

Factors Influencing Drug Absorption

Presented By

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❖ PHARMACOKINETICS:

➤ *Pharmacokinetics* is the science of the kinetics of drug absorption, distribution, and elimination (i.e., excretion and metabolism).

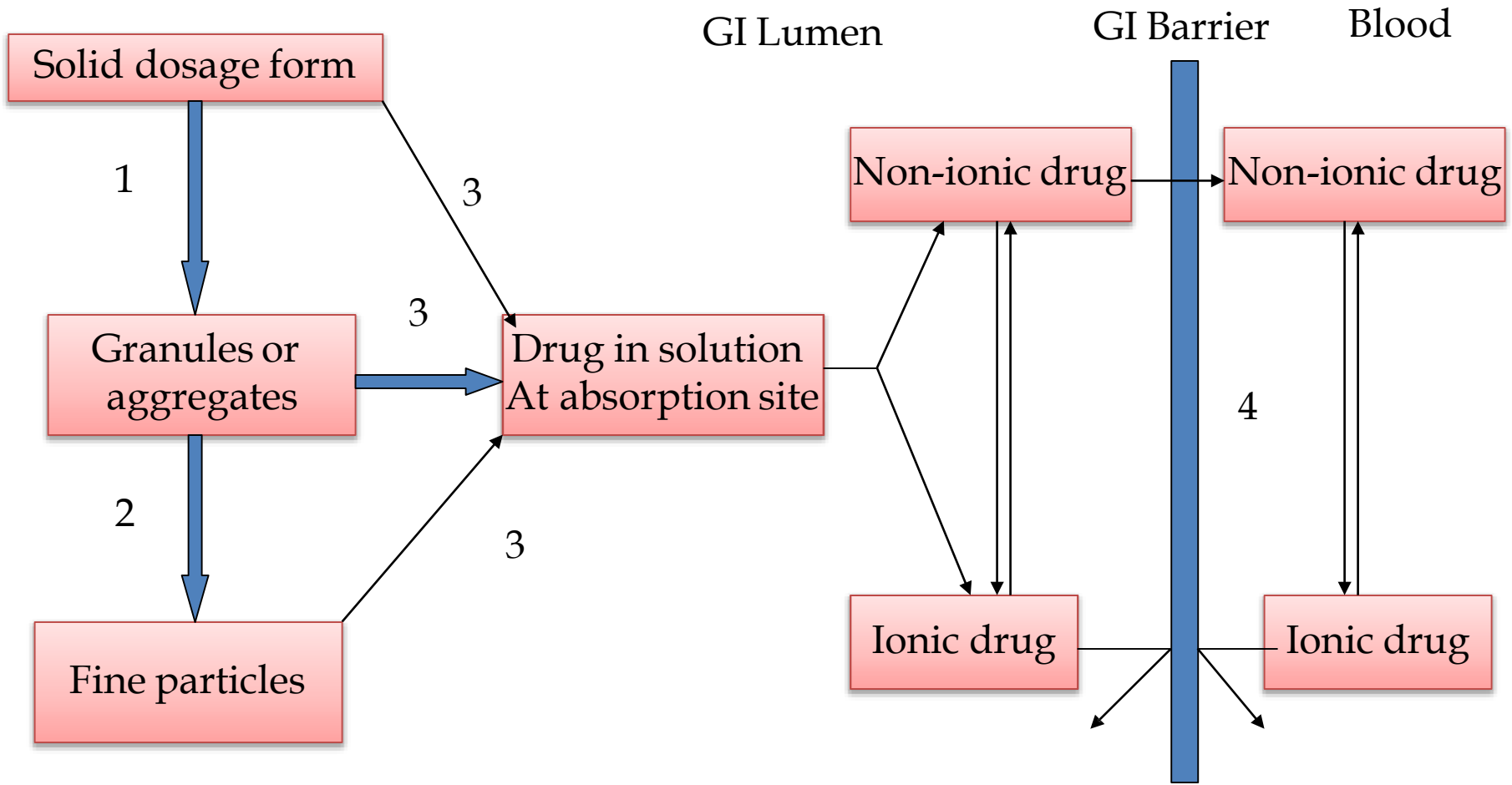
❖ PHARMACODYNAMICS:

➤ *Pharmacodynamics* refers to the relationship between the drug concentration at the site of action (receptor) and pharmacologic response.

❖ ABSORPTION:

➤ “The process of movement of unchanged drug from the site of administration to systemic circulation is called as absorption”.

➤ It 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.



- Means of
- 1 Disintegration
 - 2 Deaggregation
 - 3 Dissolution
 - 4 Absorption

Sequence of events in the absorption of drugs from orally administered solid dosage forms

❖ FACTORS AFFECTING DRUG ABSORPTION

A. Physicochemical factors:

- 1) Drug solubility & dissolution rate
 - 2) Particle size & effective surface area
 - 3) Polymorphism & amorphism
 - 4) Pseudopolymorphism (hydrates/solvates)
 - 5) Salt form of the drug
 - 6) Lipophilicity of the drug
 - 7) pKa of drug & gastrointestinal pH
 - 8) Drug stability
- pH- Partition hypothesis

B. Pharmaceutical factors :

- 1) Disintegration time (tablets/capsules)
- 2) Dissolution time
- 3) Manufacturing variables
- 4) Pharmaceutical ingredients (excipients/adjuvants)
- 5) Nature & type of dosage form
- 6) Product age & storage condition

C. Patient related factors :

- 1) Route of administration
- 2) Membrane physiology
 - a) Nature of cell membrane
 - b) Transport processes
- 3) Age
- 4) Gastric emptying time
- 5) Intestinal transit time

- 6) Gastrointestinal pH
- 7) Disease states
- 8) Blood flow through the GIT
- 9) Gastrointestinal contents:
 - a) Food- drug interactions
 - b) Fluids
 - c) Other normal GI contents
- 10) Presystemic metabolism by:
 - a) Luminal enzymes
 - b) Gut wall enzymes
 - c) Bacterial enzymes
 - d) Hepatic enzymes

PHYSICOCHEMICAL FACTORS

1) Drug solubility & dissolution rate :

The rate determining steps in absorption of orally administered drugs are:

