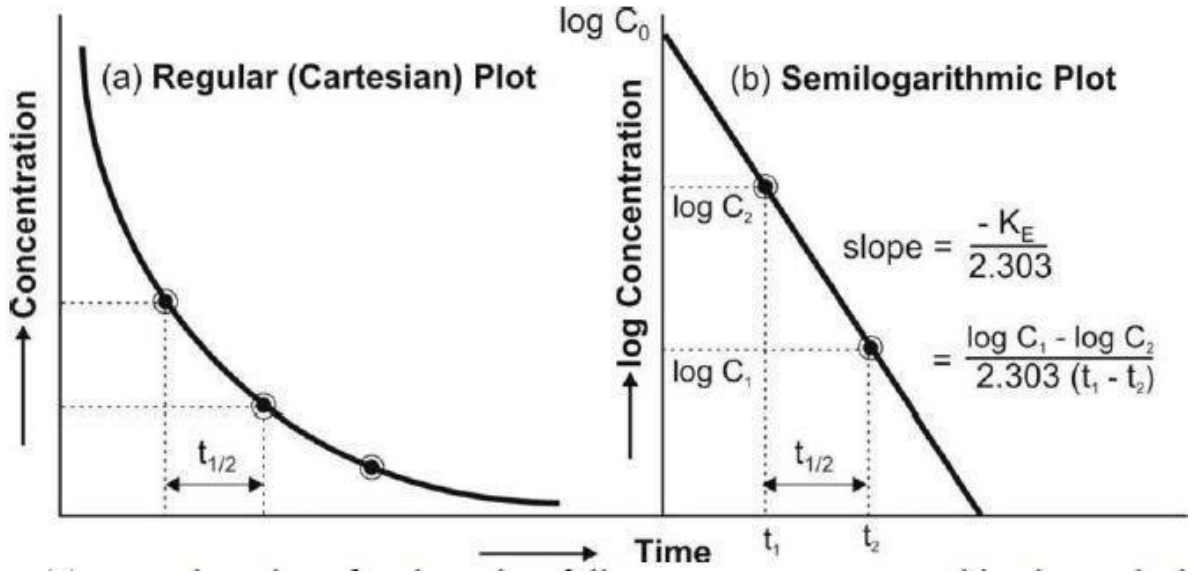


Fig. *(a) Cartesian plot of a drug that follows one-compartment kinetics and given by rapid i.v. injection, and (b) Semilogarithmic plot for the rate of elimination in a one-compartment model. Co, KE (and t½) can be readily obtained from log C versus t graph. The elimination or removal of the drug from the body is the sum of urinary excretion, metabolism, biliary excretion, pulmonary excretion, and other mechanisms involved therein. Thus, KE is an additive property of rate constants for each of these processes and better called as* ***overall elimination rate constant****.*

One-Compartment Open Model Intravenous Infusion:

Rapid i.v. injection is unsuitable when the drug has potential to precipitate toxicity or when maintenance of a stable concentration or amount of drug in the body is desired. In such a situation, the drug (for example, several antibiotics, theophylline, procainamide, etc.) is administered at a constant rate (zero-order) by i.v. infusion. In contrast to the short duration of infusion of an i.v. bolus (few seconds), the duration of constant rate infusion is usually much longer than the half-life of the drug.

Advantages of zero-order infusion of drugs include

1. Ease of control of rate of infusion to fit individual patient needs.
2. Prevents fluctuating maxima and minima (peak and valley) plasma level, desired especially when the drug has a narrow therapeutic index.

3. Other drugs, electrolytes and nutrients can be conveniently administered simultaneously by the same infusion line in critically ill patients.

