
दिलीप वळसे पाटील कला व वाणिज्य महाविद्यालय
श्री पांडुरंग ग्रामीण विकास प्रतिष्ठान मंचालित,
निमगाव सावा, पुणे.
विष्णुविण जप व्यर्थ त्याचे ज्ञान !
स्थापना
२००९

Department of Chemistry

Subject - Medicinal Chemistry

Class - T.Y.B.Sc

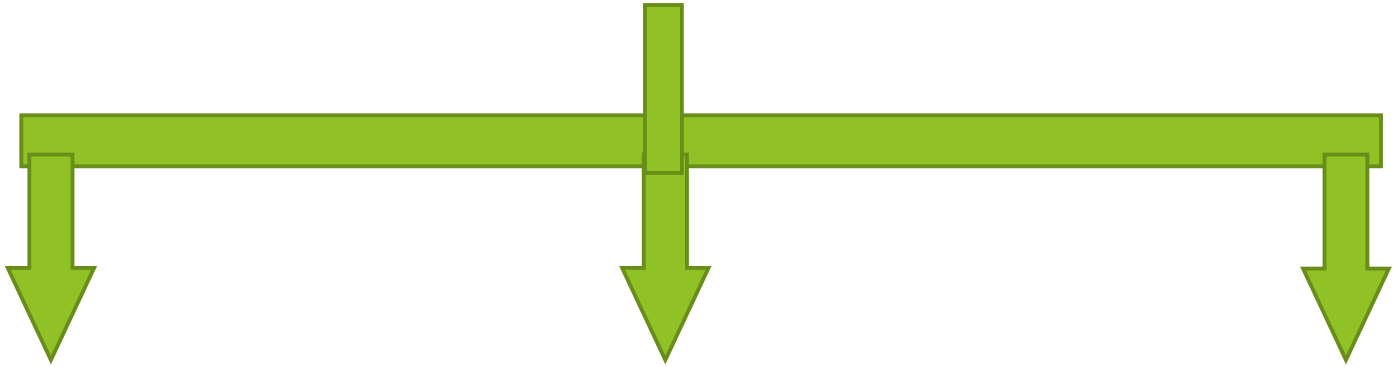
Name - Prof. Bhor Madhuri M.

Presentation on...

Pharmacokinetics and related topic

Absorption , Distribution , Metabolism , Excitation .