1. Rate of dissolution
2. Rate of drug permeation through the bio-membrane.

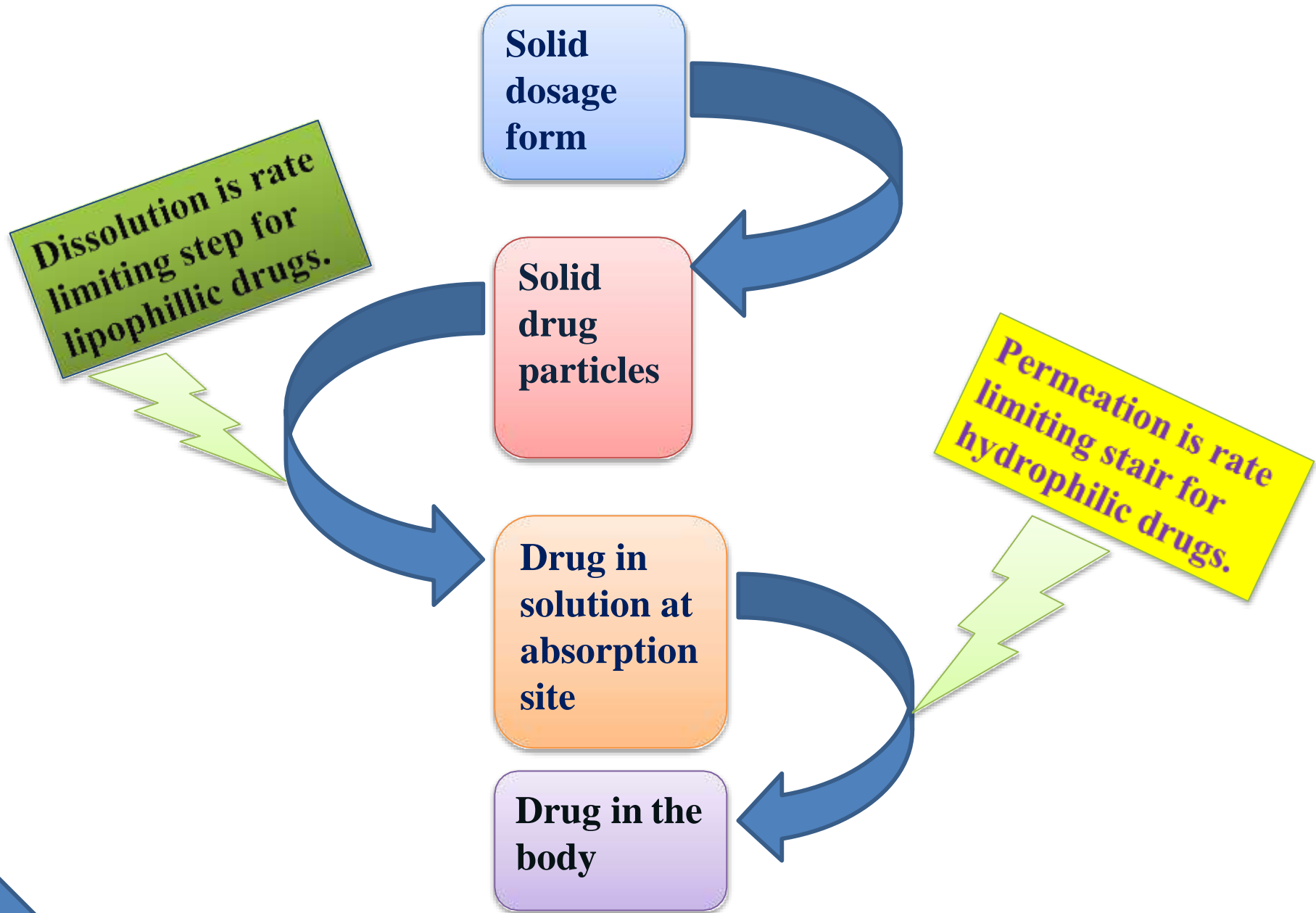
➤ Dissolution is rate determining step for hydrophobic & poorly aqueous soluble drugs.

E.g. Griesiofulvin & Spironolactone.

➤ Permeation is the rate determining step for hydrophilic & high aqueous soluble drugs.

E.g. cromolyn sodium or Neomycin.

➤ Prerequisite for the absorption of a drug is that it must be present in aqueous solution & this depends on drug's aqueous solubility & its dissolution rate.



2) Particle size and effective surface area:

- Particle size may play a major role in drug absorption.
- Dissolution rate of solid particles is proportional to surface area.
- Smaller particle size, greater surface area then higher will be dissolution rate, because dissolution is thought to take place at the surface area of the solute (Drug).
- Particle size reduction has been used to increase the absorption of a large number of poorly soluble drugs.
- E.g. Bishydroxycoumarin, digoxin, griseofulvin
- Two types of surface area
 - 1) Absolute surface area
 - 2) Effective surface area

➤ In absorption studies the effective surface area is of much more important than absolute.

➤ To increase the effective surface area, we have to reduce the size of particles up to 0.1 micron. So these can be achieved by “micronisation process”.

➤ But in these case one most important thing to be keep in mind that which type of drug is micronised if it is:

a) HYDROPHILIC OR b) HYDROPHOBIC

a) HYDROPHILIC DRUGS:

➤ In hydrophilic drugs the small particles have higher energy than the bulk of the solid resulting in an increased interaction with the solvent.

▪ Examples,

1. Griesiofulvin – Dose reduced to half due to micronisation.

2. Spironolactone – the dose was decreased to 20 times.

3. Digoxin – the bioavailability was found to be 100% in micronized tablets.

➤ After micronisation it was found that the absorption efficiency was highly increased

b) HYDROPHOBIC DRUGS:

➤ In this micronisation techniques results in decreased effective surface area & thus fall in dissolution rate.

REASONS:

1) The hydrophobic surface of the drugs adsorbs air on to their surface which inhibits their wettability.

2)The particles reaggregates to form large particles due to their high surface free energy, which either float on the surface or settle on the bottomof the dissolution medium.

3)Electrically induced agglomeration owing to surface charges prevents intimate contact of the drug with the dissolution medium.

➤ Such hydrophobic drugs can be converted to their effective surface area.

a) Use of surfactant as a wetting agent which

- decrease the interfacial tention.

- displace the absorbed air with the solvent. Eg. phenacetin

b) Add hydrophilic diluents like PEG, PVP, dextrose etc.

which coat the surface of hydrophobic drug particles.

3) Polymorphism & Amorphism:

➤ Depending upon the internal structure, a solid can exist either in a crystalline or amorphous form. When a substance exists in more than one crystalline form, the different forms are designated as polymorphs, and the phenomenon as polymorphism.

➤ Polymorphs are of two types:

1) **Enantiotropic polymorph** is the one which can be reversibly changed into another form by altering the temperature or pressure. E.g. Sulfur.

2) **Monotropic polymorph** is the one which is unstable at all the temperature or pressures. E.g. glyceryl strarates.

➤ The polymorphs differ from each other with respect to their physical properties such as solubility, melting point, density, hardness and compression characteristics. Thus, these change in physical properties affect the dissolution properties and hence the absorption.

➤ E.g. The vitamin riboflavin exists in several polymorphic forms, polymorphic form III of riboflavin is 20 times more water soluble than the form I.

➤ **AMORPHISM:** Some drugs can exist in amorphous form (i.e. having no internal crystal structure). Such drug represents the highest energy state.

➤ They have greater aqueous solubility than the crystalline forms because a energy required to transfer a molecule from the crystal lattice is greater than that required for non-crystalline (amorphous form).

➤ For example: the amorphous form of Novobiocin is 10 times more soluble than the crystalline form. Thus, the order of different solid dosage forms of the drugs is

Amorphous > Meta-stable > stable

4) Pseudopolymorphism: When the solvent molecules are entrapped in the crystalline structure of the polymorph, it is known as pseudo-polymorphism.

➤ **Solvates:** the stoichiometric type of adducts where the solvent molecules are incorporated in the crystal lattice of the solid are called as the solvates, and the trapped solvent as solvent of crystallization.

➤ **Hydrates:** when the solvent in association with the drug is water, the solvate is known as a hydrate.

➤ Hydrates/Solvates are pseudo-polymorphs where hydrates are less soluble and solvates are more soluble and thus affect the absorption accordingly.

➤ For example: n-pentanol solvates of fludrocortisone and succinyl-sulfathiazole have greater aqueous solubility than the non-solvates.

