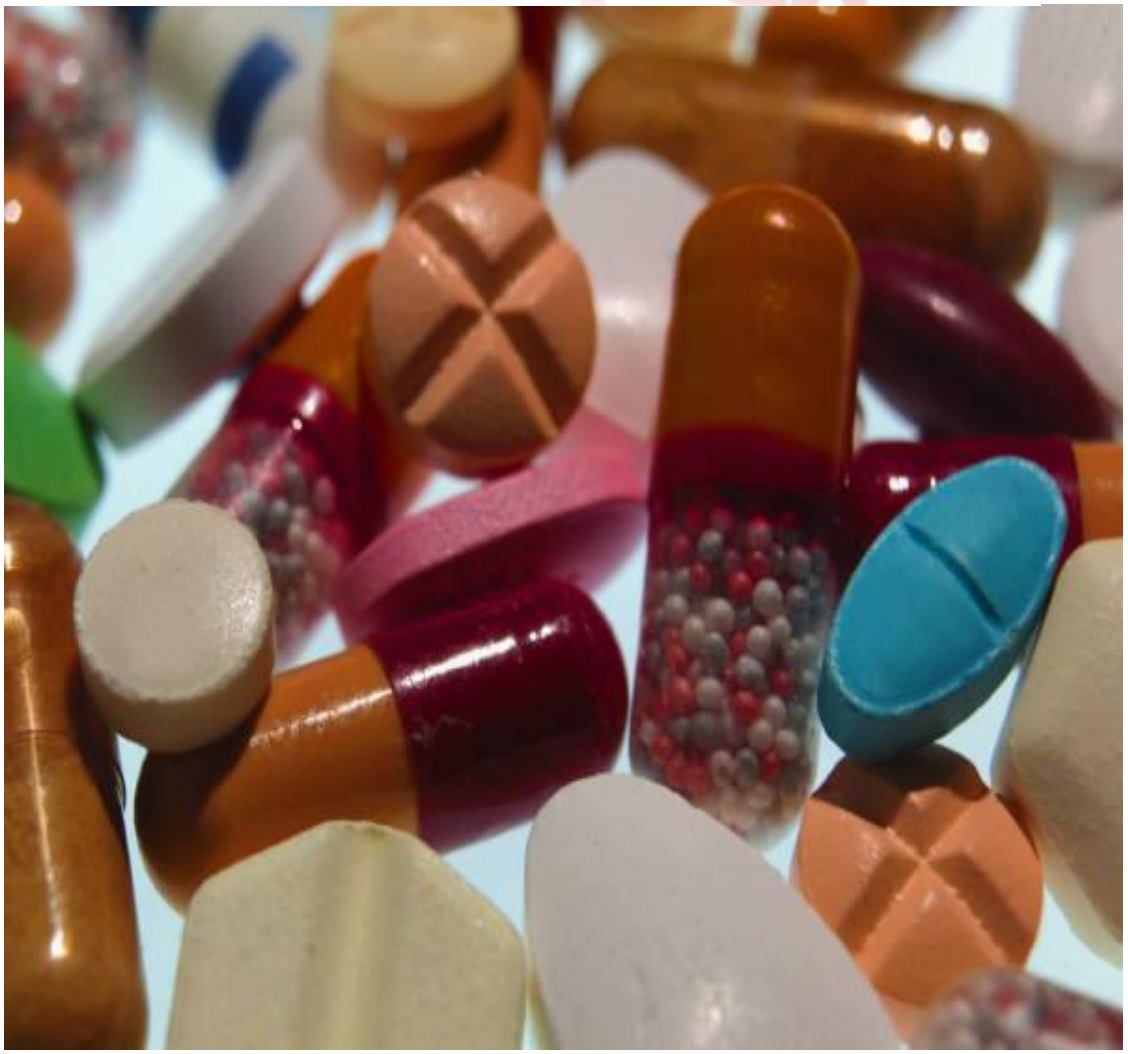
pharmacology



By:.

