Clinical Pharmacology and Drug Development

Pharmacokinetics

Module 2 Topic 4

Pharmacokinetics

- **Pharmacokinetics** is the study of the
  - **Absorption**
  - **Distribution**
  - **Metabolism**, and
  - **Excretion** of a drug
- Pharmacokinetics is **what the body does to the drugs**

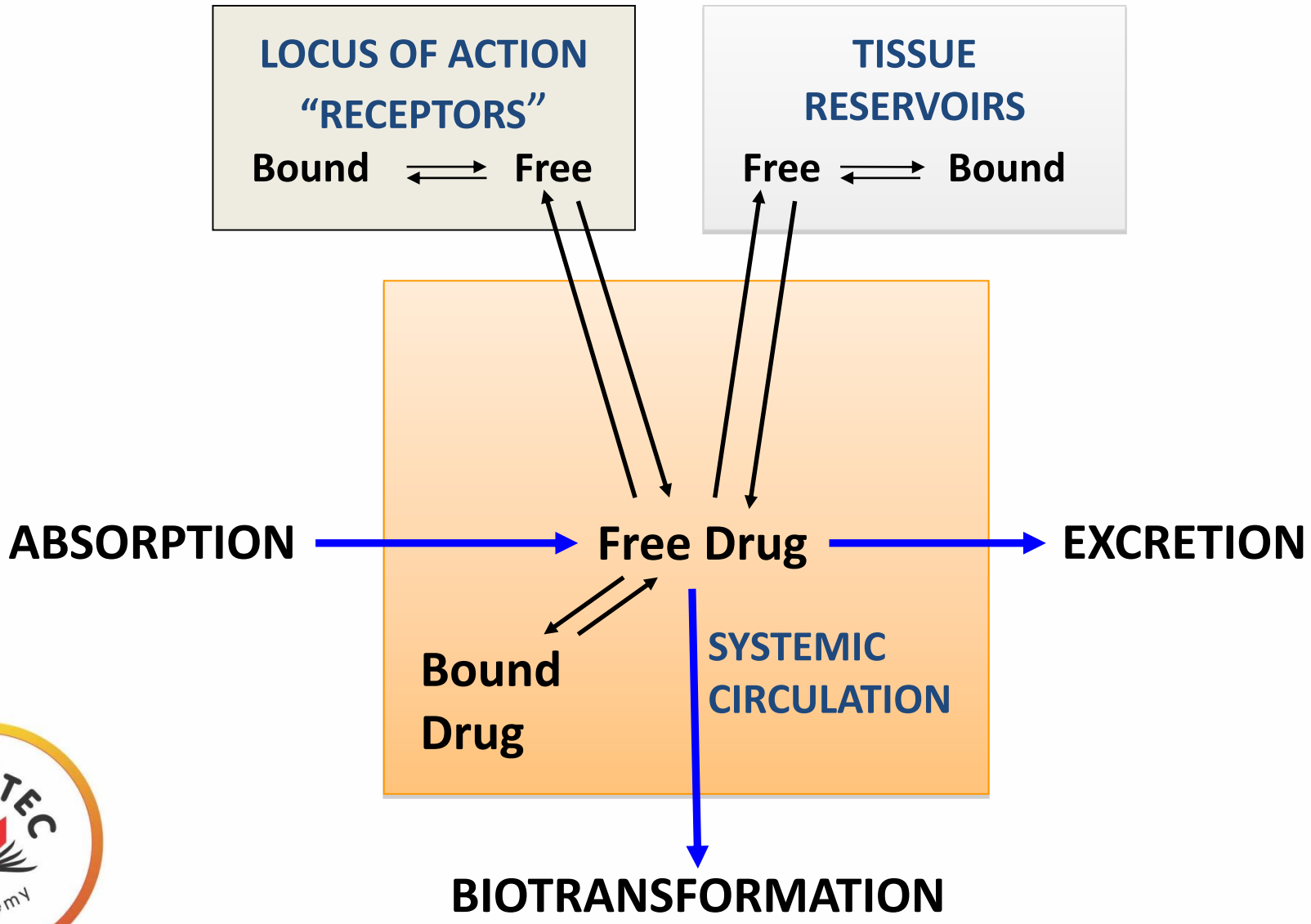
Pharmacokinetics

- **Absorption of a Drug**
  - Process of drug movement from the site of administration towards the systemic blood circulation
  - The way in which a drug is absorbed depends on its route of administration
- Routes of Drug Administration
  - **Enteral** – oral, sublingual, rectal
  - **Parenteral** – injection, inhalation, transdermal
  - **Topical**

Pharmacokinetics

Distribution of a Drug

- After a drug enters the general circulation it gets distributed throughout the body and passes into various tissues
- Protein Binding - Drugs are transported in the blood partly in solution (as free drug) and partly bound to plasma proteins – mainly albumin
  - Warfarin- 99% bound, Tolbutamide- 98% bound, Phenytoin- 90% bound
  - Free drug is active & gets metabolized & eliminated
  - Bound drug dissociates to replace the drug lost from the body


LOCUS OF ACTION
"RECEPTORS"
Bound ⇌ Free
TISSUE
RESERVOIRS
Free ⇌ Bound
ABSORPTION
Free Drug
EXCRETION
Bound
Drug
SYSTEMIC
CIRCULATION
BIOTRANSFORMATION

Pharmacokinetics

Metabolism (Biotransformation) of a Drug

- Metabolism or biotransformation is the process of chemical alteration of drugs in the body
- Metabolism facilitates elimination of the drug from the body
- Most of the drugs are eliminated from the body by the kidneys through the urine.