(5) Salt form of drug:

- While considering the salt form of drug, pH of the diffusion layer is important not the pH of the bulk of the solution.
- Example of salt of weak acid. - It increases the pH of the diffusion layer, which promotes the solubility and dissolution of a weak acid and absorption is bound to be rapid.
- Other approach to enhance the dissolution and absorption rate of certain drugs is the formation of in – situ salt formation i.e. increasing in pH of microenvironment of drug by incorporation of a buffering agent. E.g. aspirin, penicillin
- But sometimes more soluble salt form of drug may result in poor absorption. e.g. sodium salt of phenobarbitone viz., its tablet swells and did not get disintegrate, thus dissolved slowly and results in poor absorption.

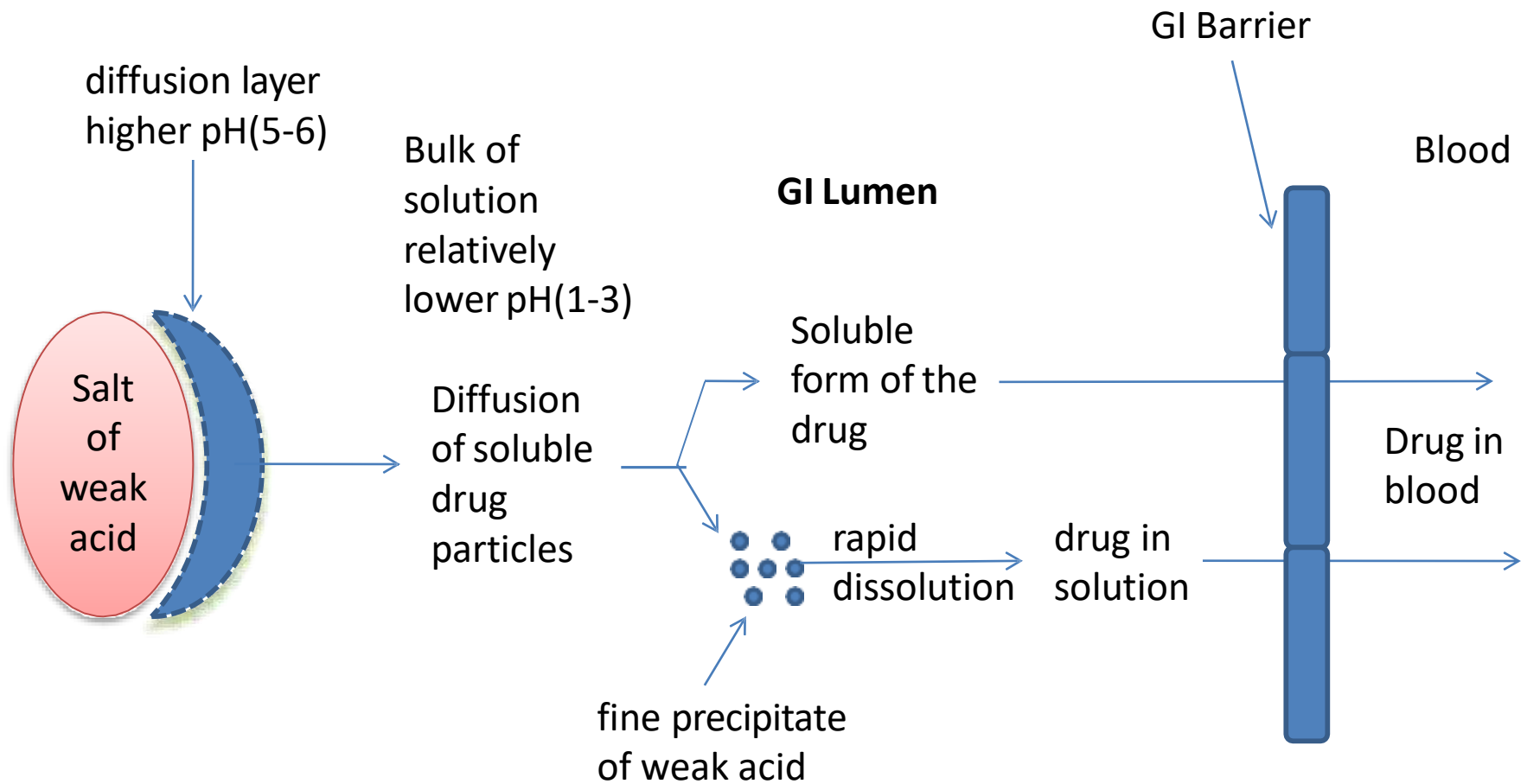


Fig: Dissolution and absorption of an acidic drug administered in a salt form

6 & 7) pH-Partition hypothesis:

➤ The theory states that for drug compounds of molecular weight more than 100, which are primarily transported across the bio-membrane by passive diffusion, the process of absorption is governed by:

1. The dissociation constant pK_a of the drug.
2. The lipid solubility of the un-ionized drug.
3. The pH at the absorption site.

A) DRUG pKa AND GI pH:

➤ Amount of drug that exists in un-ionized form and in ionized form is a function of pKa of drug and pH of the fluid at the absorption site, and it can be determined by **Handerson-Hasselbach equation**:

• **For weak acids,**

$$\text{pH} = \text{pKa} + \log \frac{[\text{ionized}]}{[\text{un-ionized}]} \quad \dots(1.1)$$

$$\% \text{ Drug ionized} = \frac{10^{\text{pH}-\text{pKa}}}{1+10^{\text{pH}-\text{pKa}}} \times 100 \quad \dots (1.2)$$

• **For weak bases,**

$$\text{pH} = \text{pKa} + \log \frac{[\text{un-ionized}]}{[\text{ionized}]} \quad \dots(1.3)$$

$$\% \text{ Drug ionized} = \frac{10^{\text{pKa}-\text{pH}}}{1+10^{\text{pKa}-\text{pH}}} \times 100 \quad \dots(1.4)$$

➤ If there is a membrane barrier that separates the aqueous solutions of different pH such as the GIT and the plasma, then the theoretical ratio R of drug concentration on either side of the membrane can be given by the following equations:

• **For weak acids,**

$$R_a = \frac{C_{GIT}}{C_{plasma}} = \frac{1 + 10^{pH_{GIT} - pK_a}}{1 + 10^{pH_{plasma} - pK_a}} \dots (1.5)$$

• **For weak bases,**

$$R_b = \frac{C_{GIT}}{C_{plasma}} = \frac{1 + 10^{pK_a - pH_{GIT}}}{1 + 10^{pK_a - pH_{plasma}}} \dots (1.6)$$

B) LIPOPHILICITY AND DRUG ABSORPTION:

➤ The lipid solubility of the drug is determined from its oil/water partition coefficient (K_o/w) value, whereby the increase in this value indicates the increase in percentage drug absorbed.

➤ $K_o/w = \frac{\text{Distribution of the drug in the organic phase (octanol)}}{\text{Distribution of the drug in the aqueous phase}} \dots\dots\dots (1.7)$

8) Drug stability:

- A drug for oral use may destabilize either during its shelf life or in the GIT.
- Two major stability problems resulting in poor bioavailability of an orally administered drug are _ degradation of the drug into inactive form, and interaction with one or more different component(s) either of the dosage form or those present in the GIT to form a complex that is poorly soluble or is unabsorbable.