The three phase of drug action

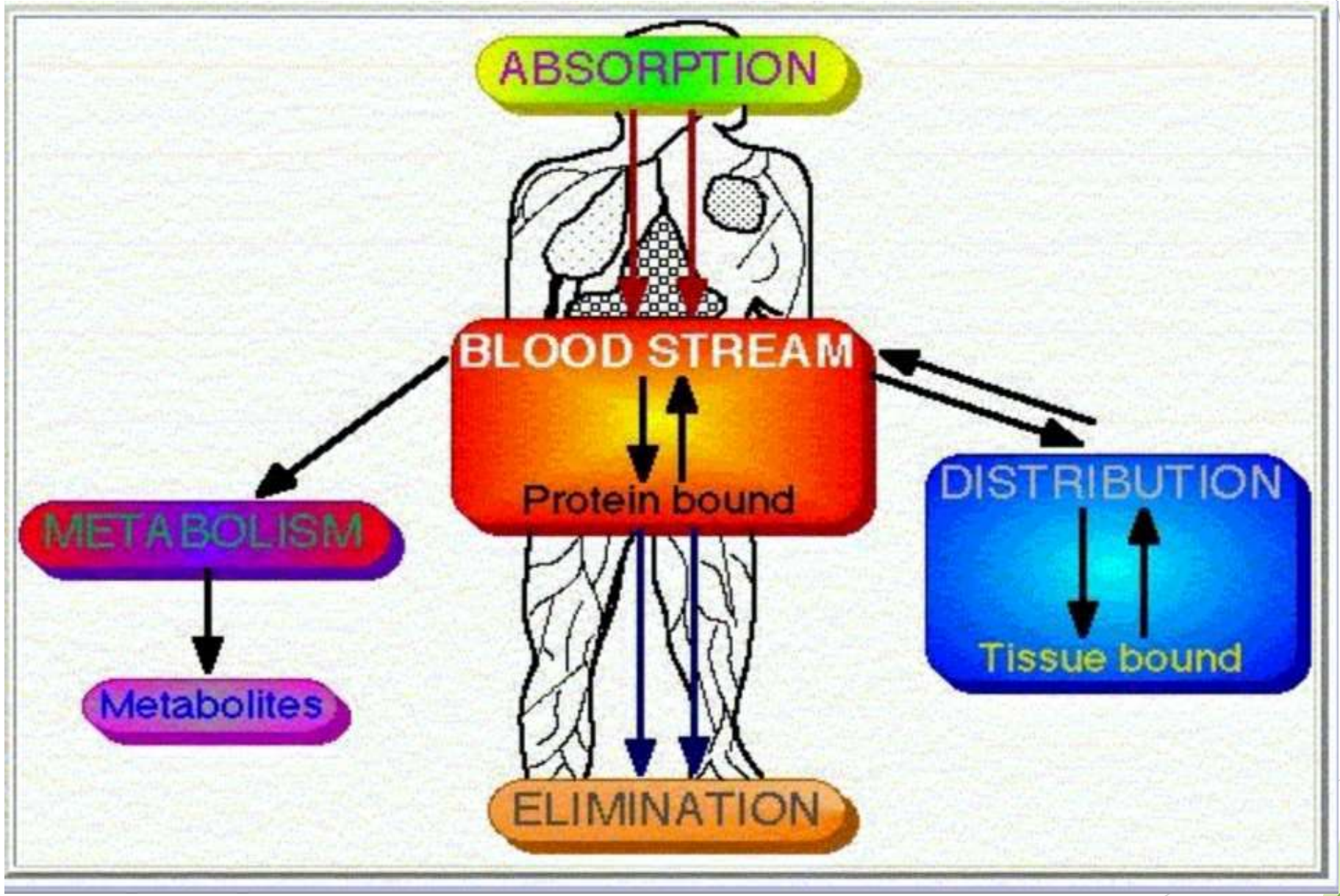


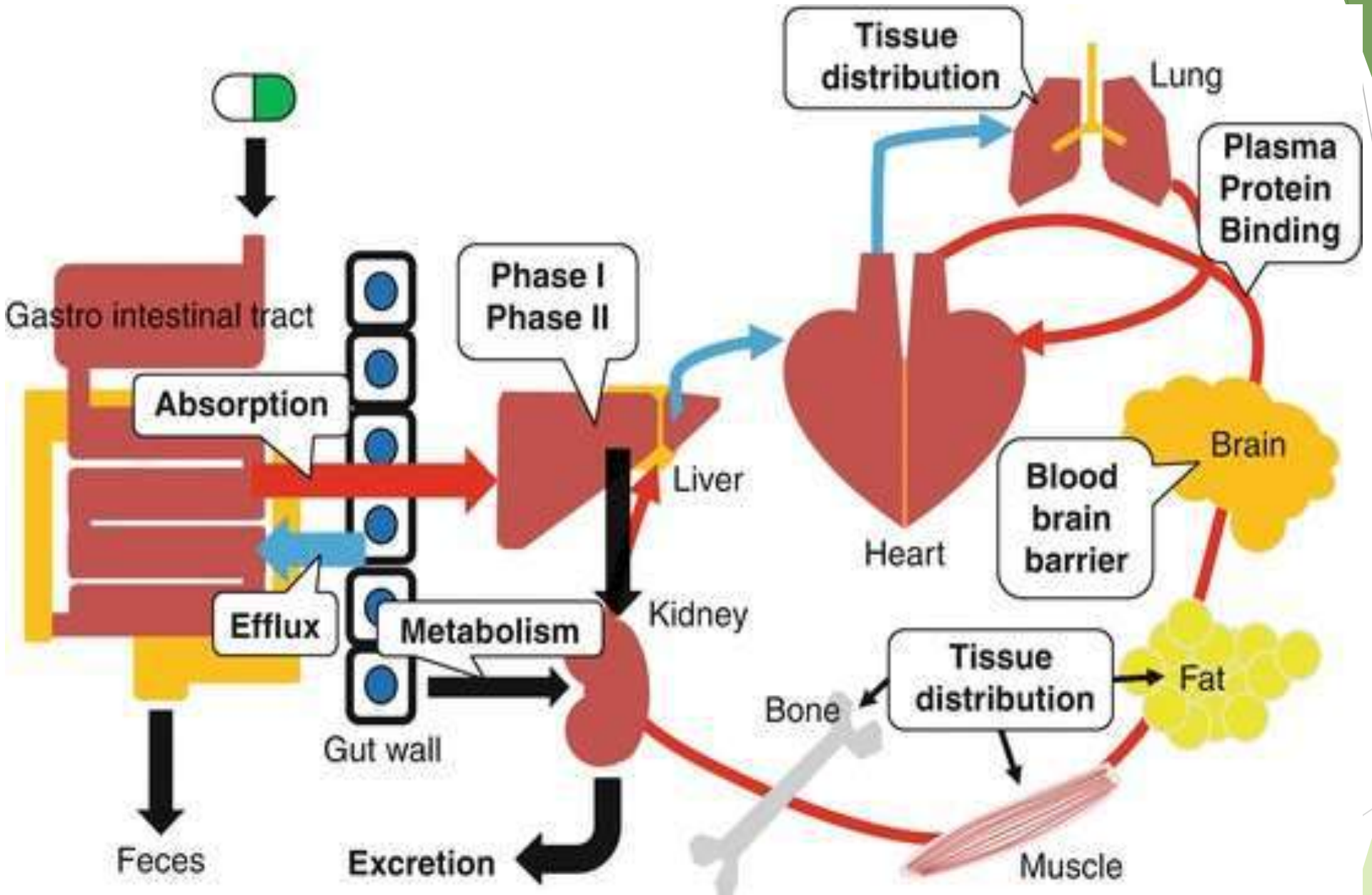
1. Pharmaceutical Phase.
2. Pharmacokinetics Phase.
3. Pharmacodynamics Phase