The model can be represented as follows:

At any time during infusion, the rate of change in the amount of drug in the body, dX/dt is the difference between the zero-order rate of drug infusion Ro and first-order rate of elimination,

–KEX:

$$\frac{dX}{dt} = R_0 - K_E X$$

Integration and rearrangement of above equation yields:

$$X = \frac{R_0}{K_E}(1 - e^{-K_E t})$$

Since X = Vd C, the above equation can be transformed into concentration terms as follows:

$$C = \frac{R_0}{K_E V_d}(1 - e^{-K_E t}) = \frac{R_0}{Cl_T}(1 - e^{-K_E t})$$

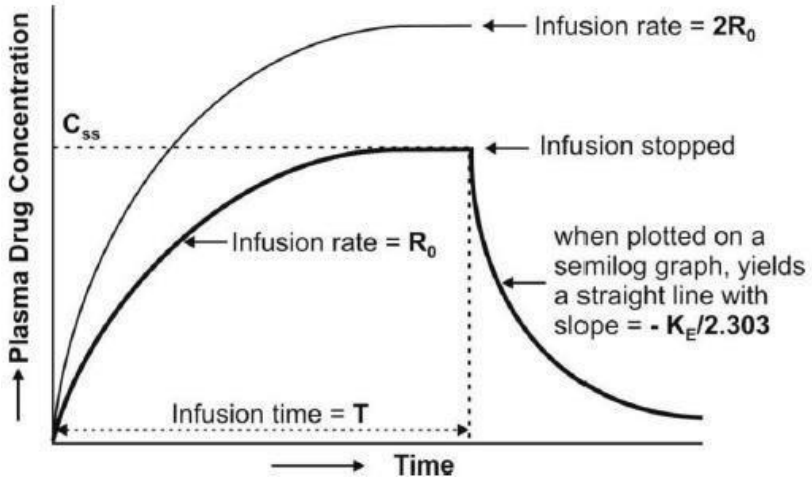


Fig. Plasma concentration-time profile for a drug given by constant rate i.v. infusion (the two curves indicate different infusion rates Ro and 2Ro for the same drug)

At the start of constant rate infusion, the amount of drug in the body is zero and hence, there is no elimination. As time passes, the amount of drug in the body rises gradually (elimination rate less than the rate of infusion) until a point after which the rate of elimination equals the rate of infusion i.e. the concentration of drug in plasma approaches a constant value called as **steady-state**, **plateau** or **infusion equilibrium.**

At steady-state, the rate of change of amount of drug in the body is zero, hence, the equation becomes:

$$\text{Zero} = R_0 - K_E X_{ss}$$

$$K_E X_{ss} = R_0$$

Transforming to concentration terms and rearranging the equation:

$$C_{ss} = \frac{R_0}{K_E V_d} = \frac{R_0}{Cl_T} \text{ i.e. } \frac{\text{Infusion rate}}{\text{Clearance}}$$

Where, Xss and Css are amount of drug in the body and concentration of drug in plasma at steady-state respectively. The value of KE (and hence t½) can be obtained from the slope of straight line obtained after a semilogarithmic plot (log C versus t) of the plasma concentration-time data gathered from the time when infusion is stopped. Alternatively,KE can be calculated from the data collected during infusion to steady-state as follows:

Substituting Ro/ClT = Css we get

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

Rearrangement yields:

$$\left[\frac{C_{ss} - C}{C_{ss}}\right] = e^{-K_E t}$$

Transforming into log form, the equation becomes:

$$\log\left[\frac{C_{ss} - C}{C_{ss}}\right] = \frac{-K_E t}{2.303}$$

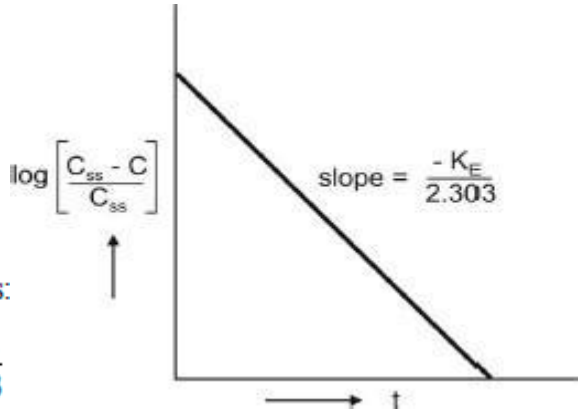


Fig. *Semilog plot to compute KE from infusion data upto steady-state*

One-Compartment Open Model Extravascular Administration(First Order):