PHARMACEUTICAL FACTORS

1. Disintegration time (tablets/capsules):

- Rapid disintegration is important to have a rapid absorption so lower disintegration time is required.
- Disintegration time of tablet is directly proportional to – amount of binder & Compression force.
- 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.
- E.g. COATED TABLETS: they have long disintegration time.
- Fast dispersible tablets have short disintegration time.

2) Dissolution time:

- Dissolution is a process in which a solid substance solubilises in a given solvent i.e... mass transfer from the solid surface to the liquid phase.
- Dissolution time is also an important factor which affect the drug absorption.

3) Manufacturing variables:

- Several manufacturing processes influence drug dissolution from solid dosage forms.
- For example: For tablet it is
 - ✓ Method of granulation
 - ✓ Compression force

▪ **Method of granulation:**

- The wet granulation process is the most conventional technique
- The tablets that dissolve faster than those made by other granulation methods.
- But wet granulation has several limitations like formation of crystal bridge or chemical degradation.
- The method of direct compression force has been utilized to yield the tablets that dissolve at a faster rate.

▪ **Compression force:**

- The compression force employed in tableting process influence density, porosity, hardness, disintegration time and dissolution rate of tablets.
- Higher compression force increases the density and hardness of the tablet, decreases porosity and hence penetrability of the solvent into the tablet and thus in slowing of dissolution and absorption (Fig .A)

- On the other hand, higher compression force causes deformation, crushing or fracture of drug particles into smaller ones and causes a large increase in effective surface area. This results in an increase in dissolution rate of tablets (Fig B)
- A combination of both the curves A and B is also possible as shown in curves C & D.

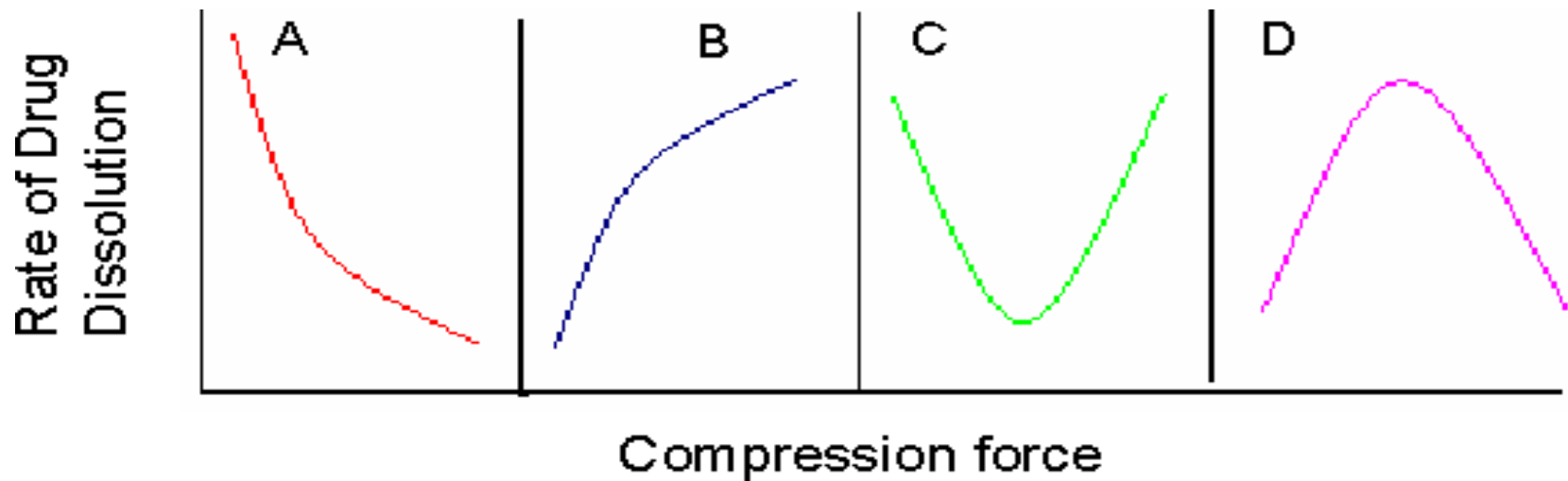


Fig. Influence of compression force on the dissolution rate of tablets

4) Pharmaceutical ingredients (excipients/adjuvants):

- More the number of Excipients in the dosage form, more complex it is & greater the potential for absorption and Bioavailability problems.
- Commonly used excipients in various dosage forms are,

a) Vehicle:

- Rate of absorption – depends on its miscibility with biological fluid
- Miscible vehicles causes rapid absorption e.g. propylene glycol.
- Immiscible vehicles – Absorption depends on its partitioning from oil phase to aqueous body fluid.

b) Diluents:

➤ Hydrophilic diluents – Imparts Absorption

Hydrophobic diluents – Retards Absorption

➤ Also, there is a drug-diluent interaction, forming insoluble complex and retards the absorption. E.g. Tetracycline-DCP

c) Binders & granulating agent:

➤ Hydrophilic binders – Imparts hydrophilic properties to the granule surface – gives better dissolution properties. E.g. Starch, Gelatin. PVP.

➤ More amount of binder increases the hardness of the tablet and retards the absorption rate.

d) Disintegrants:

➤ Mostly hydrophilic in nature.

➤ Decrease in amount of disintegrants – significantly lowers bioavailability.

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 un-absorbable 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.
- e.g. Griseofulvin, steroids
- It may decrease absorption when it forms the un-absorbable complex with drug above CMC.

h) Coating:

➤ In general, deleterious effects of various coatings on the drug dissolution from a tablet dosage form are in the following order.

Enteric coat > sugar coat > non-enteric coat

➤ The dissolution profile of certain coating materials change on aging; e.g. shellac coated tablets, on prolonged storage, dissolve more slowly in the intestine. This can be however, be prevented by incorporating little PVP in the coating formulation.

i) Buffers:

➤ Buffers are sometimes useful in creating the right atmosphere for drug dissolution as was observed for buffered aspirin tablets.

➤ However, certain buffer systems containing potassium cations inhibit the drug absorption as seen with Vitamin B₂ and sulfanilamide.

j) Colorants:

- Even a low concentration of water soluble dye can have an inhibitory effect on dissolution rate.
- The dye molecules get absorbed onto the crystal faces and inhibit the drug dissolution.
- For example: Brilliant blue retards dissolution of sulfathiazole.

k) Complexing agents:

- Complex formation has been used to alter the physicochemical & biopharmaceutical properties of a drug.