Pharmacokinetics

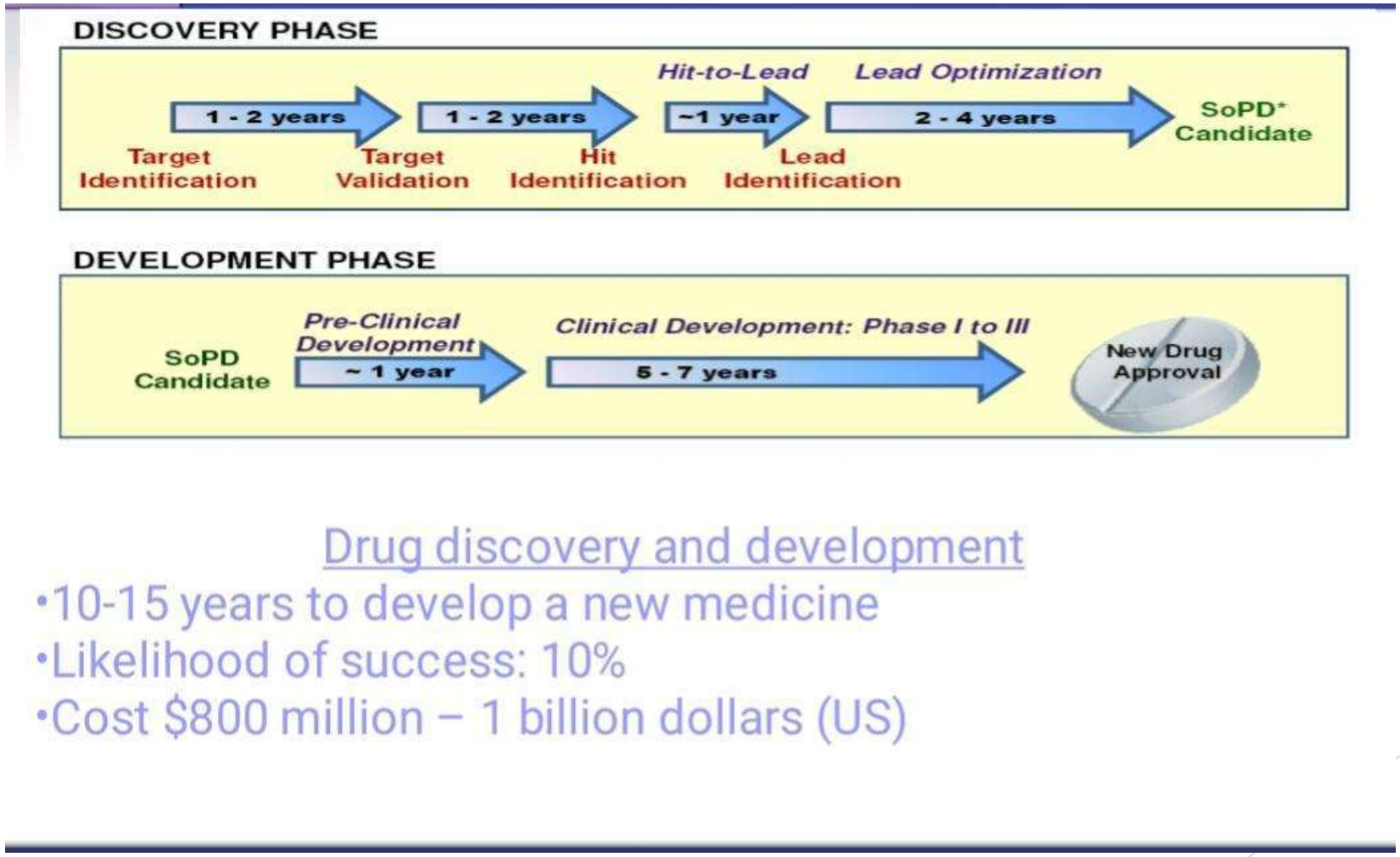
Introduction

- Pharmacokinetics is the movement of drug through the body.
- It is described as What the body does to the drug.
- It is the study of absorption, distribution, metabolism, excretion of drug


ABSORPTION
BLOOD STREAM
Protein bound
METABOLISM
Metabolites
DISTRIBUTION
Tissue bound
ELIMINATION


Tissue distribution
Lung
Plasma Protein Binding
Phase I
Phase II
Gastro intestinal tract
Absorption
Liver
Heart
Brain
Blood brain barrier
Efflux
Metabolism
Kidney
Tissue distribution
Fat
Bone
Gut wall
Feces
Excretion
Muscle

