ABSORPTION OF DRUGS

(Unit Objective: Student able to understand the rate and Mechanism of Drug absorption)

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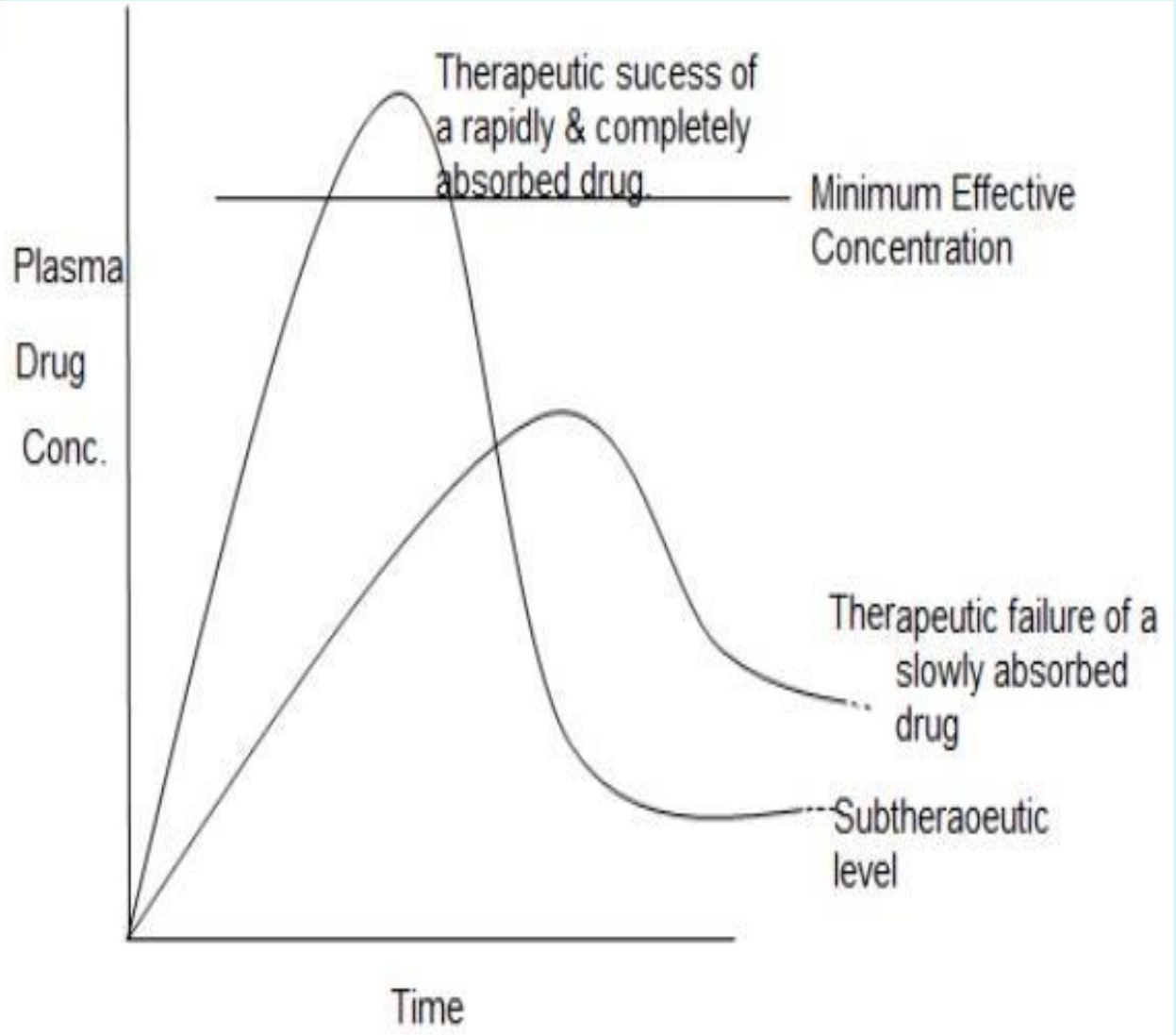
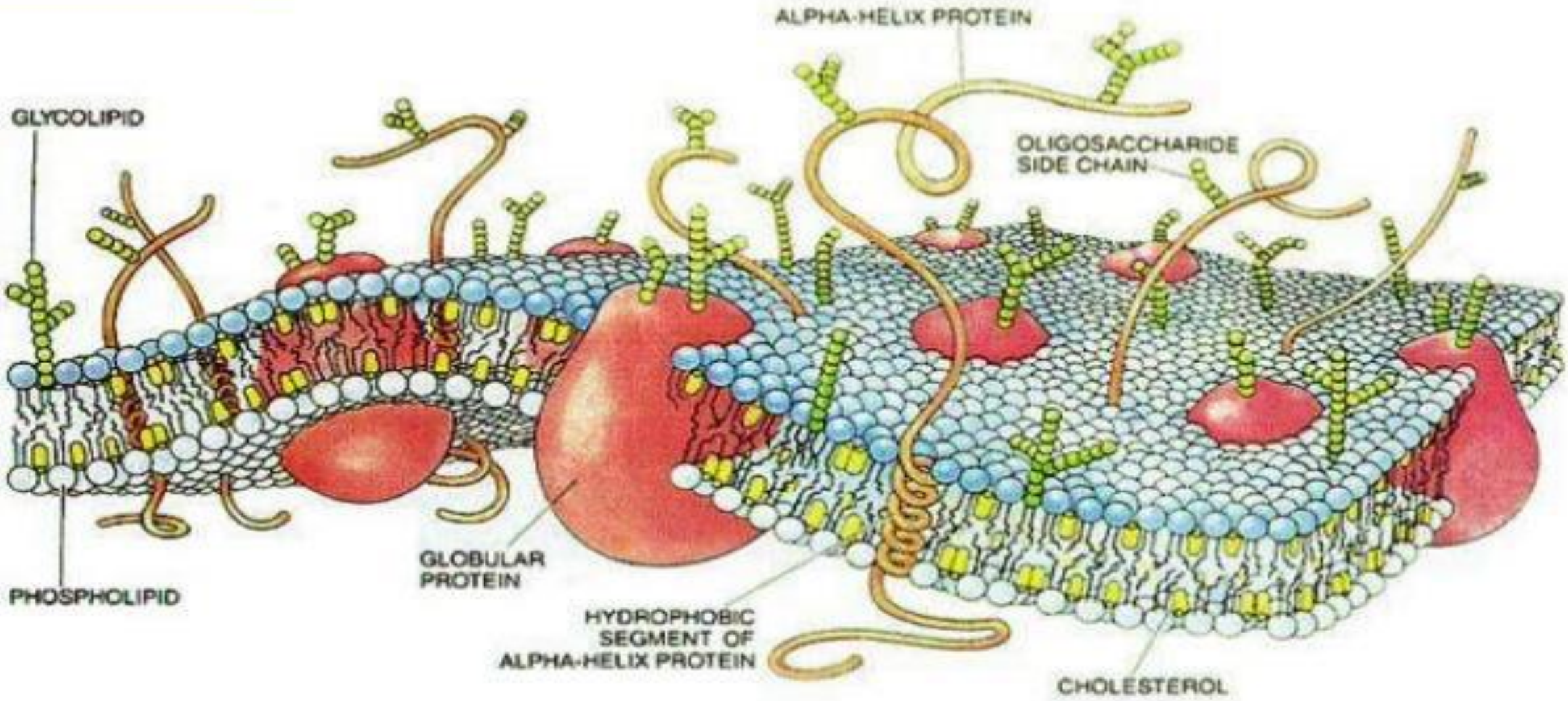
DEFINATION

- It is defined as the process of movement of unchanged drug from the site of administration to the systemic circulation.
- There always present a correlation between plasma concentration of a drug & the therapeutic response & thus, absorption can also be defined as the process of movement of unchanged drug from the site of administration to the site of measurement. i.e., plasma.



STRUCTURE OF CELL MEMBRANE



MECHANISM OF DRUG ABSORPTION

1. Passive diffusion
2. Carrier Mediated transport
    1. Active transport
    2. Facilitated diffusion
3. Pore transport
4. Ionic or Electrochemical diffusion
5. Ion Pair transport
6. Endocytosis

Passive Diffusion

Characteristics:

- Common
- Occurs along concentration gradient non selective
- Not saturable
- Requires no energy
- No carrier is needed
- Depends on lipids solubility
- Depends on pKa of drug – pH of medium

Expressed by *Fick's first law* of diffusion -

"The drug molecules diffuse from a region of *higher* concentration *to* one of *lower* concentration until equilibrium is attained & the rate of diffusion is directly proportional to the concentration gradient across the membrane".