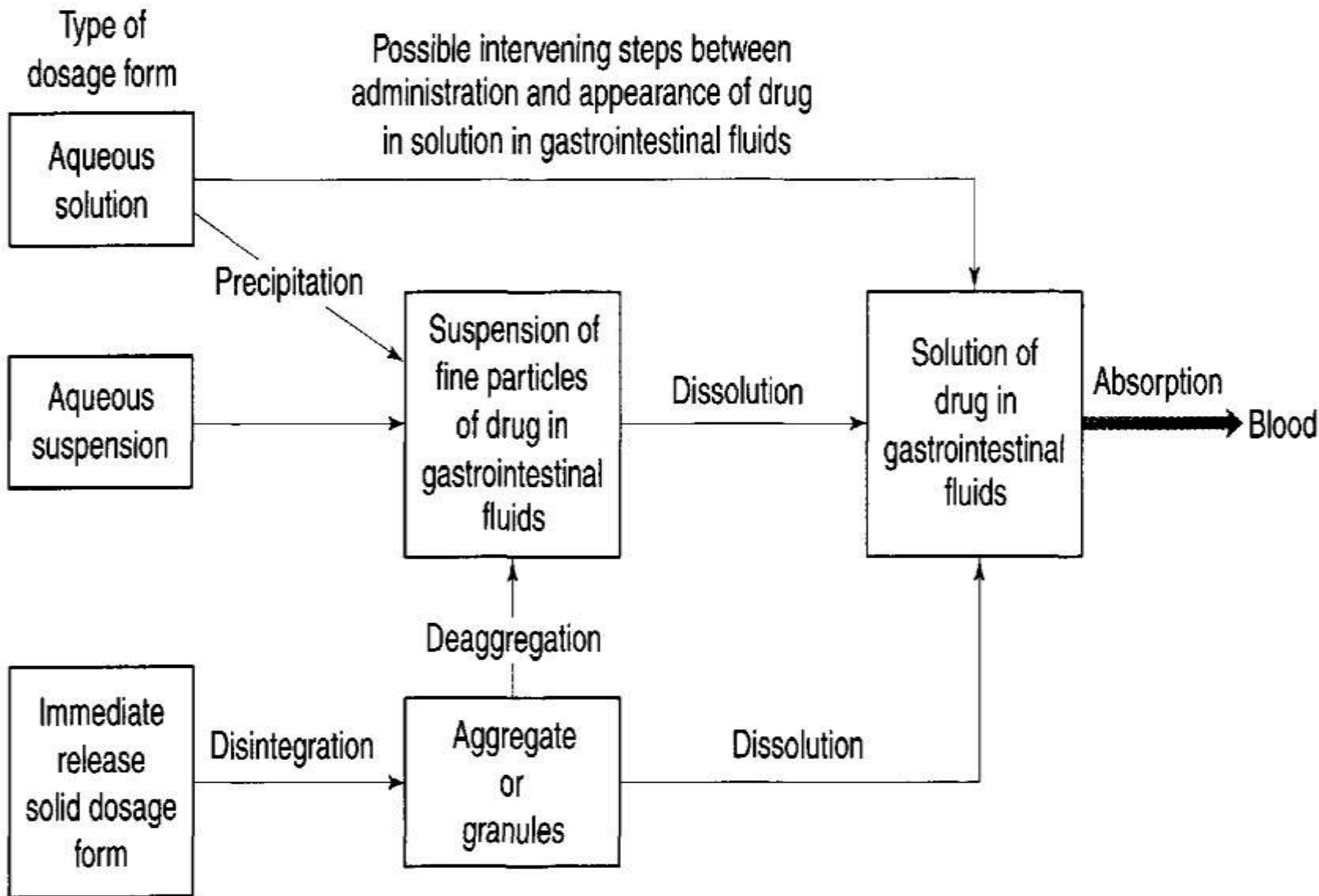
▪ Example

- 1) Enhanced dissolution through formation of a soluble complex.
 - E.g. ergotamine tartarate-caffeine complex & hydroquinone-digoxin complex.
- 2) Enhanced lipophilicity for better membrane permeability.
 - E.g. caffeine-PABA complex.

5) Nature & type of dosage form:

➤ Apart from the proper selection of the drug, clinical success often depends to a great extent on the proper selection of the dosage form of that drug.

➤ As a general rule, the bio-availability of a drug form various dosage forms decrease in the following order:
Solutions > Emulsions > Suspensions > Capsules > Tablets > Coated Tablets > Enteric Coated Tablets > Sustained Release Products.



3 Schematic outline of the influence of the dosage form on the appearance of drug in solution in the gastrointestinal tract.

➤ **6) Product age & storage condition:**

➤ Product aging and storage conditions can adversely affect the bio-availability by change in especially the physico-chemical properties of the dosage forms.

➤ For example:

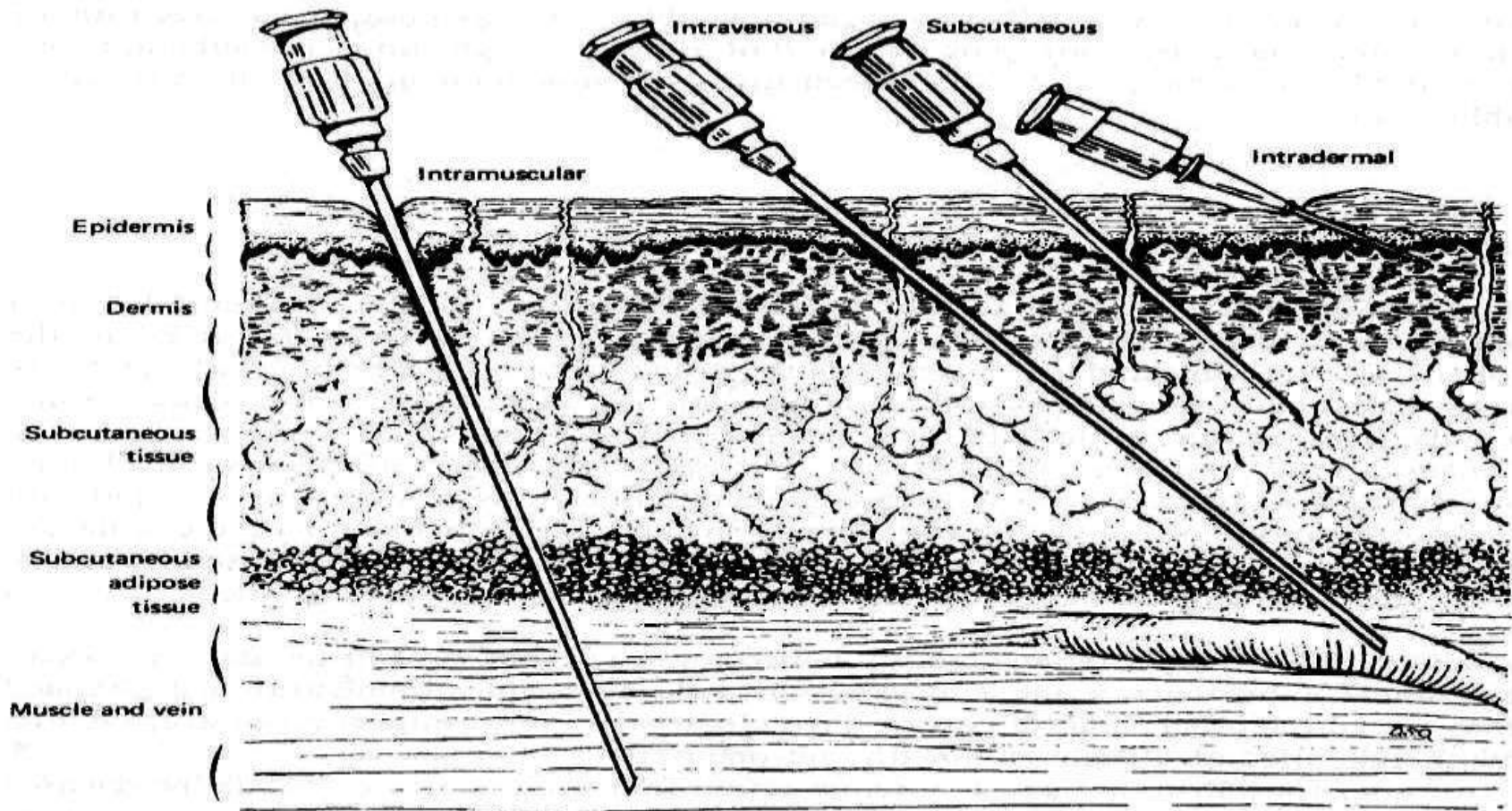
1. Precipitation of the drug in solution
2. Hardening of tablet
3. Change in particle size of suspension.