Drug formation process



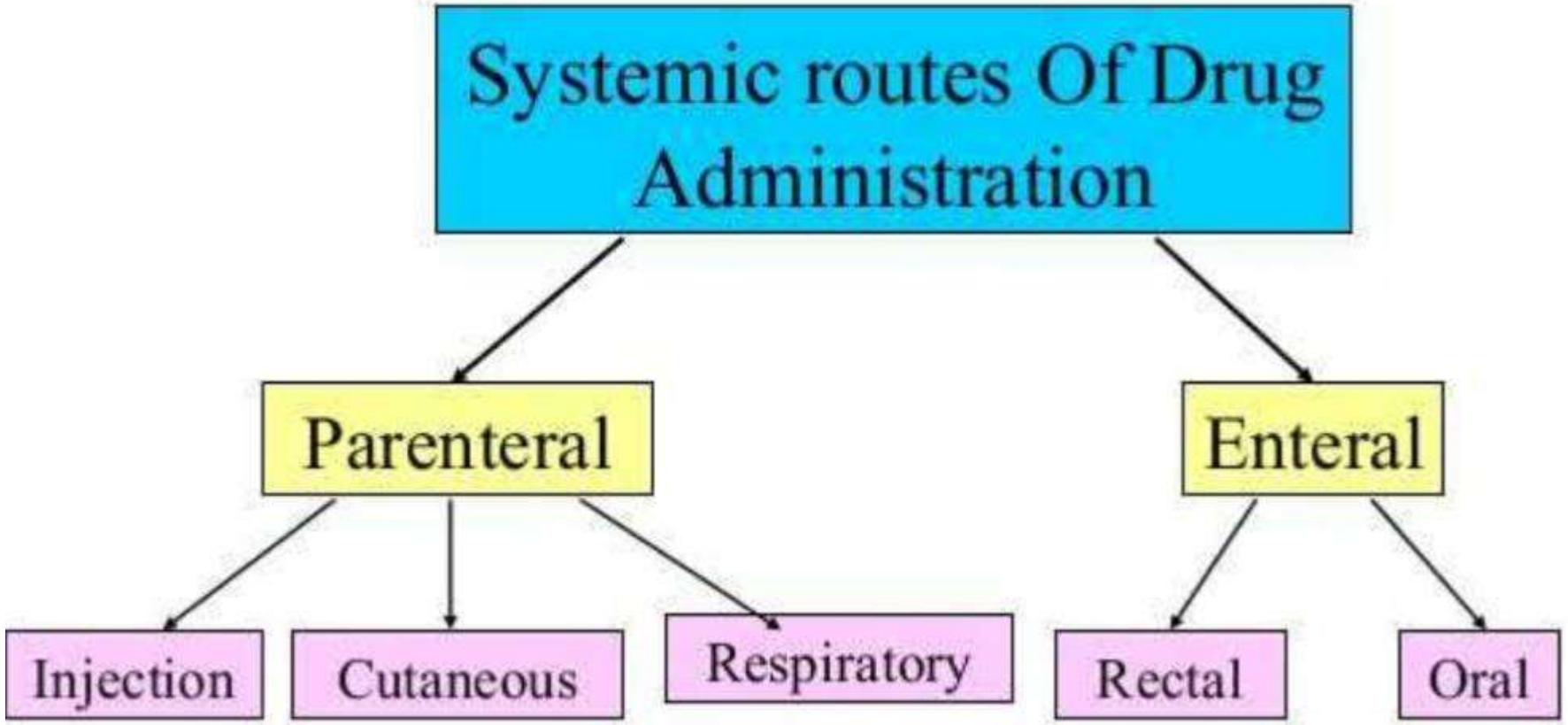
Drug discovery and development

- 10-15 years to develop a new medicine
- Likelihood of success: 10%
- Cost $800 million – 1 billion dollars (US)

Absorption

- A drug must have the right balance of water and fat solubility...
- If the drug is too polar (hydrophilic),It does not pass through the fatty cell membranes of the gut well.
- If the drug is too hydrophobic,it will be poorly soluble.
- The drug must be stable to chemical and enzyme.
- Necessary for the production of a therapeutic effect.
- Most drug undergo gastrointestinal absorption
- Absorption must be efficient

Routes Of Administration



Factors affecting drug absorption

- Physio-chemical properties

1) Partical size (drug molecule)
2) Formation (dosage form).
3) Ionisation.
4) pH
5) Liquid solubility and concentration.

Henderson-Hasselbalch Equation

$$pH = pK_a + \log\left(\frac{[base]}{[acid]}\right)$$

pH = pH of the buffered solution

pK_a = pK_a of the weak acid

[base] and [acid] are initial [ ]'s of the conjugate acid/base pair

Lipinski's rule of five.

- The rule of thumb, orally absorbed drugs tend to obey is known as Lipinski's rule of five.

