PHARMACOKINETICS

- Duration of drug therapy ranges from a single dose (acute condition) to drugs taken life-long(chronic conditions).
- The frequency of administration of a drug in a particular dose is called as dosage regimen
- Depending upon the therapeutic objective , the duration of drug therapy and the dosage regimen decided
- Therapeutic and the toxic effects depend on the concentration of drug .

- 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

- To achieve this, knowledge of not only ADME but also of the kinetics of these processes is a must .

Pharmacokinetics

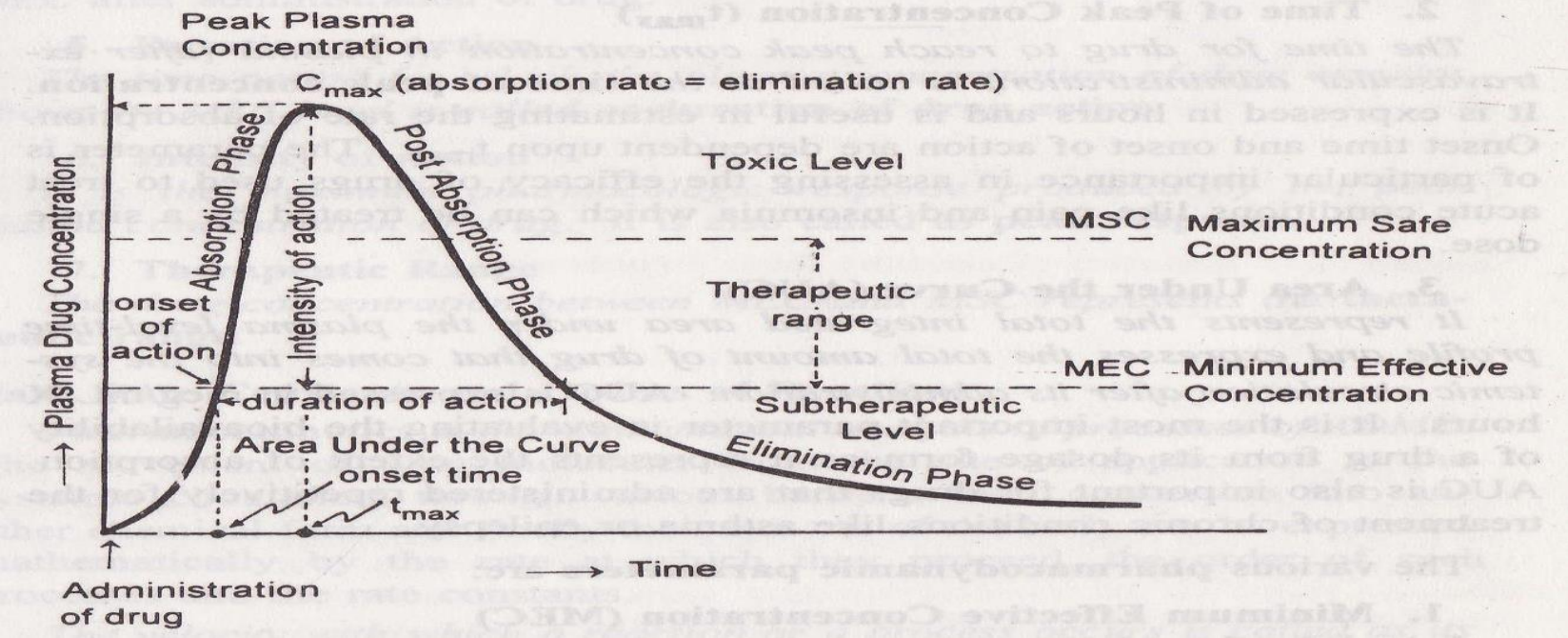
- Defined as the kinetics of ADME and their relationship with the pharmacological, therapeutic or toxicological response in man and animals

- Theoretical aspect: Involves development of pharmacokinetic models to predict drug disposition.

- Experimental aspect : Involves development of biological sampling techniques, analytical methods for measurement of drug concentration in biological samples .

Plasma Drug Concentration-Time Profile

- A direct relationship exists between the drug concentrations at the site of action & the concentration of drug in plasma.
- Pharmacokinetic & Pharmacodynamic parameters can be evaluated



PHARMACOKINETIC PARAMETERS

Peak plasma concentration (C_{max})

- The point of maximum concentration of drug in plasma is called as the peak & the concentration of drug at peak is known as peak plasma concentration or peak height concentration

- Represents maximum drug concentration & is expressed in µg/ml

- It depends upon administered dose, rate of absorption & elimination. It is related to the intensity of pharmacological response

- Absorption rate equals elimination rate of drug

Time of Peak Concentration (t_{max})

- The time for drug to reach C_{max} after extravascular administration & is expressed in hours
- Useful in estimating the rate of drug absorption
- Useful for assessing the efficacy of drugs used to treat acute condition

Area under the curve (AUC)

- Represents the total integrated area under the plasma level-time profile & expressed in µg/ml*hours
- Express the total amount of drug that's comes into the systemic circulation i.e. extent of absorption
- Determined by Planimeter Method, Cut and weigh Method etc.