PATIENT RELATED FACTORS

1) Route of administration:

❖ *Parenteral route:*

- They avoid the possibility of hepatic first-pass metabolism.



• **Intra-arterial:**

➤ Intra-arterial injection is used to deliver drugs directly to organs, for example, in cancer chemotherapy, and in the use of vasopressin for GI bleeding.

• **Intrathecal:**

➤ Injection directly into the cerebrospinal fluid (CSF) ensures complete CNS bioavailability for drugs that can not cross the blood-brain barrier.

➤ E.g. Mepivacaine and prilocaine for spinal anesthesia.

• **Intravenous (IV):**

➤ IV administration introduces drug directly into the venous circulation.

➤ IV bolus is used for immediate therapeutic effect, typically for general anesthesia and for treatment of cardiac arrhythmia.

•**Intramuscular (IM):**

- Intramuscular injection is used mainly for drugs and vaccines that are not absorbed orally, for example, aminoglycosides, insulin, and hepatitis vaccine.
- The IM route is often used for sustained medication and specialized vehicles, such as aqueous suspensions, oily vehicles

❖ *Topical route:*

•**Transdermal:**

- This drug delivery route include continuous release of drug over a specified period, low presystemic clearance, and facile drug withdrawal by simply removing the device, and good patient convenience and compliance.

- Some disadvantages relate to barrier properties of the skin, skin reactions, and the relatively large dose size.
- Generally small dose is delivered (<10mg)
- E.g. clonidine, estradiol

• **Intranasal:**

- Intranasal administration may be used for local or systemic effects. Local effects include treatment of nasal allergies, rhinitis, and nasal congestion. Nasal delivery for systemic effects is established for a small number of drugs
- E.g. Vasopressin analogues and oxytocin are commercially available for intranasal dosage.

• **Vaginal:**

- Vaginal drug delivery is used mostly for local effects, but vaginal absorption can give rise to rapid and efficient systemic delivery.
- E.g. vaginal rings and biodegradable microspheres.

❖ *Enteral routes:*

• **Rectal:**

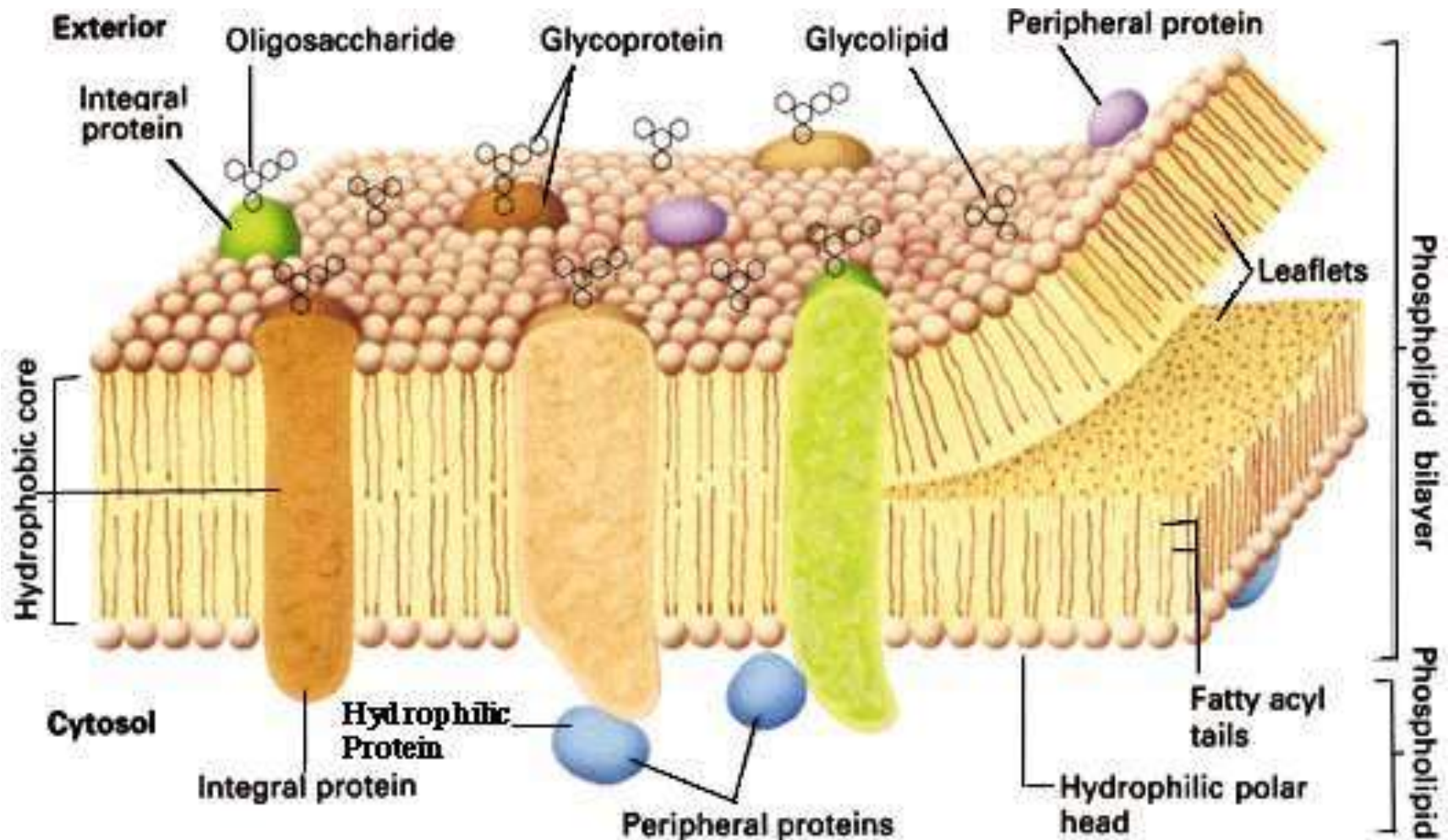
- Rectal absorption is generally slower than oral absorption, but for some drugs, rectal absorption exceeds oral absorption presumably due to avoidance of first-pass metabolism after rectal delivery.
- E.g. Metoclopramide, ergotamine, lidocaine

• **Buccal:**

- Drugs can be absorbed from the oral cavity itself or sublingually. Absorption from either route is rapid, sublingual more so apparently because of greater permeability of sublingual membranes and rich blood supply.
- The mean pH of saliva is approximately 6 so that drug absorption, predominantly passive in nature, is favored for unchanged molecules, acids with pKa values >3 , and bases with pKa values <9 .
- E.g. organic nitrates, barbiturates, papaverine, prochlorperazine, benzodiazepines.