- Poor absorption are more likely when :
- There are more than 5 H- bond donar (HBD) groups;
- There are more than 10 H-bond acceptor (HBA) groups;
- The molecular weight is over 500.
- The log p value less than +5.

Distribution

- Distribuation around the blood supply is rapid
- Distribuation to the interstitial fluid surrounding tissue and organs.
- Some drug have to enter cell in order to reach their target.
- A drug may be absorbed into fatty tissue and bound to macromolecules.
- Drug entering the CNS have to cross the blood-brain barrier.

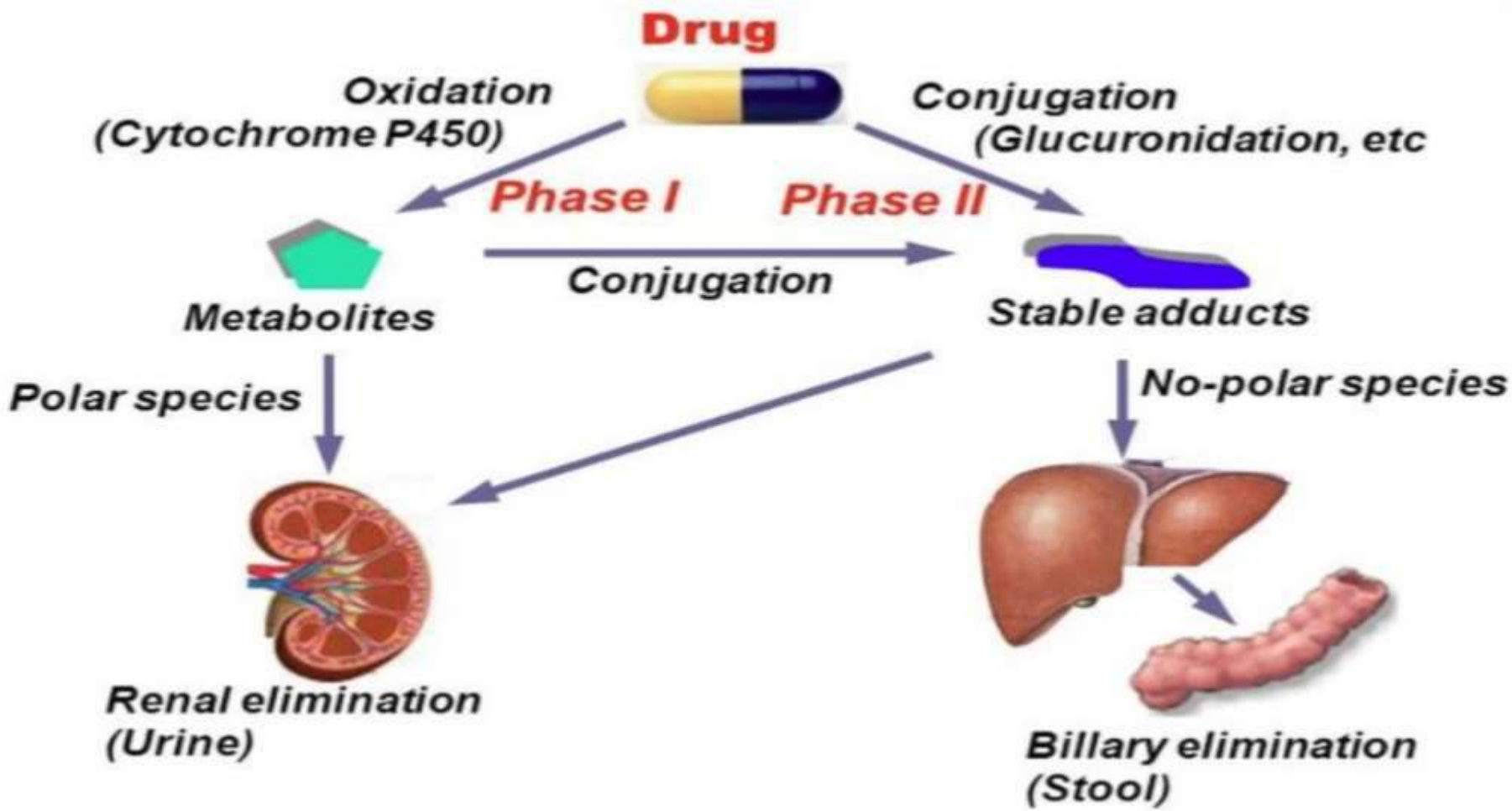
- All of the glide in the body,in which a drug can be dissolved,
- Can be roughly divided into three compartments.