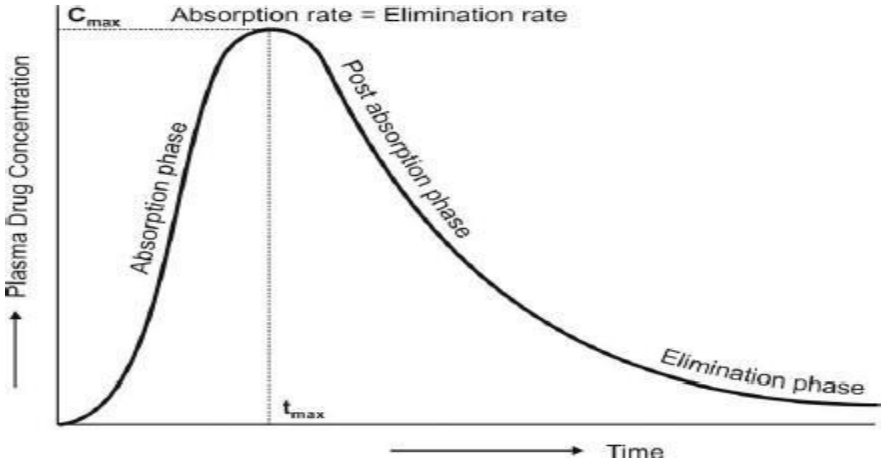
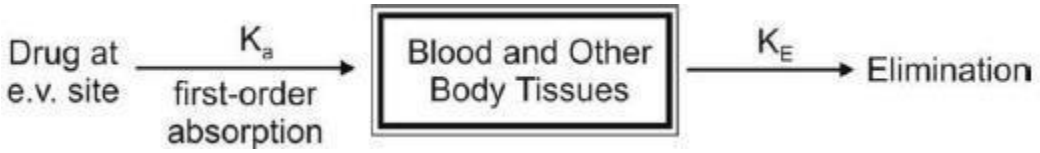


Fig. *The absorption and elimination phases of the plasma concentration-time profile obtained after extravascular administration of a single dose of a drug.*



The differential form of the equation is:

$$\frac{dX}{dt} = K_a X_a - K_E X$$

where, Ka = first-order absorption rate constant, and

Xa = amount of drug at the absorption site remaining to be absorbed i.e. ARA. Integration of equation yields:

$$X = \frac{K_a F X_0}{(K_a - K_E)} \left[e^{-K_E t} - e^{-K_a t} \right]$$

Transforming into concentration terms, the equation becomes

$$C = \frac{K_a F X_0}{V_d (K_a - K_E)} \left[e^{-K_E t} - e^{-K_a t} \right]$$

where F = fraction of drug absorbed systemically after e.v. administration.

Assessment of Pharmacokinetic Parameters

C max and t max: At peak plasma concentration, the rate of absorption equals rate of elimination i.e. KaXa =KEX and the rate of change in plasma drug concentration dC/dt = zero. This rate can be obtained by differentiating equation

$$\frac{dC}{dt} = \frac{K_a F X_0}{V_d (K_a - K_E)} \left[K_E e^{-K_E t} + K_a e^{-K_a t} \right] = \text{Zero}$$

On simplifying, the above equation becomes:

$$K_E\, e^{-K_E t} = K_a\, e^{-K_a t}$$

Converting to logarithmic form,

$$\log K_E - \frac{K_E t}{2.303} = \log K_a - \frac{K_a t}{2.303}$$

where t is t_{max}. Rearrangement of above equation yields:

$$t_{max} = \frac{2.303 \log (K_a / K_E)}{K_a - K_E}$$

URINARY EXCRETION DATA

(Disposition Viewed from Urine only)

In the absence of plasma level-time data, useful information can still be obtained from urine data regarding elimination kinetics of a drug. The method has several *advantages* in the analysis of a pharmacokinetic system:

1. The method is useful when there is lack of sufficiently sensitive analytical techniques to measure concentration of drugs in plasma with accuracy.
2. The method is non-invasive and therefore better subject compliance is assured.
3. The method is more convenient since it involves collection of urine samples in comparison to drawing of blood periodically.
4. A less sensitive analytical method is required for determining urine drug concentration as compared to plasma concentrations. If urine drug concentrations are low, assaying of larger sample volumes is relatively easy.
5. First-order elimination, excretion and absorption rate constants and fraction excreted unchanged can be computed from such data. First-order metabolism or extra-renal excretion rate constant can also be calculated subsequently from the difference (KE – Ke) = Km.