Pharmacodynamic Parameters

Minimum Effective Concentration (MEC)

- Minimum concentration of drug in plasma (receptor site) required of produce the therapeutic effect.
- Concentration of drug below MEC is said to be in the sub-therapeutic level

Maximum safe concentration (MSC) / Minimum toxic concentration (MTC)

- Concentration of drug in plasma above which adverse or unwanted effect are precipitated
- Concentration above MSC is said to be in the toxic level.

Onset of action: Beginning of pharmacological response is onset of action & occurs when the plasma drug concentration just exceeds MEC.

Onset time : It corresponds to the time for the plasma concentration to reach MEC

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.

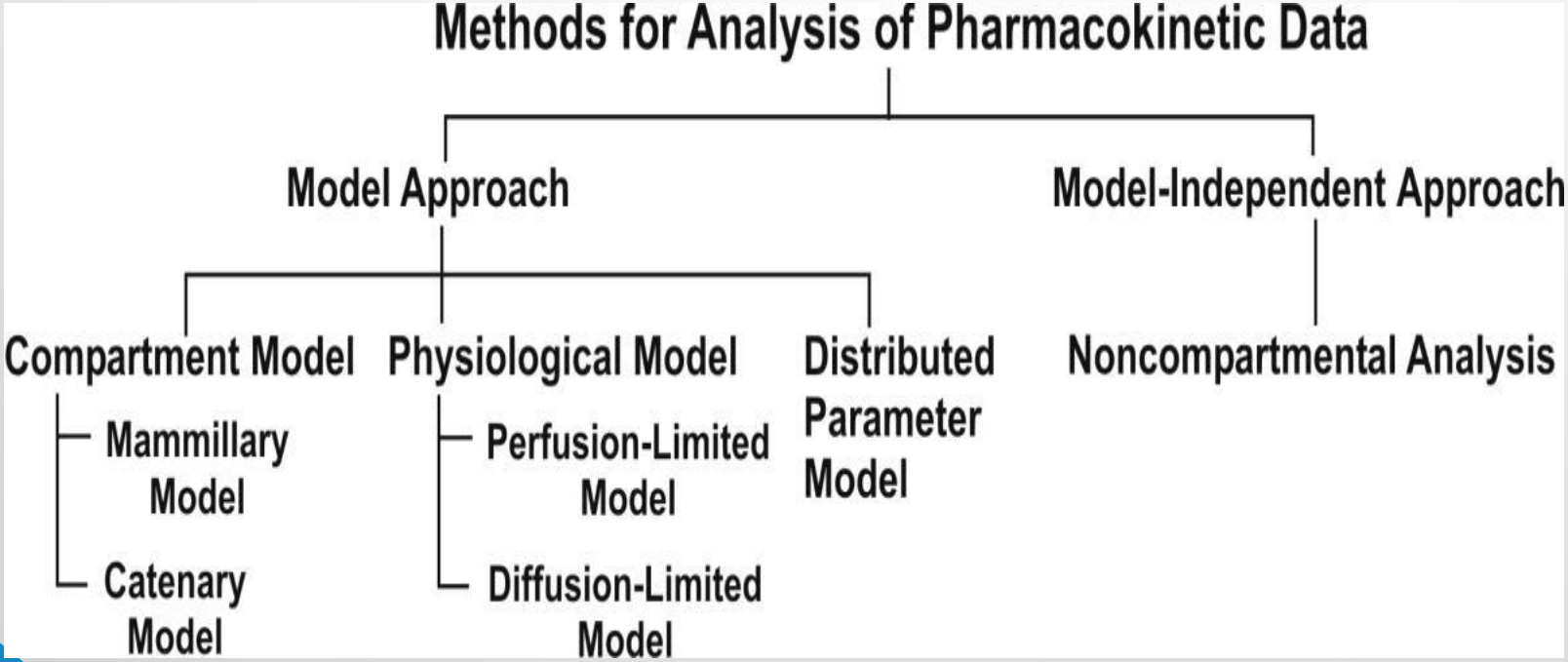
Intensity of action : Maximum pharmacological response produced by the peak plasma concentration of drug.

Therapeutic range : 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. It is also defined as the ratio of dose required to produce toxic or lethal to therapeutic effect.

Pharmacokinetic Approaches

- Drug movement within the body is a complex process. Major objective is to develop a simple approach to describe, analyse and interpret the data obtained during *in vivo* drug disposition studies.



A model is a hypothesis that provide concise means of expressing mathematically or quantitatively, the time course of drug(s) throughout the body & compute meaningful PK parameters.

Applications of Pharmacokinetic models.

- Characterizing the behavior of drugs in patients
- Predicting the concentration of drug in various body fluids with any dosage regimen.
- Predicting the multiple-dose concentration curves from single dose experiments.

- Calculating the optimum dosage regimen for individual patients.
- Evaluating the risk of toxicity with certain dosage regimens.
- Correlating plasma drug concentration with pharmacological response.
- Evaluating the bioequi/bioinequivalence between different formulations of the same drug.
- Determining the influence of altered physiology/diseased sate on drug ADME.