1) Intravascular (blood plasma found within blood vessel)

2) Interstitial / tissue (fluid surrounding cells).
3) Intracellular (fluid within cells)

The distribution of a drug into this compartments is directed by its physical and chemical properties.

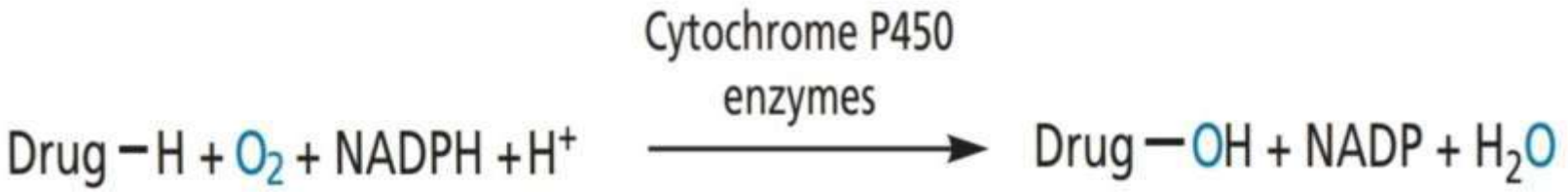
Metabolism



- The chemical modification of drug with the overall goal of getting rid of the drug.
- Enzymes are typical involved in metabolism.

Phase I drug metabolism

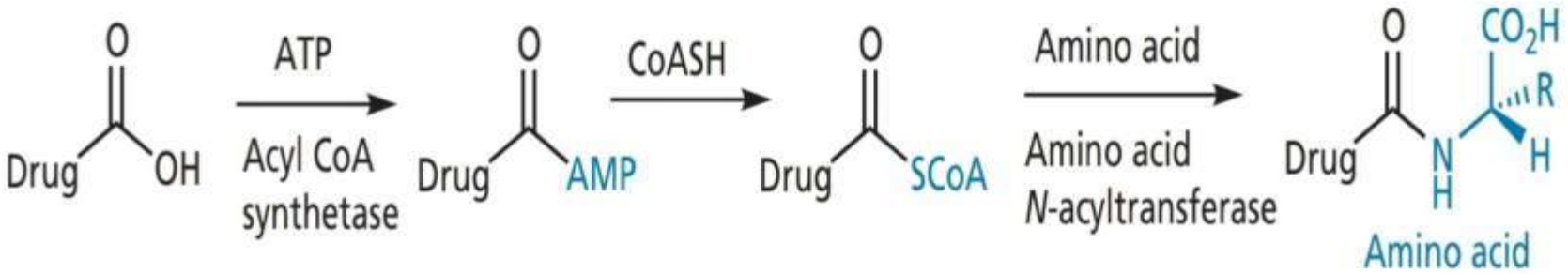
- Reaction
- Convert parents compound into a more polar (hydrophilic) metabolite by adding functional groups (-OH, -SH, -NH2, -COOH, etc.)
- Ex. Oxidation.