6. Direct measurement of bioavailability, both absolute and relative, is possible without the necessity of fitting the data to a mathematical model.

Criteria for Obtaining Valid Urinary Excretion Data

1. A significant amount of drug must be excreted unchanged in the urine (at least 10%).
2. The analytical method must be specific for the unchanged drug; metabolites should not interfere.
3. Water-loading should be done by taking 400 ml of water after fasting overnight, to promote diuresis and enable collection of sufficient urine samples.
4. Before administration of drug, the bladder must be emptied completely after 1 hour from water-loading and the urine sample taken as blank.
5. The drug should then be administered with 200 ml of water and should be followed by 200 ml given at hourly intervals for the next 4 hours.
6. Volunteers must be instructed to completely empty their bladder while collecting urine samples.
7. Frequent sampling should be done in order to obtain a good curve.
8. During sampling, the exact time and volume of urine excreted should be noted.
9. An individual collection period should not exceed one biological half-life of the drug and ideally should be considerably less.
10. Urine samples must be collected for at least 7 biological half-lives in order to ensure collection of more than 99% of excreted drug.
11. Changes in urine pH and urine volume may alter the urinary excretion rate.

IMPORTANT QUESTIONS

Very short answer question 2 Marks:

1. Define pharmacokinetics.
2. In compartment modelling why does excretion takes place from central compartment
3. What are the limitations of one compartment model
4. Define elimination rate constant?
5. Describe the influence of Ke on Cmax , Tmax and AUC.
6. Mention the methods for calculating of AUC.
7. Define biological half life.
8. Enumerate the applications of pharmacokinetics.
9. What is first order and second order reaction?
10. What is Zero order reaction?
11. Write equation for zero and first order half life.
12. What do mean by therapeutic index?
13. Give an example for Mono exponential equation.
14. Give an example for Bi exponential equation.
15. Draw the blood level profiles for oral and intravenous route of administration.
16. Enlist different pharmacokinetic parameters.
17. Define Cmax and Tmax.
18. Classify Pharmacokinetic models.
19. What is multi compartment model?
20. Give the schematic representation of one compartment open model-oral.
21. Give the schematic representation of one compartment open model-IV.
22. Give the schematic representation of two compartment open model-oral.
23. Give the schematic representation of two compartment open model-IV.
24. Give the schematic representation of three compartments model-oral.
25. Give the schematic representation of three compartments model-IV.
26. What are the assumptions of one compartment model?
27. Give the formula AUC0-t & AUC0-∞.

Short answer question 5 Marks:

1. Write a note on Catenary and mammillary modeling.
2. Write the importance of Compartment modeling in pharmacokinetic study.
3. With a neat labeled diagram explain the drug levels in blood after oral administration.
4. Explain various pharmacokinetic parameters after oral administration of drug.
5. Write the applications of pharmacokinetic models.
6. Explain how steady state level of the drug is achieved through I.V infusion.
7. Give schematic representation of two and three compartment models with brief explanation.
8. Explain the assumptions of one-compartment open model
9. Write about the advantages and disadvantages of compartment modeling.
10. Compare blood level curves between I.V and oral routes with a graph.
11. Give the mono exponential and bi exponential equations for drugs administered as IV bolus and explain the terms.
12. How do you determine KE using rate of excretion method from urine data.
13. How do you determine KE using sigma minus method from urine data.

Long answer questions 10 Marks:

1. What do you understand by pharmacokinetic model? Classify the pharmacokinetic models, give their salient features, advantages and disadvantages.
2. Discuss in detail one-compartment open model for a drug administered as IV Bolus. Give the schematic representation, graphs and equations for the same.
3. Discuss in detail one-compartment open model for a drug administered as IV infusion. Give the schematic representation, graphs and equations for the same
4. Discuss in detail two-compartment open model for a drug administered as IV Bolus. Give the schematic representation, graphs and equations for the same.
5. What is a compartment? Classify the compartment models. Give the schematic representation of the same.