2) Membrane physiology:

a) Nature of cell membrane:



- The cell membrane consists of globular proteins embedded in a dynamic fluid, lipid bilayer matrix
- Cell membranes are generally thin, approximately 70 to 100 Å in thickness.
- Cell membranes are composed primarily of phospholipids in the form of a bilayer interdispersed with carbohydrates and protein groups. The plasma membrane to be composed of two layers of phospholipid between two surface layers of proteins, with the hydrophilic "head" groups of the phospholipids facing the protein layers and the hydrophobic "tail" groups of the phospholipids aligned in the interior.
- lipid-soluble drugs tend to penetrate cell membranes more easily than polar molecules.
- proteins provide a pathway for the selective transfer of certain polar molecules and charged ions through the lipid barrier.

3) Age:

- In infants, the gastric pH is high and intestinal surface and blood flow to the GIT is low resulting in altered absorption pattern in compare to adults.
- In elderly persons, gastric emptying altered, decreased intestinal surface area and GI blood flow, higher incidents of achlorhydria so impaired drug absorption.

4) Gastric emptying time:

- The process by which food leaves the stomach and enters the duodenum.
- Rapid gastric emptying is required when the drug is best absorbed from distal part of the small intestine.

- Delayed gastric emptying is required when drugs are absorbed from proximal part of the small intestine and prolonged drug absorption site contact is desired.
- Gastric emptying is a first order process.
- **Gastric emptying rate:** This is the speed at which the stomach contents empty into the intestine.
- **Gastric emptying time:** Which is the time required for the gastric contents to the SMALL INTESTINE.
- **Gastric emptying half-life:** which is the time taken for half the stomach contents to empty.

Volume of Ingested Material	As volume increases initially an increase then a decrease. Bulky material tends to empty more slowly than liquids
Type of Meal	Gastric emptying rate: carbohydrates > proteins > fats
Physical state of gastric contents	Solutions or suspensions of small particles empty more rapidly than do chunks of material that must be reduced in size prior to emptying.
Body Position	Lying on the left side decreases emptying rate and right side promotes it
Drugs Anticholinergics Narcotic analgesics Ethanol	Reduction in rate of emptying Reduction in rate of emptying Reduction in rate of emptying
Emotional state	Anxiety promotes where as depression retards it
Disease states	gastric ulcer, hypothyroidism retards it, while duodenal ulcer, hyperthyroidism promotes it.

5) Intestinal transit time:

➤ Intestinal transit time is the major site of absorption of most of drugs.

➤ The mixing movement of the intestine that occurs due to peristaltic contractions promotes drug absorption, firstly, by increasing the drug intestinal membrane contact and secondly by enhancing drug dissolution of especially of poorly soluble drugs, through induced agitation.

➤ Delayed intestinal transit is desirable for

A) Drugs that dissolve or release slowly from their dosage form (sustained release products)

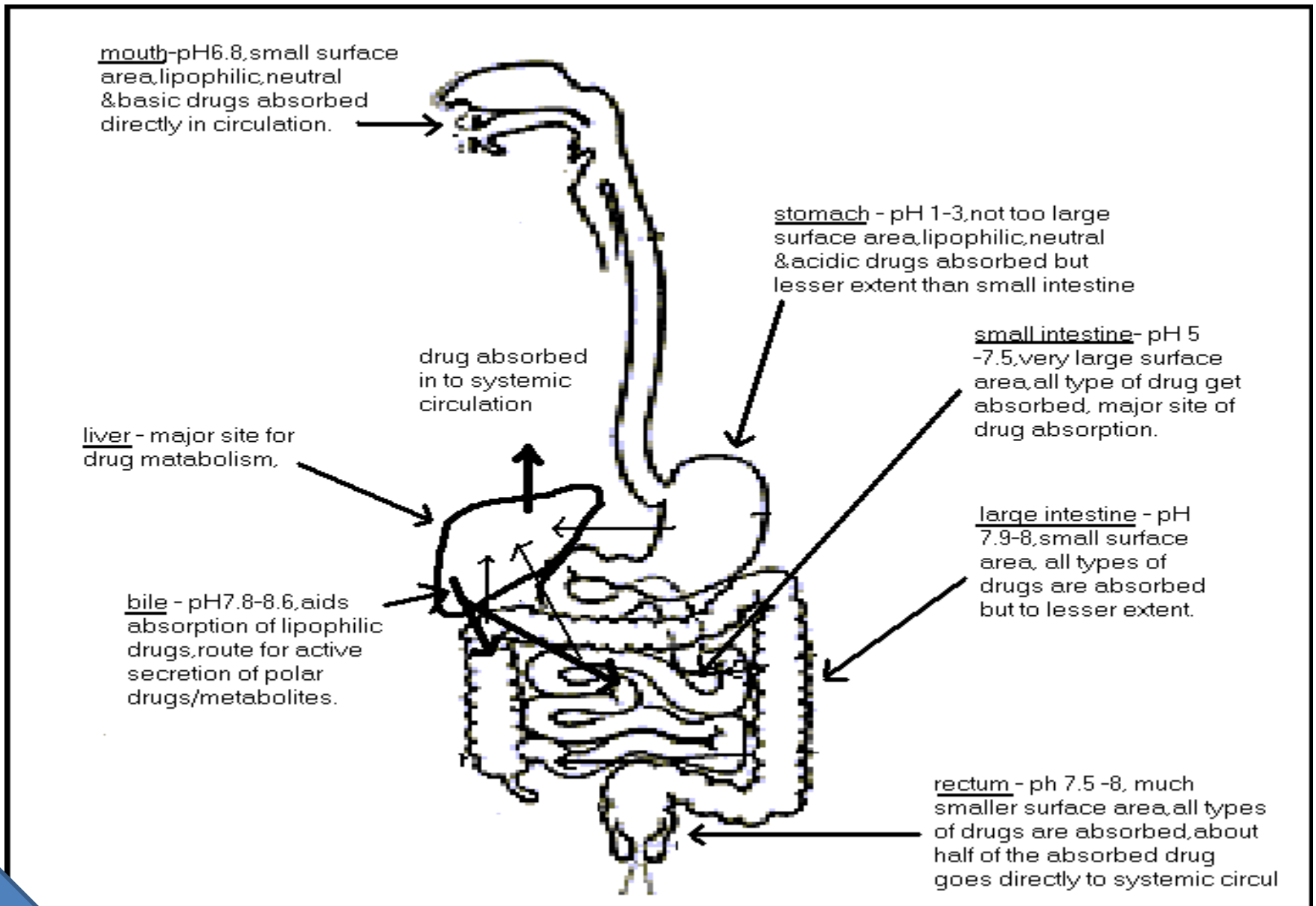
B) Drugs that dissolve only in intestine (enteric coated formulations)

C) Drugs absorbed from specific sites in the intestine (several B vitamins)

Intestinal region	Transit time
Duodenum	5 minutes
Jejunum	2 hours
Ileum	3 to 6 hours
Caecum	0.5 to 1 hour
Colon	6 to 12 hours

- Intestinal transit time is influenced by various factors such as food, diseases and drugs
- E.g. metoclopramide which promotes intestinal transit, enhance absorption of rapidly soluble drugs while anticholinergic retards intestinal transit and promotes the absorption of poorly soluble drugs.

6) Gastrointestinal pH:



7) Disease states:

Gastric diseases (Achlorhydric patients):

- They may not have adequate production of acids in the stomach; stomach HCl is essential for solubilizing insoluble free bases.
- Many weak-base drugs that cannot form soluble salts & remain undissolved therefore unabsorbed. Salt forms of these drugs cannot be prepared because the free base readily precipitates out.
- E.g. Dapsone, itraconazole, and ketoconazole .