$$dq/dt = D\,A\,K_{o/w}\,(C_{git} - C_{plm})/Vh$$

$$\frac{dQ}{dt} = \frac{DAK_{m/w}}{h}(C_{GIT} - C)$$

Sink condition

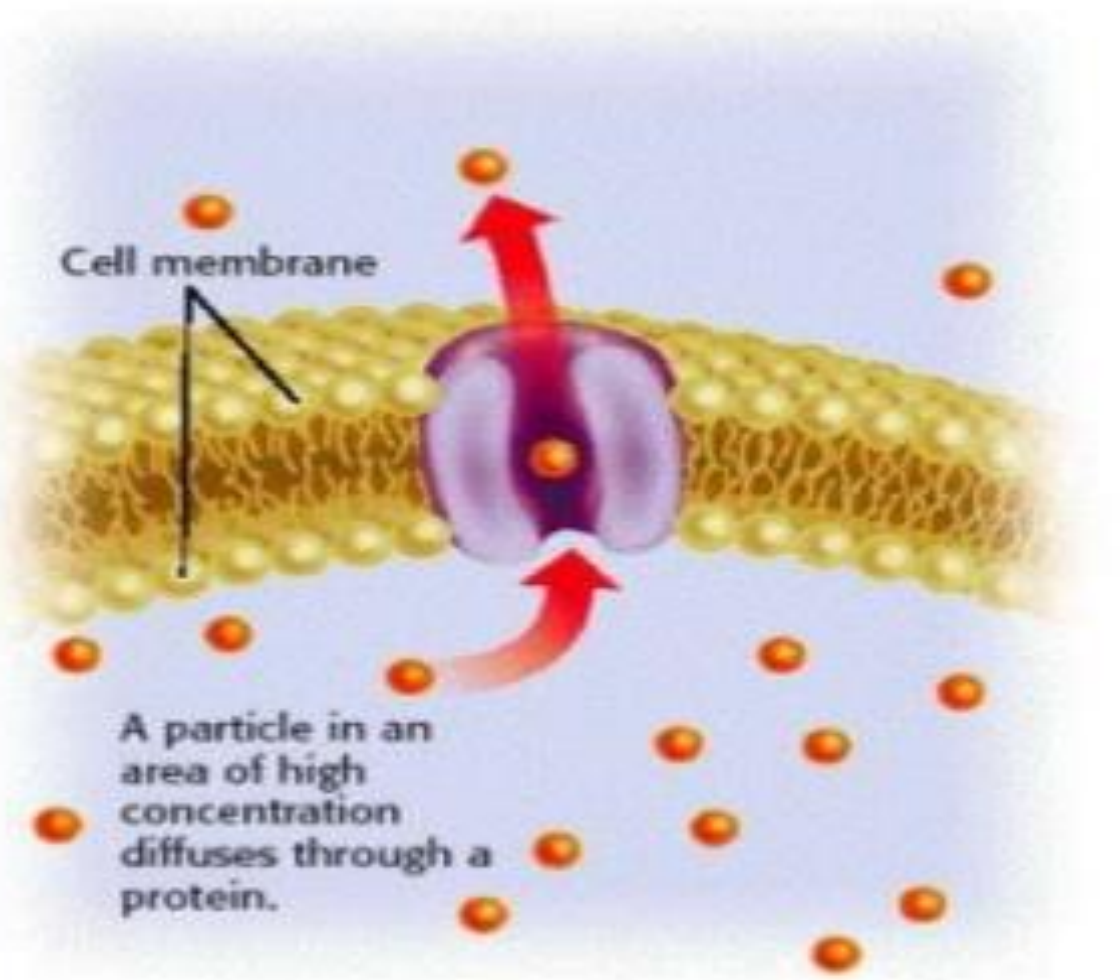
$$dQ/dt = P\,C_{GIT}$$

Active Diffusion

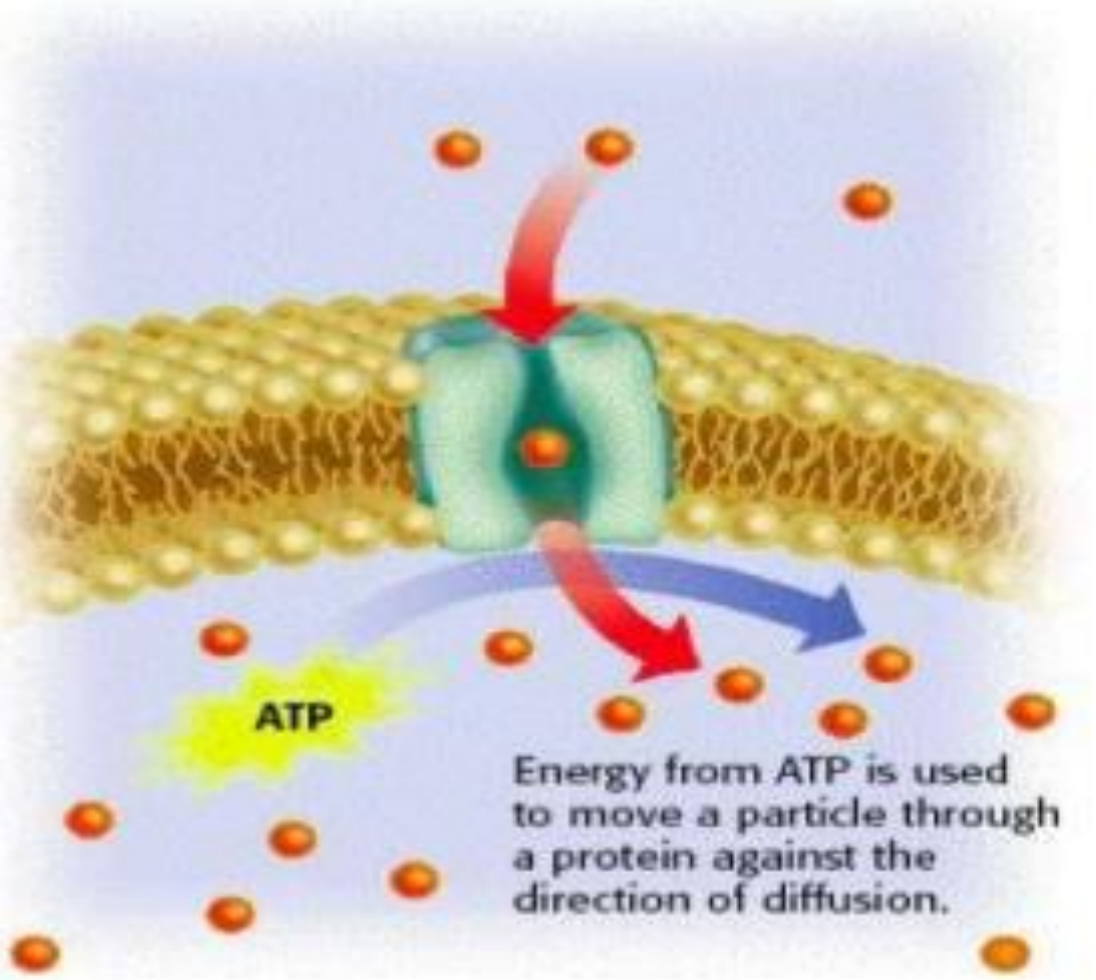
Characteristics:

- Relatively unusual
- Occurs against concentration gradient
- Requires carrier and energy
- Specific
- Saturable
- Iron, K, Na, Ca
- Uptake of levodopa by brain

PASSIVE TRANSPORT



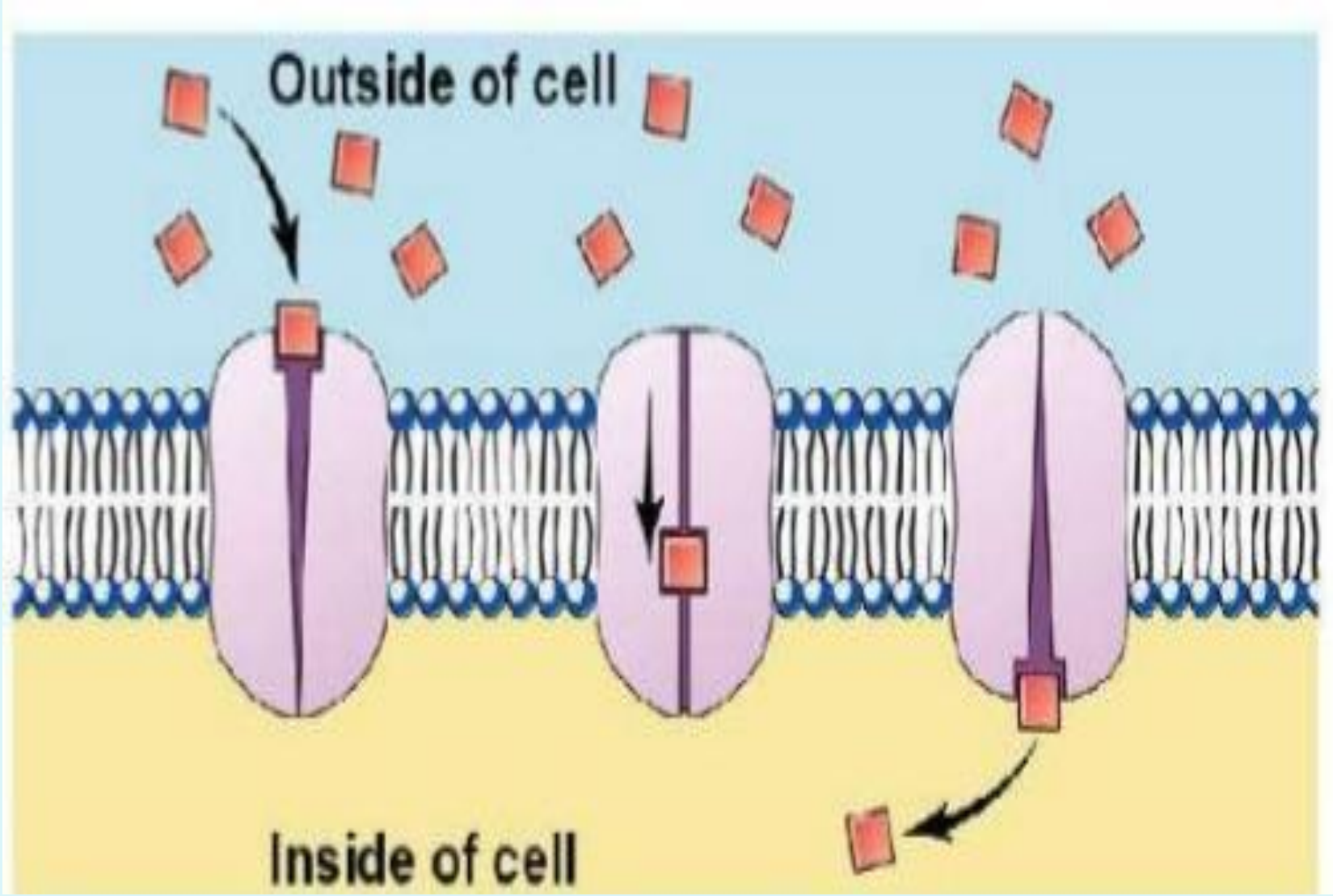
ACTIVE TRANSPORT



Facilitated Diffusion

Characteristics:

- Occurs along the concentration gradient
- Requires carrier
- Saturable
- Structure specific
- No energy required
- Mixed order kinetics
- Monosaccharides, Amino acids, Vitamins



Pore Transport

- Also known as convective transport, bulk transport, filtration.
- Important in absorption of low molecular weight (less than 100), low molecular size (smaller than the diameter of the pore) and generally water-soluble drugs.
- The driving force for the passage of the drug is the hydrostatic or the osmotic pressure difference across the membrane.

Rate of absorption via pore Transport depends on the number & size of the pores, & given as follows:

$$\frac{dc}{dt} = \frac{N \cdot R^2 \cdot A \cdot \Delta C}{(\eta)\,(h)}$$

where,

$\frac{dc}{dt}$ = rate of the absorption.

N = number of pores

R = radius of pores

ΔC = concentration gradient

η = viscosity of fluid in the pores

Ionic and Electrochemical Diffusion

- Charge on membrane influences the permeation of drugs.
- Molecular forms of solutes are unaffected by the membrane charge and permeate faster than ionic forms.
- The permeation of anions and cations is also influence by pH.
- Once inside the membrane the cations are attached to negatively charged intracelluar membrane, thus giving rise to an electrical gradient.
- If the same drug is moving from a higher to lower concentration, i.e. Moving down the electrical gradient, the phenomenon is known as electrochemical diffusion.
- Thus, at a given pH, the rate of permeation may be as follows

Unionized molecule > anions > cations

Ion- Pair transport

- It is another mechanism to expalin the absorption of such drugsw which ionize at all pH conditions.
- Quaternary ammonium compounds, sulfonic acids,
- Although they have low o/w partition coefficient values, they will penetrate the membrane by forming reversible neutral complex with endogenous ions

Such neutral complexes have both the required lipophilicity as well as aqueous solubility for passive diffusion.

Endocytosis

- It involves engulfing extracelluar materials within a segment of the cell membrane to form a saccule or a vesicle whcih is then pinched off intracellularly.
- fats, starch, oil soluble vitamins, insulin
- Absorbed into lymphatic circulation by passing first pass metabolism.

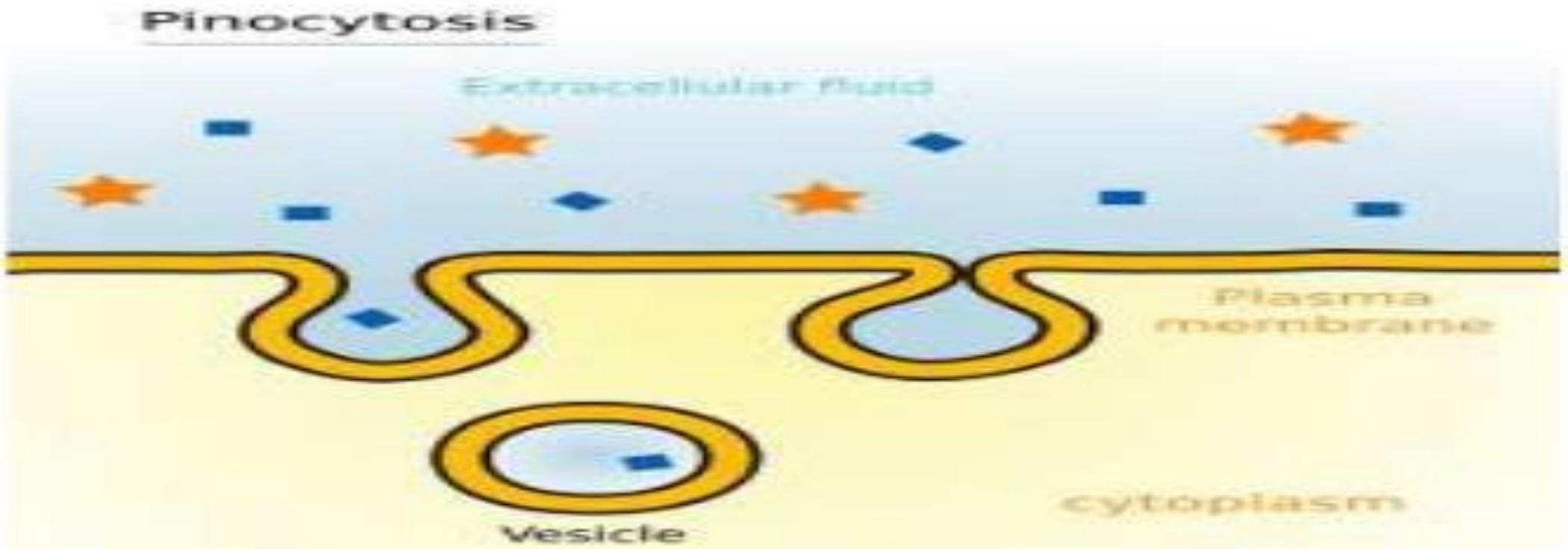
In endocytosis, there are two process

A) Phagocytosis

B) Pinocytosis

Pinocytosis

This process is important in the absorption of oil soluble vitamins & in the uptake of nutrients.



Factor Affecting Absorption of Drugs

A. Pharmaceutical factors:

1. Physicochemical properties of drug
   a. Drug solubility and dissolution rate
   b. Particle size and effective surface area
   c. Polymorphism and amorphism
   d. Pseudopolymorphism(hydrates or solvates)
   e. Salt form of the drug
   f. Lipophilicity of the drug
   g. Drug stability
   h. Stereochemical nature of the drug

2. Formulation factors:

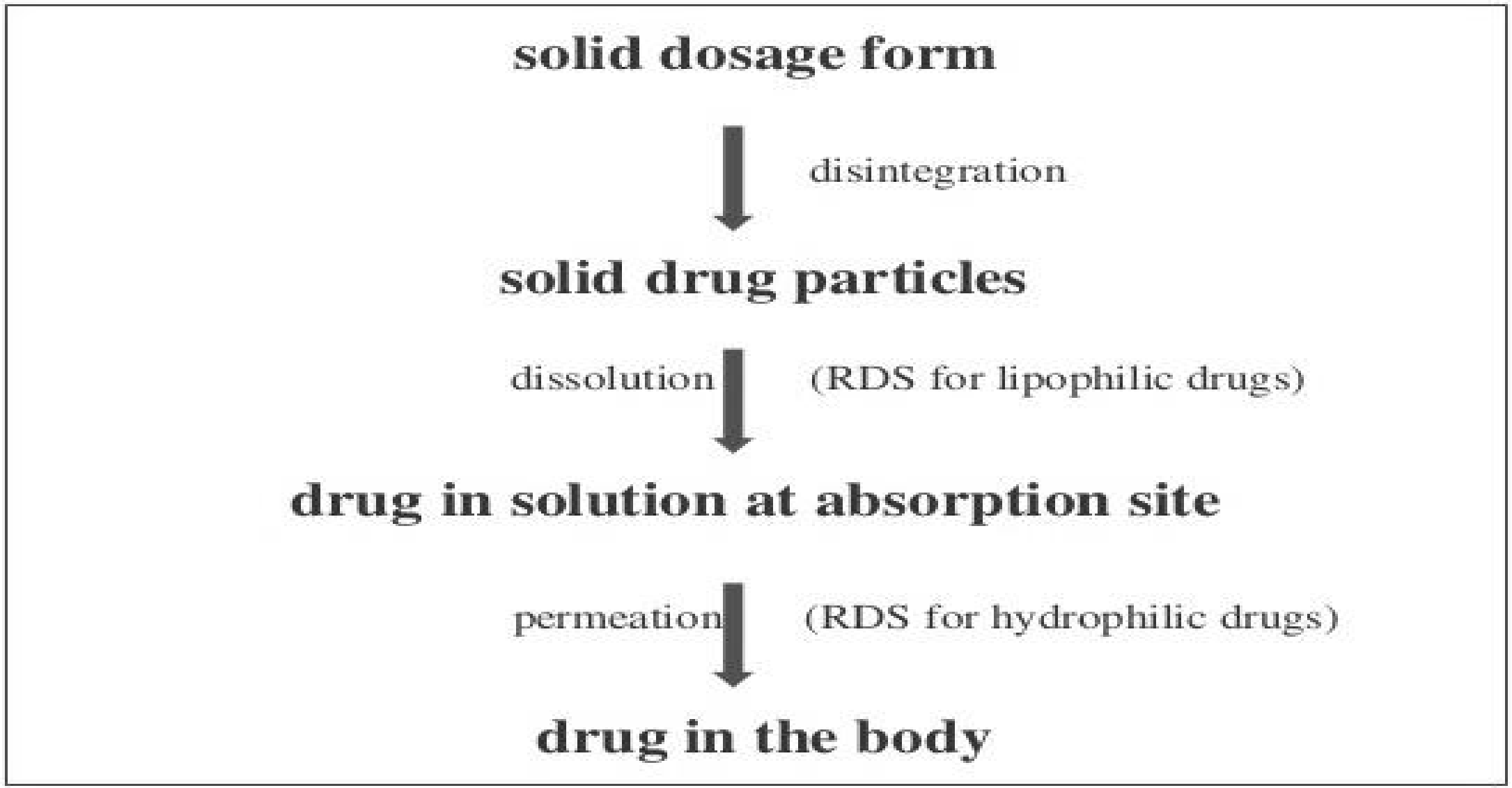
a. disintegration time
b. manufacturing variables
c. nature and type of dosage form
d. pharmaceutical ingredients (excepients)
e. product age and storage conditions

