

## Ion trapping

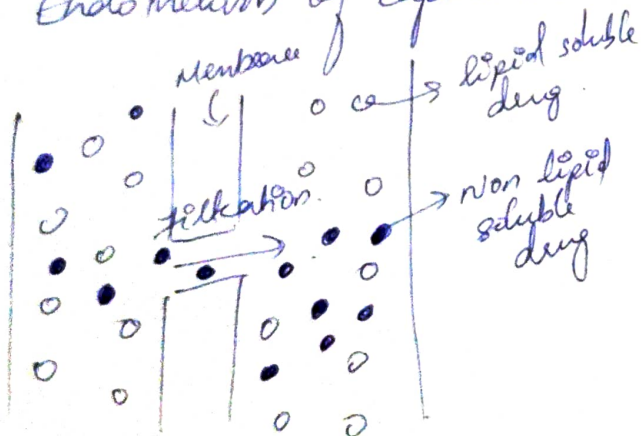
Acidic drugs (ionized) cross gastric mucosal cell  $\rightarrow$  intracellular pH is 7, hence reverts to ionized form  $\rightarrow$  slowly pass to ECF

$\rightarrow$  Result in gastric mucosal cell damage aspirin.

## Paracellular / Filtration

$\rightarrow$  Passage of drugs through aqueous pores in the membrane/through paracellular space.

eg. Endothelium of capillaries.



## Carrier Mediated Transport

$\rightarrow$  Cell membrane  $\rightarrow$  transmembrane proteins; act as carriers

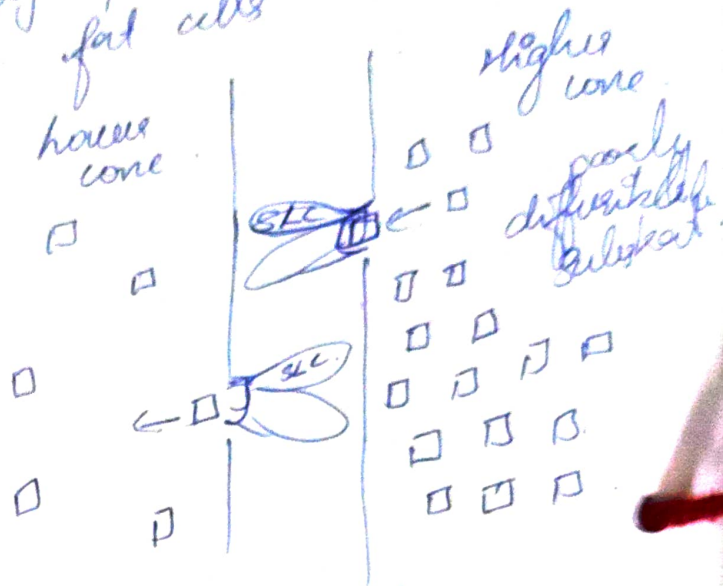
$\rightarrow$  carrier is specific for the substrate

$\rightarrow$  Rate of transport depends on % saturation of carrier protein.

## Facilitated Diffusion

$\rightarrow$  SLC  $\rightarrow$  solute carrier transporters

$\rightarrow$  No energy needed  
 $\rightarrow$  Along concentration gradient  
 eg. Glucose into muscle, fat cells



## Active Transport

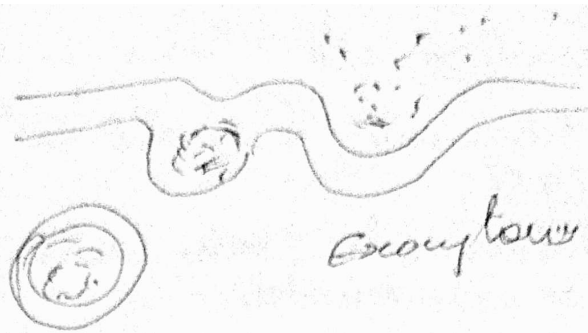
$\rightarrow$  Carrier mediated  
 $\rightarrow$  Energy is required  
 $\rightarrow$  Against the concentration gradient

types:

1. Primary
2. Secondary
  - a) symport
  - b) antiport

## Primary Active Transport

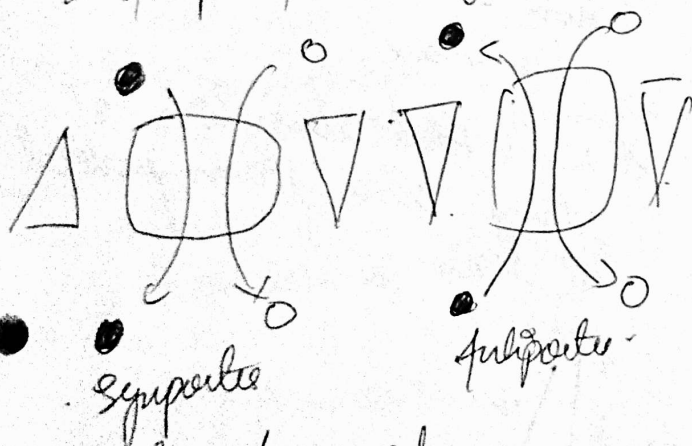
$\rightarrow$  Energy from ATP hydrolysis  
 $\rightarrow$  Against the concentration gradient  
 $\rightarrow$  ABC (ATP-Binding cassette) transporters.



Secondary Active Transport  
 → Uses the energy produced by the electrochemical gradient created by one molecule for transport of another molecule

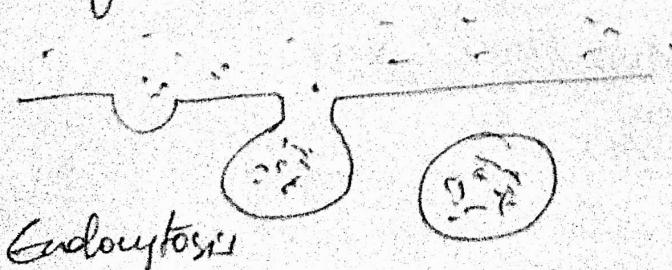
Types:

1. Symport / Co-transporters
2. Antiport / Exchange transporters



Vesicular transport

→ Large molecules transported into the cell (endocytosis) or extruded from the cell (exocytosis) by endocytosis in tiny vesicles.  
 Eg: Hormones



## ABSORPTION

Movement of the drug from its site of administration into the circulation.

Depends on:

- aqueous solubility
- concentration
- Area of absorbing surface
- Vascularity of absorbing surface
- Route of drug administration

Oral Route

- Epithelial lining of GIT is lipoidal.
- Non ionized, lipophilic drug is readily absorbed.
- Presence of food can retard absorption.
- Certain drugs degraded in GIT (ineffective orally) eg: Insulin.
- Luminal effect (insoluble complexes) eg: tetracycline & calcium salts, phenytoin with succinylate.

## Parenteral sites

- Intravenous → complete and rapid
- Intramuscular (more vascularity) > subcutaneous.

## Lung

- simple diffusion
- rapid
- large surface area.
- high vascularity

## Topical sites

- Infant skin → poor absorption
- Cornea, mucous membranes → permeable to lipid soluble drugs

## X Bioavailability (Question)

Bioavailability is a measure of the fraction (F) of administered dose of a drug that reaches the systemic circulation in the unchanged form."

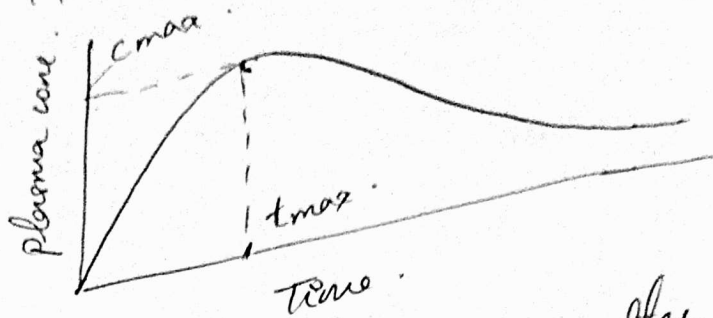
Indicated by 'F'

Bioavailability through intravenous route is 100%.