Cardio-vascular diseases:

- Several changes associated with congestive cardiac failure influence bio-availability of a drug viz., edema of the intestine, decreased blood flow to the GIT and gastric emptying rate and altered GI pH, secretions and microbial flora.

8) Blood flow through the GIT:

- It plays a major role in absorption by continuously maintain the concentration gradient across the epithelial membrane.
- The GIT is extensively supplied by blood capillary network.
- Blood flow is imp for actively absorption of drugs.
- Absorption of polar molecules doesn't depends on the blood flow but lipid soluble molecules highly depends on the blood flow.
- Food influences blood flow to the GIT. Perfusion increases after meals & persist for few hours but absorption is not affected.

9) Gastrointestinal contents:

- 1) **Food- drug interactions:** The presence of food in the GI tract can affect the bioavailability of the drug .
 - Digested foods contain amino acids, fatty acids, and many nutrients that may affect intestinal pH and solubility of drugs.
 - Some effects of food on the bioavailability of a drug from a drug product include:

Delay in gastric emptying

Stimulation of bile flow

A change in the pH of the GI tract

An increase in splanchnic blood flow

- Presence of food will affect absorption in following way
- a) Decreased absorption: ex. Penicillin, erythromycin, ethanol, tetracycline, levodopa etc.
 - b) Increased absorption: ex griseofulvin, diazepam, vitamins etc.

2) **Fluid volume:**

- Large fluid volume results in better dissolution, rapid gastric emptying and enhanced absorption-
- Ex. Erythromycin is better absorbed when taken with a glass of water under fasting condition than when taken with meals.

3) **Interaction of drug with normal GI constituents:**

- The GIT contains a number of normal constituents such as mucin which is a protective mucopolysaccharides that lines the GI mucosa, interact with streptomycin.

10) Presystemic metabolism:

➤ The loss of drugs through bio-transformation by such eliminating organs during the passage to systemic circulation is called as first-pass or pre-systemic metabolism.

➤ complete absence of the drug in plasma after oral administration is indicative of the first-pass effects. The four primary systems which affect the pre-systemic metabolism of a drug

- 1) Luminal Enzymes
- 2) Gut wall enzymes/mucosal enzymes
- 3) Bacterial enzymes
- 4) Hepatic enzymes

1) Lumenal Enzymes:

- The primary enzyme found in gastric juice is pepsin. Lipases, amylases and proteases are secreted from the pancreas into the small intestine in response to ingestion of food.
- Pepsins and the proteases are responsible for the degradation of protein and peptide drugs in the lumen.

2) Gut wall enzymes:

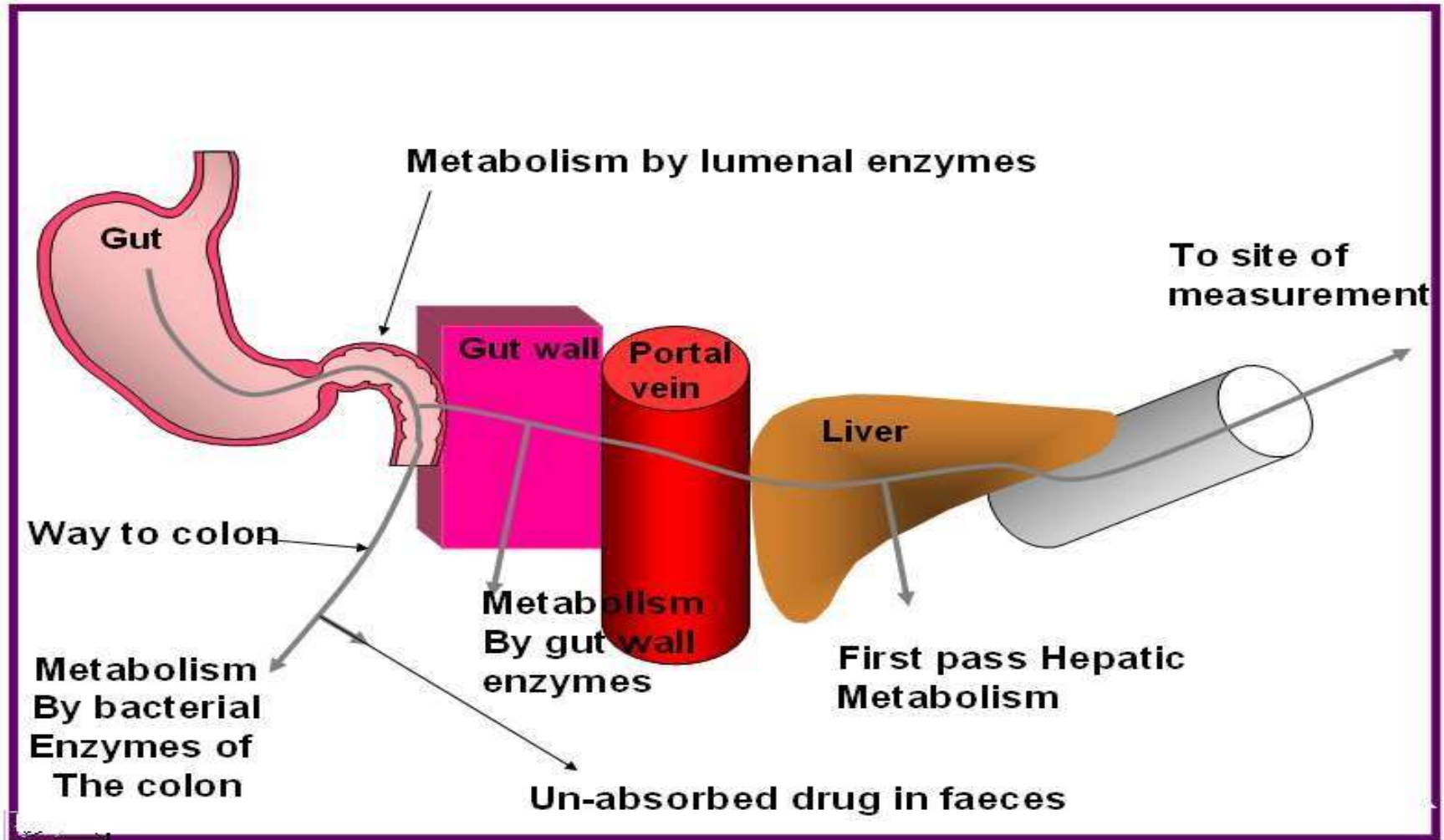
- These also called mucosal enzymes, they are present in stomach, intestine and colon. Alcohol dehydrogenase (ADH) is an enzyme of stomach mucosa that inactivates ethanol.
- E.g. sulfation of ethinyl estradiol & isoprenaline.

3) Bacterial enzymes:

- Which are mainly localized within the colonic region of the gastrointestinal tract, also secrete enzymes which are capable of a range of reactions.
- E.g. Sulphasalazine, is a prodrug of 5-aminosalicylic acid linked via an azo bond to sulphapyridine.

4) Hepatic enzymes:

➤ Several drugs undergo first-pass hepatic metabolism, the highly extracted ones being Isoprenaline, propranolol, diltiazem, etc.



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THANK
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