Factor Affecting Absorption of Drugs

B. Patient related factors:

a. age
b. gastric emptying time
c. intestinal transit time
d. Gastrointestinal pH
e. disease state
f. blood flow through the GIT
g. gastrointestinal contents
    a. Other drugs
    b. Food
    c. fuilds
h. presystemic metabolism by
    i. luminal enzymes
    ii. gut wall enzymes
    iii. bacterial enzymes
    iv. hepatic enzymes

a. Drug solubility and dissolution rate :



For Hydrophobic drugs:

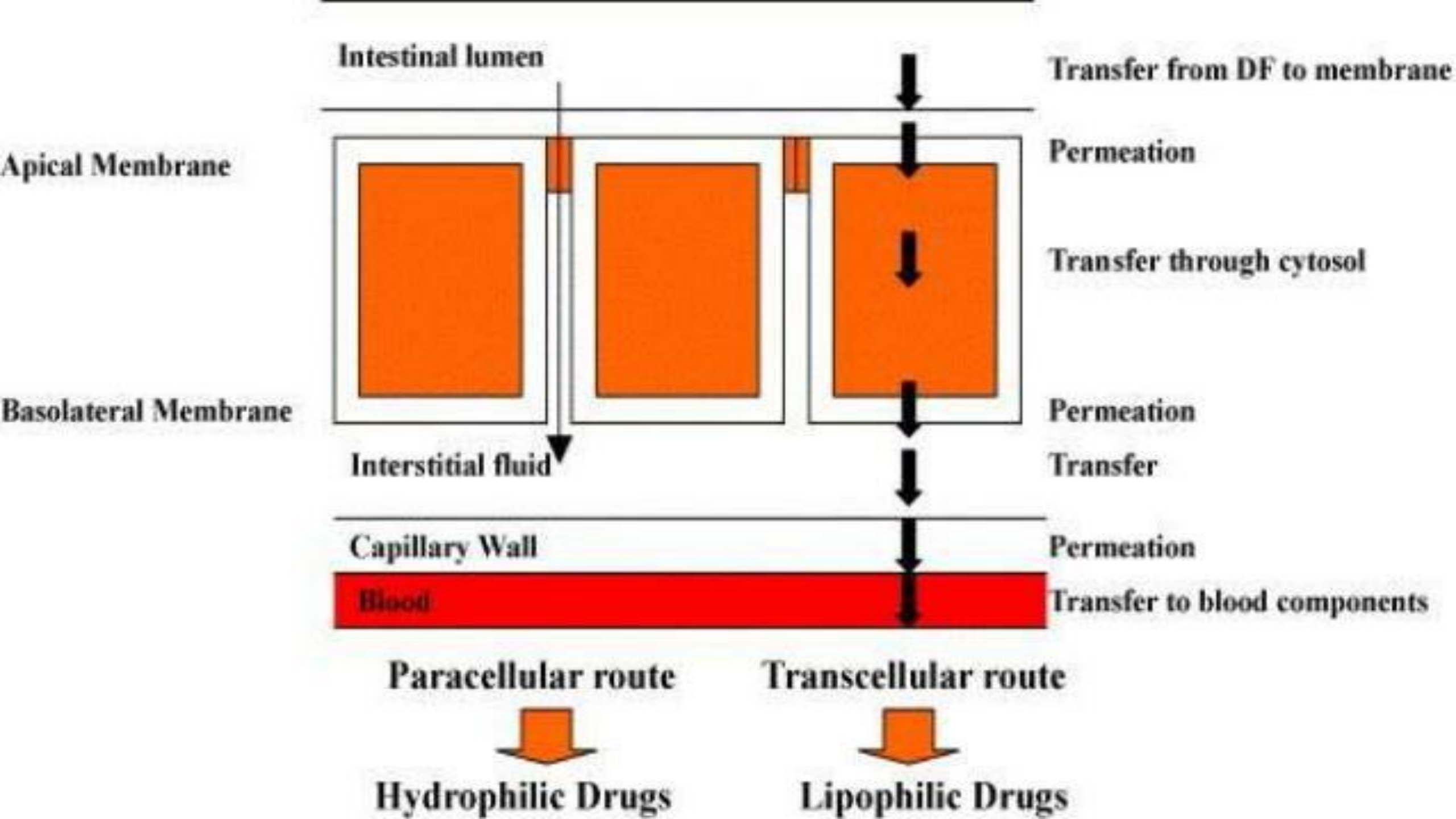
Dissolution is rate limited step.

eg: griseofulvin , spironolactone.

For Hydrophilic drugs:

Permeation is rate limited step.

eg: cromolyn sodium, neomycin.


Intestinal lumen
Transfer from DF to membrane
Apical Membrane
Permeation
Transfer through cytosol
Basolateral Membrane
Permeation
Interstitial fluid
Transfer
Capillary Wall
Permeation
Blood
Transfer to blood components
Paracellular route
Transcellular route
Hydrophilic Drugs
Lipophilic Drugs

b. Particle size and effective surface area of drug:

Smaller the drug particle, greater the surface area.

surface area

- absolute surface area → total surface area of solid surface of particle
- effective surface area → area of solid surface exposed to dissolution medium

✓Smaller the particle size (by micronization) greater is the effective surface area more intimate contact b/w solid surface and aq solvent higher is the dissolution rate increase in absorption efficiency.

✓Particle size reduction has been used to increase the absorption of a large number of poorly soluble drugs, such as bishydroxycoumarin, digoxin, griseofulvin, nitrofurantoin,and tolbutamide.

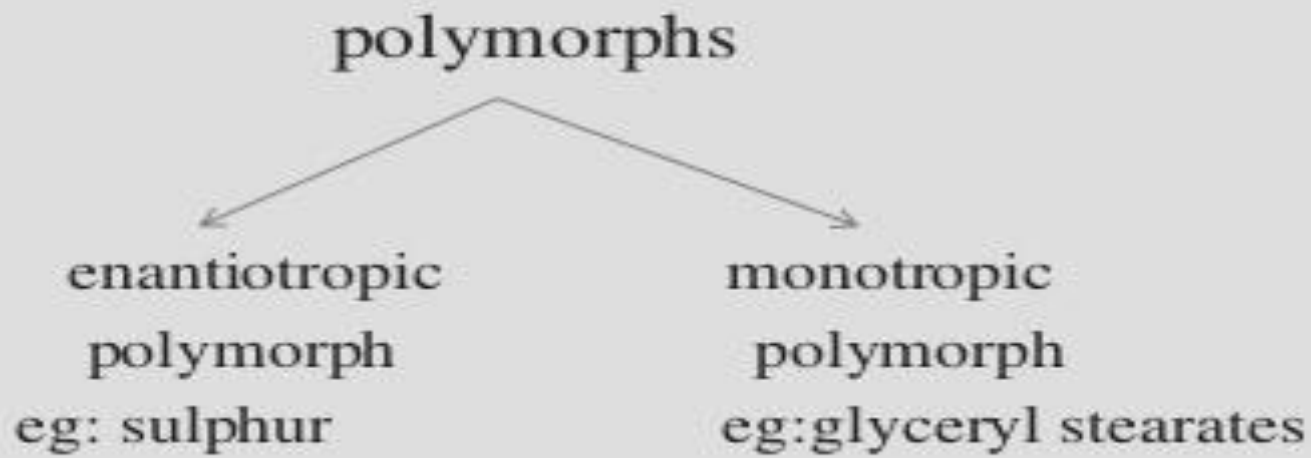
✓Griseofulvin has extremely low aqueous solubility, and material of normal particle size gave rise to poor and erratic absorption.

✓Microsize particles improve absorption, but it is improved even more when it is formulated in ultramicrosize particles as a monomolecular dispersion in polyethylene glycol.

Polymorphism and Amorphism:

Many compounds form crystals with different molecular arrangements, or polymorphs.

These polymorphs may have different physical properties, such as dissolution rate and solubility.