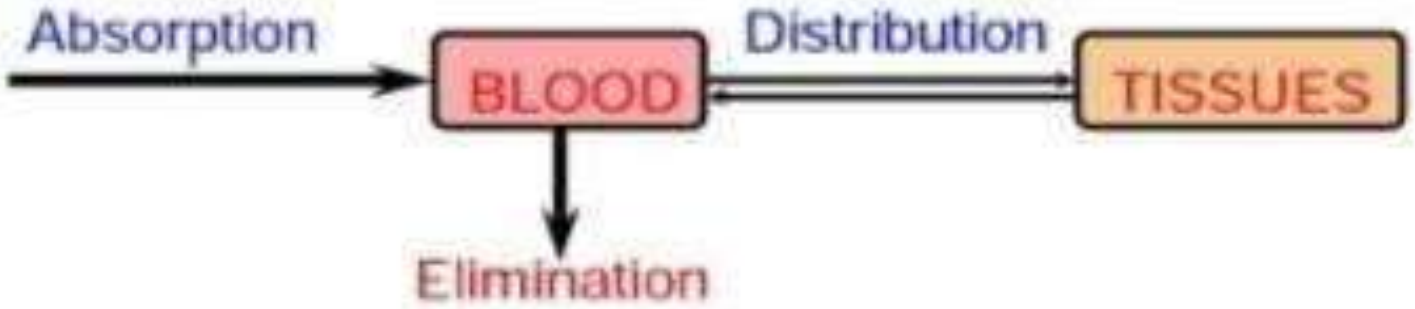
- Oxidation by cytochrome P450 enzyme.

Phase II

- Conjugation with endogenous substrate to further increase aqueous solubility.
- Conjunction with glucoronide, sulphate, acetate,amino acid.



Excretion (Elimination)



Elimination: the *irreversible* transfer of a drug from the systemic circulation

Major routes of elimination:

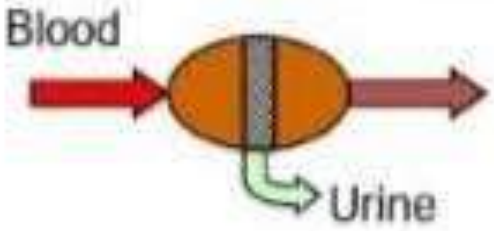
Metabolism

Renal excretion (for free drug, ie low logD)

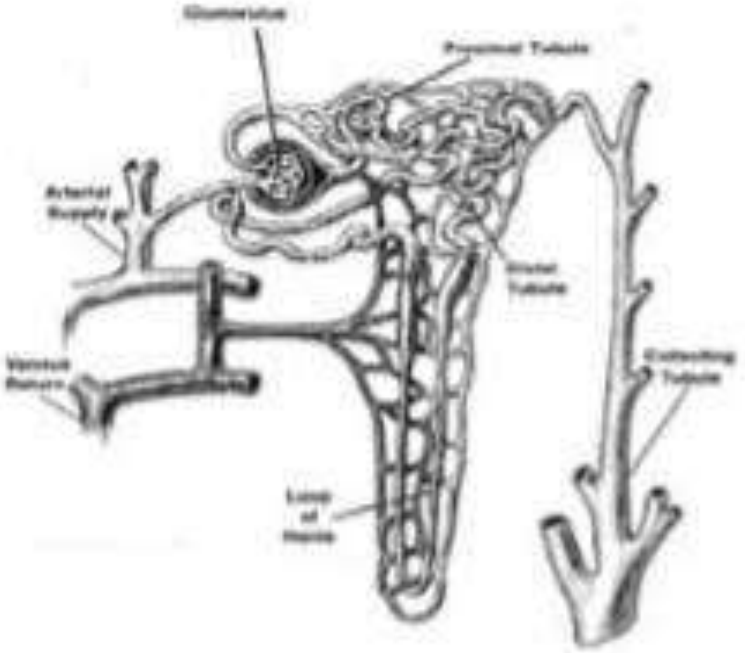
Biliary excretion

Also lungs, sweat etc.

Renal Excretion



Nephron



1. *All* **unbound** drug in plasma is filtered in the glomerulus. Only significant for very polar compounds, log D < 0.

2. Some compounds are actively secreted into urine along the proximal tubule.

3. Unionised drug can undergo passive reabsorption from urine into blood along the length of the nephron (net excretion may be zero).

4. Drug that is bound to plasma proteins is not filtered.


Thank
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