Pharmacokinetics

Liver is by far the most important organ involved in the metabolism of drugs

- Liver cells contain a number of enzymes that are responsible for many metabolic reactions
- The most important enzyme system of metabolism is cytochrome P-450 (CYP450), a superfamily of isoenzymes that catalyzes the oxidation of many drugs

Pharmacokinetics

Excretion of a Drug

- Excretion is the process by which a drug is eliminated from the body.
- The major organ responsible for excretion of a drug is the kidney, which eliminates drugs via urine
- Other routes by which drugs are excreted from the body include:
  - Bile
  - Saliva
  - Sweat
  - Breast milk
  - Lungs, etc.

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Bioavailability

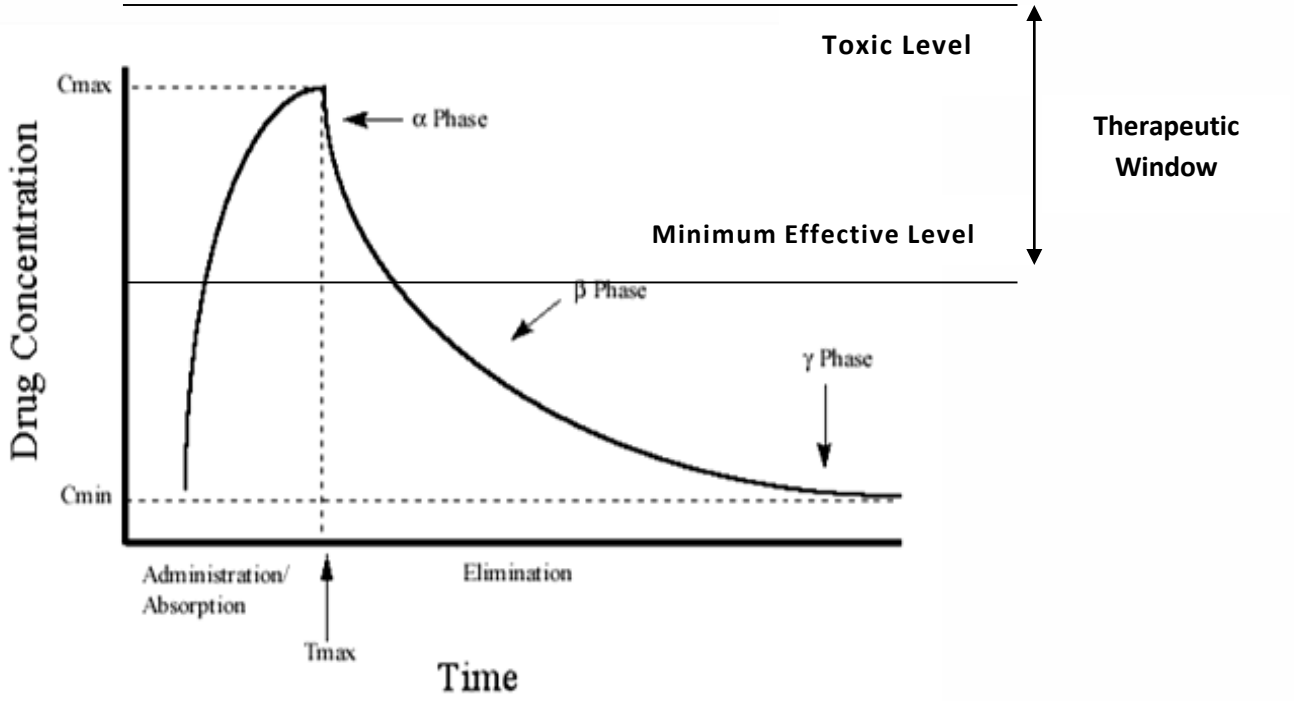
- Bioavailability is the rate and extent to which the drug enters the general circulation following administration by oral route

Bioequivalence

- Bioequivalence indicates that the drug products, when given to the same patient in the same dosage regimen, result in equivalent concentrations of drug in plasma and tissues

Pharmacokinetics

Estimation of Bioavailability



Time V/s Concentration curve

Pharmacokinetics

Half – Life ($t_{½}$) :

- Time taken for the blood concentration (or the amount of drug in the body) to be reduced by 50 % of the previous reading
  - For example, if 500 mg is present in the body at time zero, after metabolism, 250 mg may be present at 1 h and 125 mg at 2 h illustrating a half-life of 1 h

Steady State:

- Situation when the amount of drug entering the circulation equals that being removed from it
- Seen after many doses of drug given at fixed intervals
- A steady state is achieved after approximately four to five half-lives