✓40 % of all organic compounds – exist in various polymorphic forms.

✓70% of barbiturates & 65% of sulphonamides exhibit polymorphism.

Amorphous form:

These have greater aqueous solubility than the crystaline forms because the energy required to transfer a molecule from crystal lattice is greater than that required for non-crystalline solid .

eg: amorphous form of novobiocin - 10 times more soluble than crystalline form.

amorphous > metastable> stable

Hydrates or solvates:

- ✓ The stoichiometric type of adducts where the solvent molecule are incorporated with the crystal lattice of the solid are called as solvates.
- ✓ Trapped solvent is the solvent of crystallisation.
- ✓ The solvates can exist in diff crystalline forms called as pseudomorphs and the phenomenon is pseudopolymorphism.
- ✓ When the solvent in association with drug is water, the solvate is known as hydrate.

eg: anhydrous form of theophylline and ampicillin

high aq solubility

dissolve at a faster rate

more bioavailability than their monohydrate & trihydrate forms

Salt form of drug:

✓At given pH, the solubility of drug, whether acidic/basic or its salt, is a constant.

✓While considering the salt form of drug, pH of the diffusion layer is imp not the pH of the bulk of the solution.

For salts of weak acids,

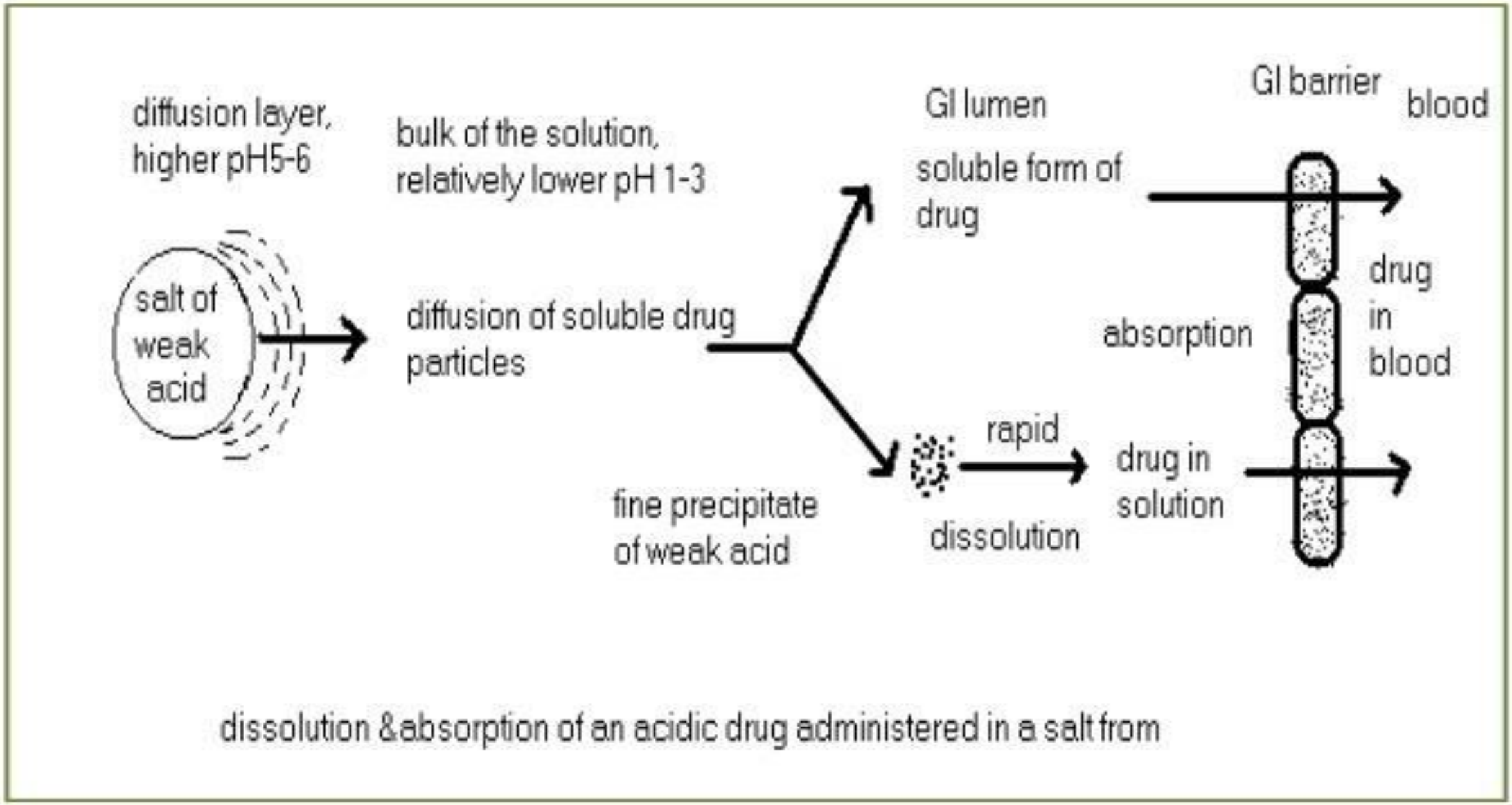
$$[H+]_d < [H+]_b$$

For salts of weak bases,

$$[H+]_d > [H+]_b$$

where $[H+]_d$ = [H+] of diffusion layer

$[H+]_b$ = [H+] of bulk of the solution



dissolution &absorption of an acidic drug administered in a salt from

✓Other approach to enhance the dissolution and absorption rate of certain drugs is by in – situ salt formation

i.e. increasing in pH of microenvironment of drug by incorporating buffer agent.

e.g: aspirin, penicillin

✓But sometimes more soluble salt form of drug may result in poor absorption.

e.g: sodium salt of phenobarbitone and phenobarbitone

↓

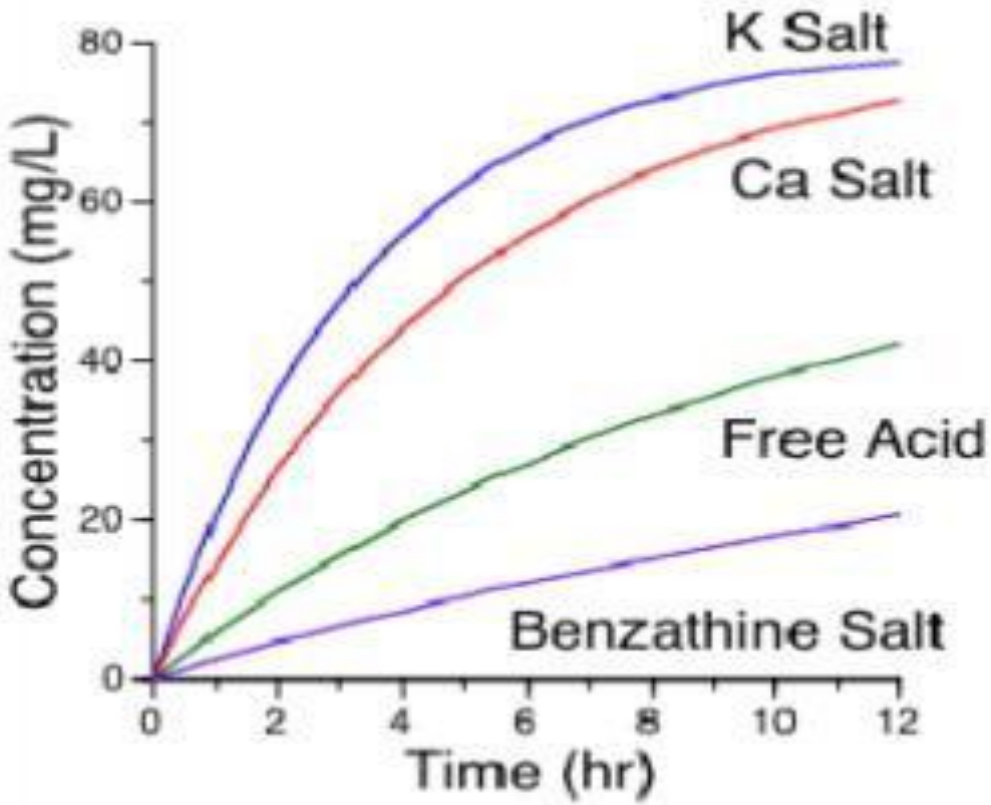
tablet of salt of phenobarbitone swelled