## Components

- Rate of BA
- Extent of BA

## Rate and Extent

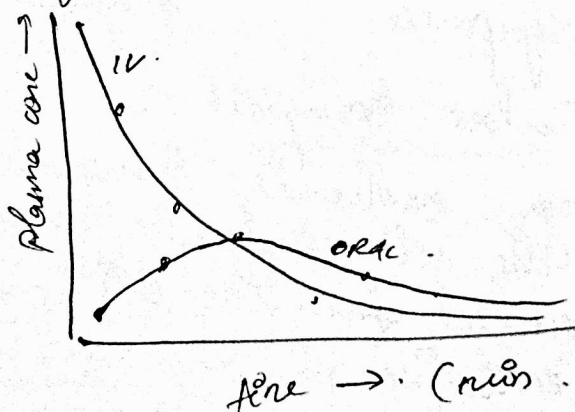


- $t_{max}$  &  $C_{max}$  measures the rate of bioavailability
- AUC (area under curve) → Extent of bioavailability

$C_{max}$  - max conc. achieved by the drug

$t_{max}$  - time taken to attain  $C_{max}$

AUC → total absorption of drug in a given period of time.



$$\text{Bioavailability (\%)} = \frac{\text{AUC (oral)} \times 100}{\text{AUC (IV)}}$$

## Factors affecting bioavailability

- Pharmaceutical factors
- Pharmacological factors

### Pharmaceutical

1. Disintegration
2. Dissolution
3. Degree of ionization
4. Particle size
5. Salt form
6. Crystal form
7. Water of hydration
8. Nature of excipients & adjuvant

### \* Formulation of drug

Oral preparation (Tablet, capsule)

↓ Disintegration

Fine particles (Powder, suspension)

↓ Dissolution

Drug into solution (solution)

↓ Absorbed from GIT.

Solutions > Suspensions > Capsule  
Tablet > Enteric coated tablet  
> SR (sustained release) tablet.

### \* Particle size

↓ particle size; ↑ BA.

Microfined aspirin, spironolactone.

### \* Crystal form

Bioavailability ↓ with crystalline form.

↑ BA: amorphous chloramphenicol palmitate

### \* Salt form

Salts of weakly acidic drugs  
↑ BA: Tollenamide sodium and Phenytoin sodium.

### \* Hydration

BA decrease when drugs associate with water to form hydrates.

BA ↑; anhydrous caffeine, theophylline.

### \* Excipients & adjuvants

Starch, gum, Ca sulfate, lactose, polysorbate 80.

BA ↑: Phenytoin, Digoxin, levodopa, warfarin.

### \* Degree of ionization

Non ionized lipid soluble drugs are better absorbed.

### Pharmacological factors

1. First pass effect
2. Route of administration
3. Gastric emptying & gastric intestinal motility

(5) 4. Food

3. Pharmacogenetic factors.
4. Miscellaneous factors.

### First pass metabolism

Metabolism of a drug during its passage from the site of absorption into the systemic circulation.

- Gut lumen
- Gut wall
- Liver.

FPM ↓ BA of drugs.

- pre systemic elimination
- Metabolism of drug before reaching systemic circulation.
- Orally administered drugs are exposed to drug metabolizing enzymes in the intestinal wall & liver → intestinal & hepatic first pass effect.
- Avoided by administering drug through different routes - parenteral, sublingual, subdermal.

Table 3.2, Tripathi  
Extent of hepatic FPM.

### Clinical Implications of FPM

- Higher oral dose, compared to parenteral dose.
- Marked inter individual

variations due to differences in FPM.

- In liver diseases, due to reduced metabolism, BA is high.

Intravenous > Intramuscular > Subcutaneous > ~~Oral~~ Oral.

### • Gastric Emptying

Increased gastric emptying enhances BA.

BA ↑ : Fasting, anxiety, lying on right side, hyperthyroidism, drugs like Metoclopramide.

BA ↓ : Fatty meal, depression, lying on left side, pyloric stenosis, hypothyroidism, drugs → Atropine, Imi.

### Disease states

- Gastroenteritis.
- Coeliac disease
- Crohn's disease
- CEF
- liver.

### Food Drug interaction.

- Absorption ↑ in empty stomach - Rifampicin.
- Absorption ↑ after meals : Lithium, phenytoin.
- Absorption of tetracycline ↓ if taken with milk.

## Drug-drug interactions

Antacids ↓ BA of tetracycline  
by forming poorly absorbed  
chelated complex.

↓ BA of drugs by  
enzyme induction.

↑ BA of drugs by  
enzyme inhibition.

Same therapeutic response,  
they are said to be therapeutically  
equivalent.

→ Pharmacokinetic factors.

→ Miscellaneous factors

## Bioequivalence

→ 2 preparations of a drug  
are considered bioequivalent  
when the rate & extent of  
bioavailability of the active  
drug from them is not  
significantly different under  
suitable test conditions.

## Chemical equivalence

→ 2 dosage forms of a drug  
contain same amount of the  
drug, they are said to be  
chemically equivalent.

## Therapeutic Equivalence

→ If 2 drugs produce the