↓

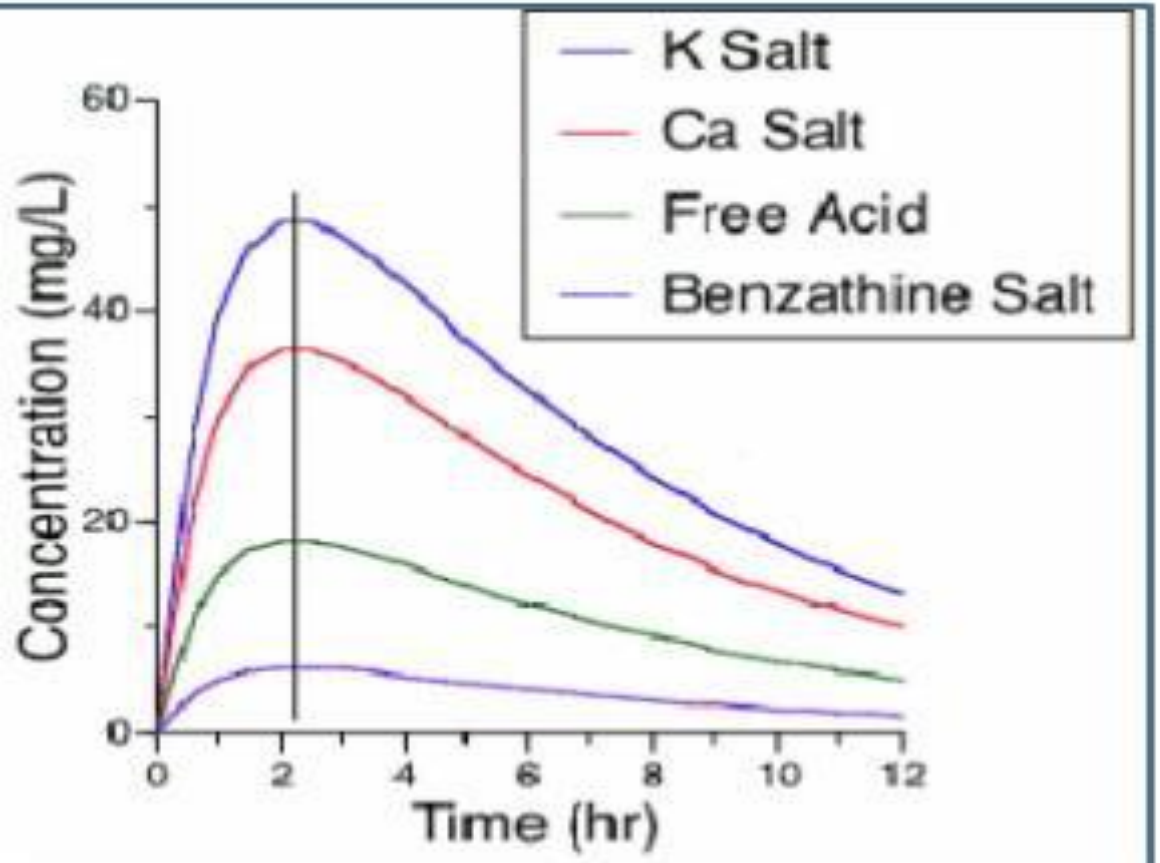
it did not get disintegrate

↓

dissolved slowly & results in poor absorption.



A) It shows the dissolution Profile of various salts



B) It shows the Penicillin plasma Conc. in fasting subjects, after oral Administration of 4×10^5 units of Penicillin in different forms.

Drug pKa & lipophilicity & GI pH --- pH partition hypothesis:

pH – partition theory states that for drug compounds of molecular weight more than 100, which are primarily transported across the biomembrane by passive diffusion,

the process of absorption is governed by

- ✓ pKa of drug
- ✓ The lipid solubility of the unionized drug
- ✓ pH at the absorption site.

Amount of drug that exist in unionized form and in ionized form is a function of pKa of drug & pH of the fluid at the absorption site and it can be determined by Hendersonhesselbach equation: -

For, Acidic drugs

$$pH = pKa + \log \frac{[\text{ionized form}]}{[\text{Unionized form}]}$$

For, Basic drugs

$$pH = pKa + \log \frac{[\text{unionized form}]}{[\text{Ionized form}]}$$

Lipophilicity and drug absorption:

✓Ideally for optimum absorption, a drug should have sufficient aq solubility to dissolve in fluids at absorption site and lipid solubility (Ko/w) high enough to facilitate the partitioning of the rug in the lipoidal biomembrane i.e. drug should have perfect HLB for optimum Bioavailability.

$$K_{o/w} = \frac{\text{Distribution of drug in organic phase (octanol)}}{\text{Distribution of drug in aq phase}}$$

As Ko/w i.e. lipid solubility, i.e. partition coefficient increases percentage drug absorbed increases.


Formulation factors:

1. Disintegration time:

✓Rapid disintegration is important to have a rapid absorption so lower D.T is required.

✓ Now D.T of tablet is directly proportional to – amount o f binder -Compression force.

And one thing should be remembered that in vitro disintegration test gives no means of a guarantee of drugs bioavailability because if the disintegrated drug particles do not dissolve then absorption is not possible.

2. Manufacturing variables: -

a) Method of granulation:

Wet granulation yields a tablet that dissolves faster than those made by other granulating methods. But wet granulation has several limitations like formation of crystal bridge or chemical degradation.

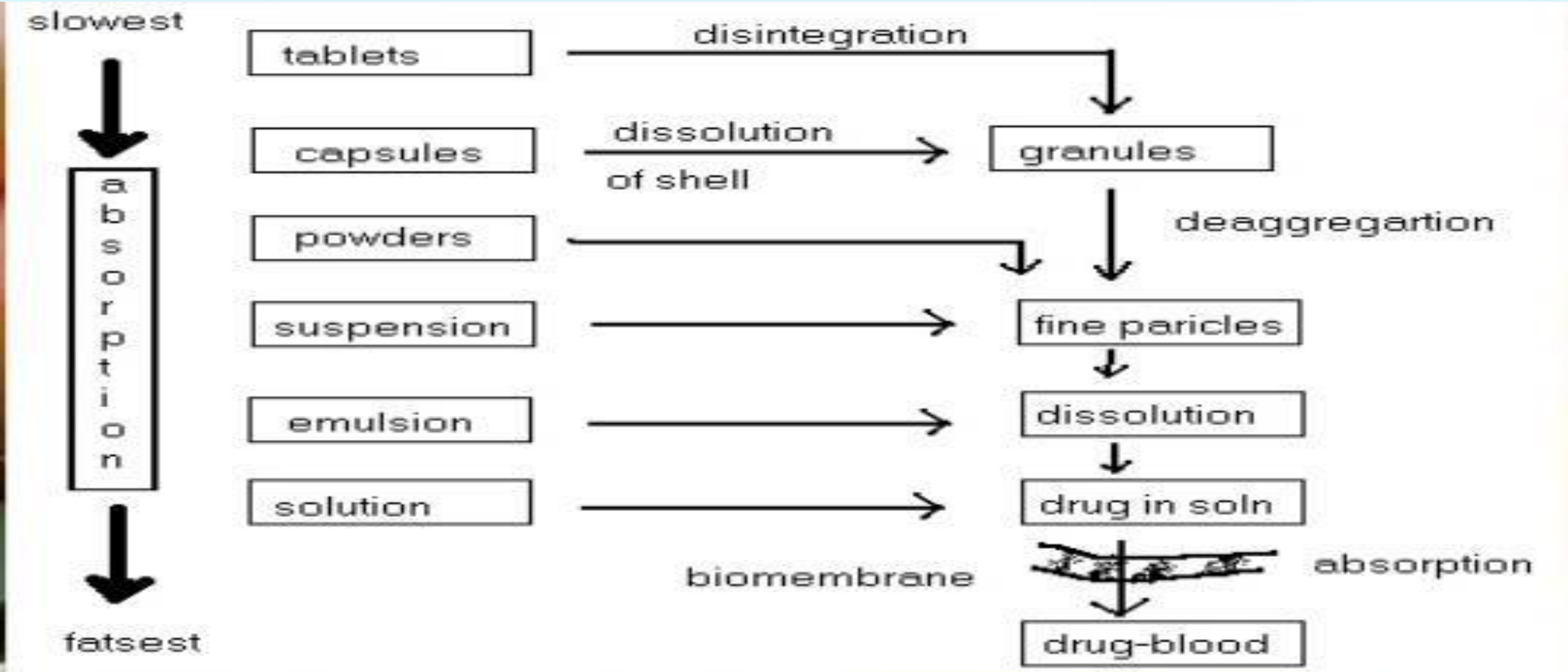
Other superior recent method named APOC (agglomerative phase of communition) that involves grinding of drug till spontaneous agglomeration and granules are prepared with higher surface area. So tablet made up of this granules have higher dissolution rate.

b) Compression force:

Higher compression force yields a tablet with greater hardness and reduced wettability & hence have a long D.T. but on other hand higher compression force cause crushing of drug particles into smaller ones with higher effective surface area which in decrease in D.T.

So effect of compression force should be thoroughly studied on each formulation.

3. Nature and types of dosage form:



Drug formulations are designed to provide an attractive, stable, and convenient method to use products. Conventional dosage forms may be broadly characterized in order of decreasing dissolution rate as solutions, solid solutions, suspensions, capsules and tablets, coated capsules and tablets, and controlled release formulations.

A. Solutions:

Aqueous solutions, syrups, elixirs, and emulsions do not present a dissolution problem and generally result in fast and often complete absorption as compared to solid dosage forms. Due to their generally good systemic availability, solutions are frequently used as bioavailability standards against which other dosage forms are compared.

B.Solid solutions

The solid solution is a formulation in which drug is trapped as a solid solution or monomolecular dispersion in a water-soluble matrix. Although the solid solution is an attractive approach to increase drug absorption, only one drug, griseofulvin, is currently marketed in this form.

C.Suspensions:

- ✓ A drug in a suspension is in solid form, but is finely divided and has a large surface area. Drug particles can diffuse readily between the stomach and small intestine so that absorption is relatively insensitive to stomach emptying rate.
- ✓ Adjusting the dose to a patient's needs is easier with solutions and suspensions than with solid dosage forms. Liquid dosage forms, therefore, have several practical advantages besides simple dissolution rate.
- ✓ However, they also have some disadvantages, including greater bulk, difficulty in handling, and perhaps reduced stability.

D. Capsules and tablets:

✓ These formulations differ from each other in that material in capsules is less impacted than in compressed tablets. Once a capsule dissolves, the contents generally disperse quickly. The capsule material, although water soluble, can impede drug dissolution by interacting with the drug, but this is uncommon.

✓ Tablets generally disintegrate in stages, first into granules and then into primary particles. As particle size decreases, dissolution rate increases due to of increased surface area.

✓Tablet disintegration was once considered a sufficient criterion to predict in vivo absorption.

✓As a general rule, the bio-availability of a drug from various dosage forms decrease in the following order:

Solutions > Emulsions> Suspensions > Capsules >Tablets > Coated Tablets > Enteric coated Tablets > Sustained Release Products.

4. Pharmaceutical ingredients/ excipients

✓ More the no. of excepients in dosage form, more complex it is & greater the potential for absorption and Bioavailability problems.

✓Changing an excipient from calcium sulfate to lactose and increasing the proportion of magnesium silicate, increases the activity of oral phenytoin.

✓ Systemic availability of thiamine and riboflavin is reduced by the presence of Fuller's earth.

✓ Absorption of tetracycline from capsules is reduced by calcium phosphate due to complexation.

✓ Most of these types of interactions were reported some time ago and are unlikely to occur in the current environment of rigorous testing of new dosage forms and formulations.

a) Vehicle:

Rate of absorption – depends on its miscibility with biological fluid.Miscible vehicles (aq or water miscible vehicle) –rapid absorption e.g. propylene glycol.

Immiscible vehicles - absorption –depends on its partitioning from oil phase to aq body fluid.

b) Diluents:

Hydrophilic diluents-form the hydrophilic coat around hydrophobic drug particles –thus promotes dissolution and absorption of poorly soluble hydrophobic drug.

c) Binders & granulating agent :

Hydrophilic binders – imparts hydrophilic properties to granule surface – better dissolution of poorly wettable drug. e.g. starch, gelatin, PVP. More amount of binder – increases hardness of tablet – decrease dissolution & disintegration rate.

d) Disintegrants :

✓ Mostly hydrophilic in nature.

✓Decrease in amount of disintegrants – significantly lowers B.A.

e) Lubricants :

✓Commonly hydrophobic in nature – therefore inhibits penetration of water into tablet and thus dissolution and disintegration.

f) Suspending agents/viscosity agent :

✓Stabilized the solid drug particles and thus affect drug absorption.

✓Macromolecular gum forms unabsorbable complex with drug e.g. Na CMC.

✓ Viscosity imparters – act as a mechanical barrier to diffusion of drug from its dosage form and retard GI transit of drug.

g) Surfactants :

✓May enhance or retards drug absorption by interacting with drug or membrane or both.

✓ Surfactants have been considered as absorption enhancers, again mostly in animals.

✓Polyoxyethylene ethers have been shown to enhance gastric or rectal absorption of lincomycin, penicillin, cephalosporins, and fosfomycin in rats and rabbits.

✓ However, in humans, oral polyoxyethylene-20-oleyl ether resulted in poor and variable insulin absorption.

✓In general, unionic surfactants have little effect on membrane structure but cationic

✓Surfactants have been associated with reversible cell loss and loss of goblet cells.

✓ Physiologic surfactants – bile salts – promotes absorption

e.g. Griseofulvin, steroids

✓ It may decrease absorption when it forms the unabsorbable complex with drug above CMC.

Colourants:

✓Even a low concentration of water soluble dye can have an inhibitory effect on dissolution rate of several crystalline drugs.

✓The dye molecules get absorbed onto the crystal faces and inhibit the drug dissolution.

e.g: Brilliant blue retards dissolution of sulfathiazole.

5. Product age and storage conditions :

✓Product aging and improper storage conditions adversely affect B.A.

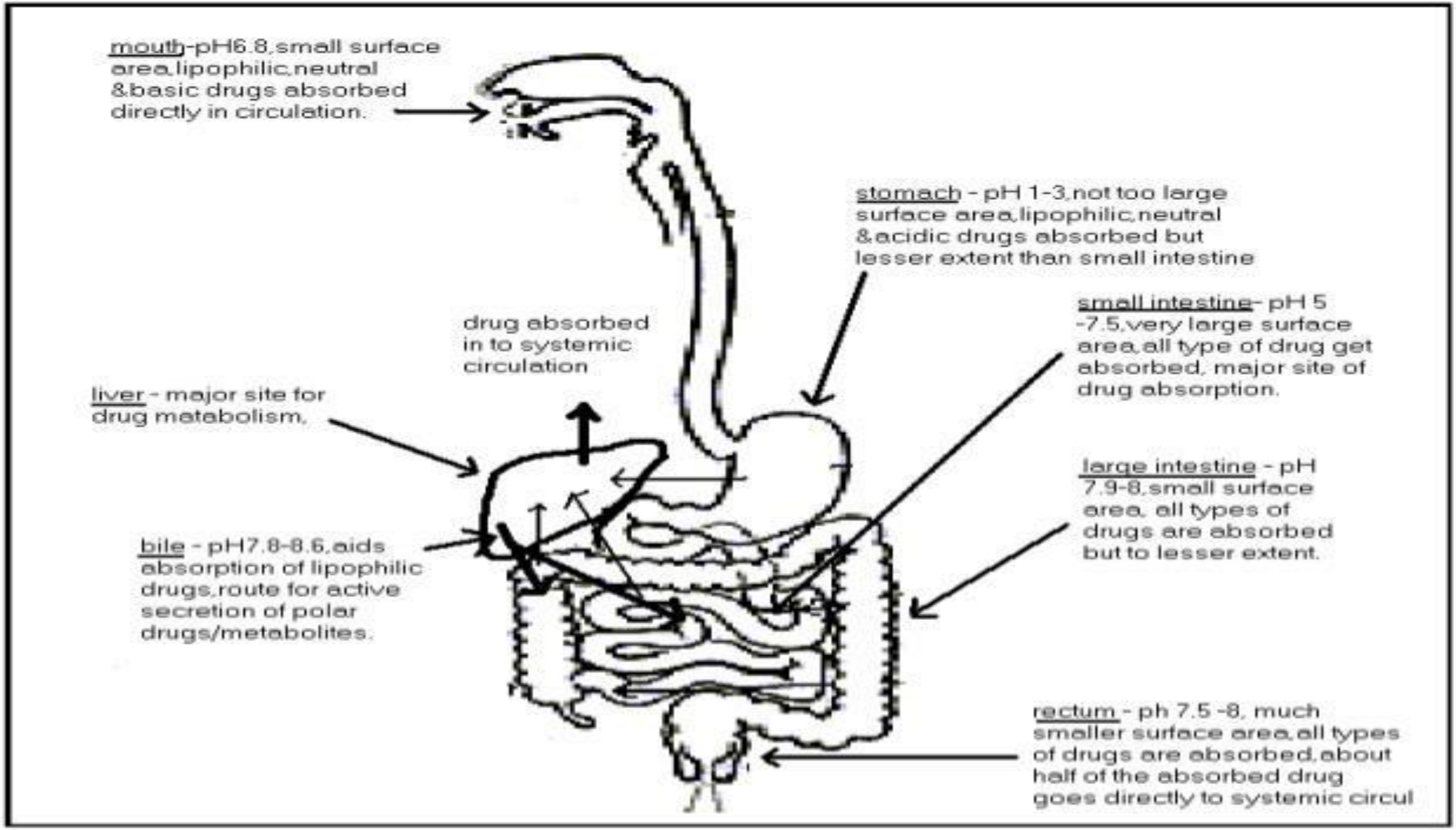
e.g:precipitation of drug in solution decrease rate of Change in particle size of suspension drug dissolution & Hardening of tablet & absorption.

Patient Related Factors

- Gastric emptying apart from the dissolution of drug and as permeation through biomembrane, the passage from stomach to small intestine, called gastric emptying also be a rate limiting step in absorption because the major site of drug absorption is intestine.

It is advisable where,

- ✓ Rapid onset of drug is desired,
- ✓ Drug not stable in gastric fluid,
- ✓ Dissolution occurring in intestine


mouth-pH6.8,small surface area,lipophilic,neutral &basic drugs absorbed directly in circulation.
stomach - pH 1-3,not too large surface area,lipophilic,neutral &acidic drugs absorbed but lesser extent than small intestine
small intestine- pH 5 -7.5,very large surface area,all type of drug get absorbed, major site of drug absorption.
drug absorbed in to systemic circulation
liver - major site for drug metabolism.
large intestine - pH 7.9-8,small surface area, all types of drugs are absorbed but to lesser extent.
bile - pH7.8-8.6,aids absorption of lipophilic drugs,route for active secretion of polar drugs/metabolites.
rectum - ph 7.5 -8, much smaller surface area,all types of drugs are absorbed,about half of the absorbed drug goes directly to systemic circul

Delay in gastric emptying is recommended in particular where:

Food promotes drug dissolution and absorption

eg: griseofulvin.

The drugs dissolve slowly. Disintegration and dissolution of dosage form is promoted by gastric fluids.

Gastric emptying is first order process. Several parameters used to quantify are:

- ✓***Gastric emptying rate:*** speed at which stomach contents empties into intestine.
- ✓***Gastric emptying time*:** time required for gastric contents to empty into small intestine
- ✓***Gastric emptying*** $\mathbf{t_{1/2}}$**:** time taken for half of the stomach contents to empty

Factors influencing gastric emptying:

Volume of meal: larger the bulk of meals, longer the gastric emptying time. An initial rapid rate of emptying observed with large volume of meal and an initial lag phase in emptying of small volume of meal.

Since gastric emptying is first order, a plot of volume of contents remaining in stomach vs time yields a straight line.

Composition of meal:

carbohydrates > proteins> fats

Delayed gastric emptying with fatty meal, is beneficial for the absorption of poorly soluble drugs like griseofulvin.

Physical state and viscosity of meal:

Liquid meals take less than hour to empty whereas a solid meal may take as long as 6 to 7 hours.

Temperature:

High or low temperature of injested fluid reduces the gastric emptying.

Gastro intestinal ph:

Retarded at low stomach ph and promoted at high ph. The inhibitory effect of various acids on emptying decreases with increase in mol wt, order is:

Hcl > acetic > lactic > tartaric> citric

Electrolytes and osmotic ph: water, isotonic solutions and of low salt concentration empty rapidly whereas high electrolyte conentration decreases gastric emptying.

Drugs that retard gastric emptying include

Poorly soluble antacids: aluminium hydroxide

Anticholinergics: atropine

Narcotic analgesics: morphine

Tricyclic anti depressents: imipramine

Disease state: like gastroenteritis, gastric ulcer, pyloric stenosis retard gastric emptying rate.

Intestinal transit:

Since small intestine is the major site for absorption of most drugs, long intestinal transit time is desirable for complete drug absorption.

Intestinal region	Transit time
Duodenum	5 min
Jejunum	2 hrs
Ileum	3to 6 hrs
Caecum	0.5 to 1hr
Colon	6 to 12 hrs

Delayed transit time is desirable for:

- ✓ Drugs that dissolve their dosage form.
- ✓ Drugs that dissolve only in intestine.
- ✓ Drugs absorbed from specific sites in the intestine.
- ✓ Laxatives promote the rate of intestinal transit.

Anticholinergic drugs: retard gastric and intestinal transit promote absorption of poorly soluble drugs

eg:propantheline

Gastro intestinal pH:

The GI ph generally increases as one moves down the stomach to the colon and rectum.GI ph influence absorption in several ways.

Disintegration:

Enteric coated formulations: ⟹ coat dissolves only in intestine followed by disintegration.

Dissolution:

weakly acidic drugs: dissolve rapidly in alkaline ph of intestine

Weakly basic drugs: dissolve in acidic ph of stomach

Absorption: depends on drug pKa and whether its an acidic or basic drug, GI ph influences drug absorption by determining amount of drug that would exist in unionised form at the site of absorption.

Stability: acidic stomach ph- affect degradation of pencillin G and erythromycin

Can be overcome by preparing prodrugs of such drugs . eg: carindacillin and erythromycin estolate.

Presystemic metabolism:

For a drug administration orally, the 2 main reasons for its decreased bioavailability are:

a. Decreased absorption and

b. First pass metabolism

✓The loss of drug through biotransformation by such eliminating organs during its passage to systemic circulations called as first pass or presystemic metabolism.

The 4 primary systems which effect presystemic metabolism of a drug are:

a. Luminal enzymes

b. Gut wall enzymes

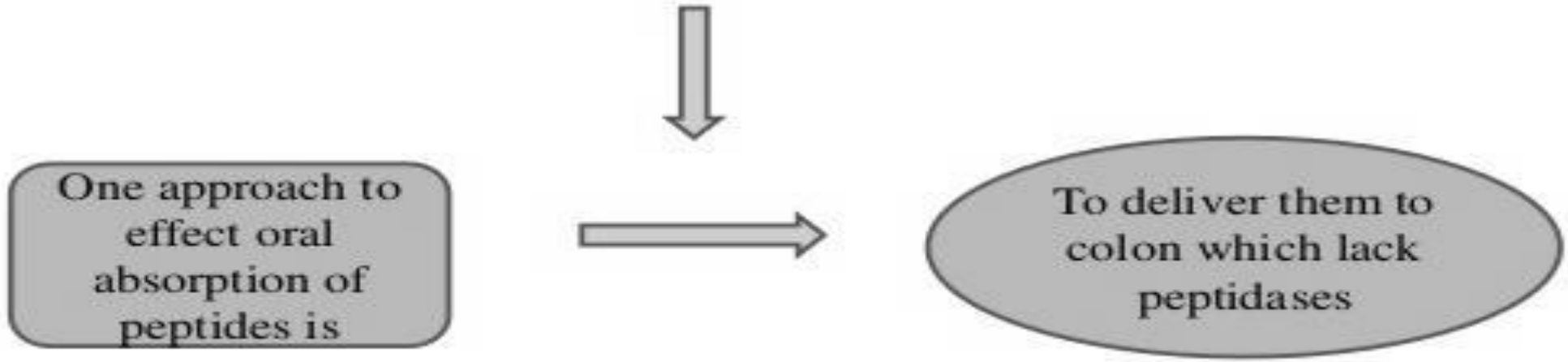
c. Bacterial enzymes

d. Hepatic enzymes

Luminal enzymes:

These are present in gut fluids and include enzymes from intestinal and pancreatic secretions. latter contain hydrolases which hydrolyse ester drugs.

chloramphenicol palmitate ⇒ active chloramphenicol, and which split amide linkages and inactivate proteins.



Gut wall enzymes: also called as mucosal enzymes present in stomach, intestine and colon.

- ✓ **Alcohol dehydrogenase:** enzyme of stomach mucosa inactivates ethanol.
- ✓ **Intestinal mucosa:** contains both phase I and phase II enzymes.

  eg: sulphation if ethinyl estradiol .
- ✓ **Colonic mucosa:** also contains both phase I and phase II enzymes.

Bacterial enzymes: colonic generally render a drug more active or toxic on biotransformation.

eg: sulphasalazine —hydrolyzation→ sulphapyridine & 5-aminsalicylic acid

(drug in ulcerative colitis)

Enzymes hydrolyse conjugates of drugs actively secreted via bile such as glucoronides of digoxin and oral contraceptives

Hepatic enzymes:

several drugs undergo first pass hepatic metabolism, the highly extracted ones being isoprenaline, propranolol, alprenolol, pentoxyphylline, nitroglycerine, diltiazem, lidocaine, morphine etc.

Gastrointestinal diseases:

Altered GI motility:

Gastrointestinal diseases and infections:

- ✓ Two of the intestinal disorders related with malabsorption syndrome that influence drug availability are celiac disease and Crohn's disease.
- ✓ Crohn's disease that can alter absorption pattern are altered gut wall microbial flora, decreased gut surface area and intestinal transit rate.
- ✓ GI infections like shigellosis, gastroenteritis, cholera and food poisoning also result in malabsorption.

Gastrointestinal surgery:

Gastrectomy can result in drug dumping in the intestine, osmotic diarrhea and reduced intestinal transit time.

Cardiovascular diseases:

Several changes associated with congestive cardiac failure influence bioavailability of a drug.

Hepatic diseases:

Disorders such as hepatic cirrhosis influence bioavailability mainly of drugs that undergo considerable first-pass hepatic metabolism.

e.g. propranolol.

Gastrointestinal Contents: A number of contents can influence drug absorption as follows:

✓ **Food-drug interactions:** Presence of food may either delay, reduce, increase or may not affect drug absorption.

Delayed	Decreased	Increased	Unaffected
Aspirin	Pencillins	Griseofulvin	Methyldopa
Paracetamol	Erythromycin	Nitrofurantoin	Propylthiouracil
Diclofenac	Ethanol	Diazepam	Sulfasomidine
Nitrofurantoin Dioxin	Tetracyclines Levodopa Iron	Actively absorbed vitamins	

Fluid volume:

Administration of drug with large fluid volume results in better dissolution, rapid gastric emptying and enhanced absorption.

e.g: erythromycin

Interaction of drug with normal GI constituents:

- ✓ The GIT contains a number of normal constituents such as mucin, bile salts and enzymes which influence drug absorption.
- ✓ Mucin a protective mucopolysaccharide that lines the GI mucosa, interacts with streptomycin and certain quaternary ammonium compounds and retards their absorption.

Drug-drug interactions in the GIT:

These interactions can be either physicochemical or physiological.

Physicochemical interactions are due to :

- ✓ Adsorption: antidiarrhoeal preparations containing adsorbents like attapulgite or kaolin-pectin retard absorption of number of drugs co-administered with them.

  e.g: promazine, linomycin.

- ✓Complexation: unabsorbable complexes are formed.

  e.g: antacids or mineral substances containing heavy metals such as Al, Ca+2 , Mg+2 retard absorption of tetracycline by forming unabsorbable complexes.

Physiological interactions are due to :

- ✓ **Decreased GI transit:**

Anticholinergics like propantheline retard GI motility and promote absorption of drugs like ranitidine and digoxin & delay absorption of paracetemol and sulphamethoxazole.

- ✓ **Increased gastric emptying:**

Metoclopramide promotes GI motility and enhances absorption of tetracycline, levodopa.

Be miserable.
Or motivate yourself.
Whatever has to be
done, it's always your
choice.

Thank
YOU