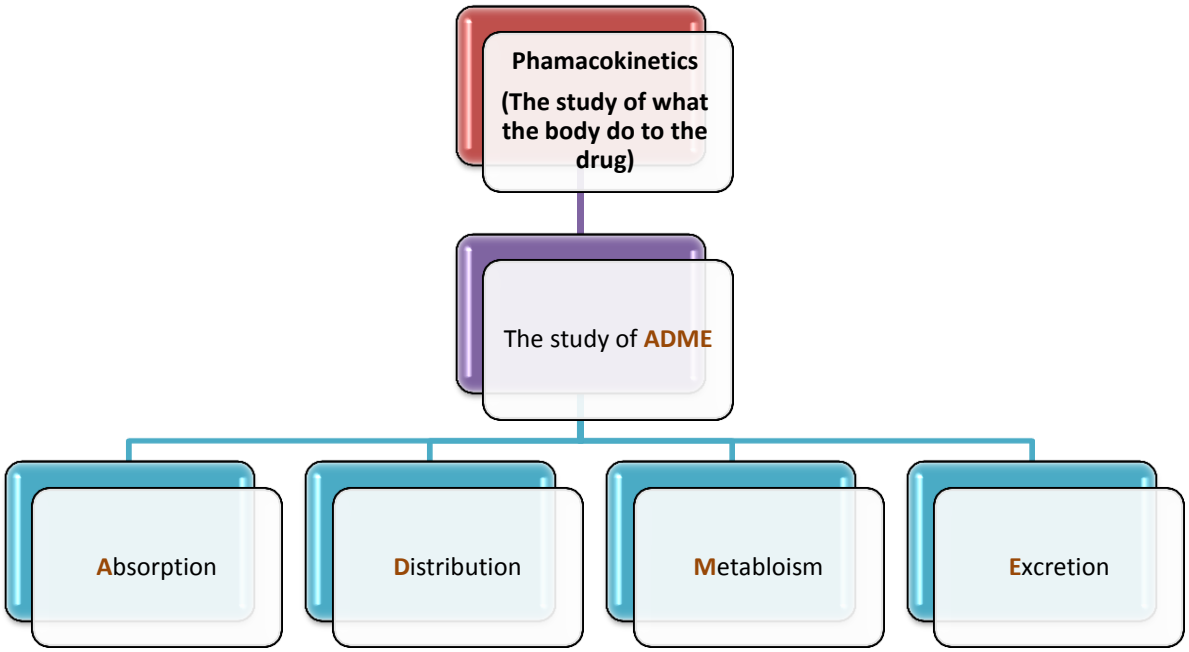
Team of pharmacology

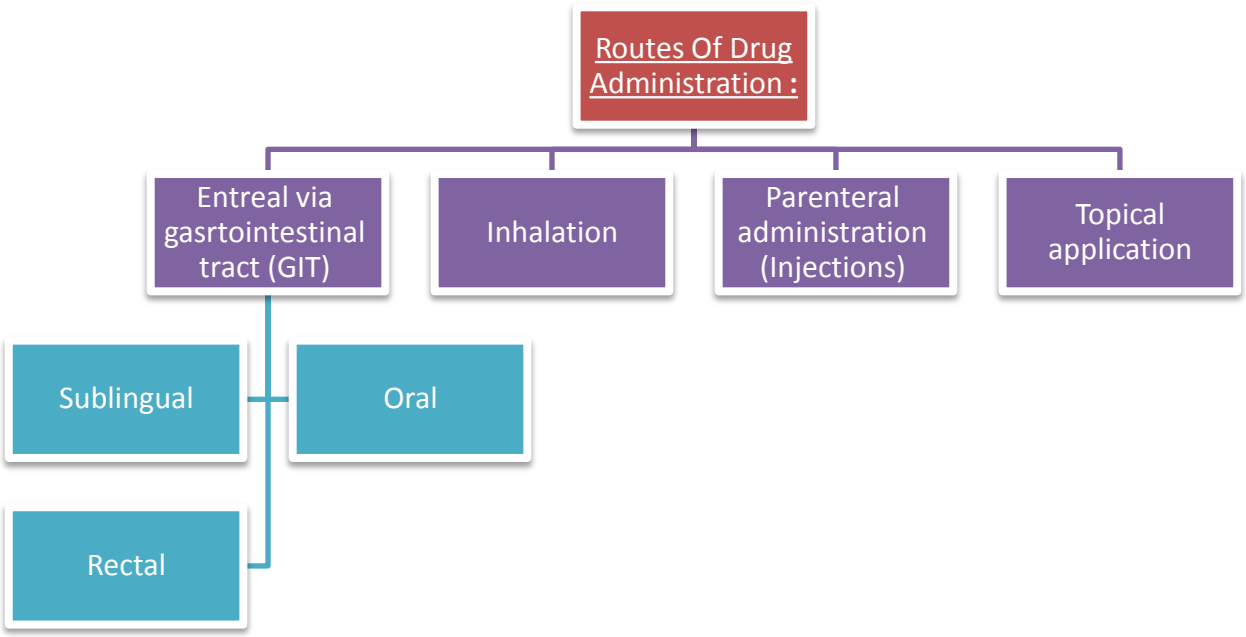
4th Pharmacology lecture

(Pharmacokinetics 1 : Drug administration and absorption)

Lecture's Objectives :

1) The study of pharmacokinetics
2) The routes of drug administration
3) Comparison between the advantages and disadvantages of (Oral administration , sublingual , Rectal administration , I.V. administration , Inhalation)
4) The factors affecting absorption from GIT and modifying drug absorption
5) First pass metabolism , where it's occurs and the results depending on it
6) Differentiate between various dosage forms
7) The types of parenteral administration, their special utilities and limitations
8) Know the topical application and transdermal patches
9) The meaning of drug absorption and its mechanisms
10) The meaning of bioavailability





Notes :

1- Parenteral : Away from the GIT.
2- Enteral: Pass the GIT and it's the simplest most common.
3- Topical medication means cream or something which is applied on the skin.

Oral administration advantages and disadvantages :

Adv.	Dis Adv.
Easy	Slow effect
Safe	No complete absorption
Self use	Destruction by PH and enzymes
Convenient	GIT irritation
cheap	Food-drug interactions
No need for sterilization	Drug-drug interactions
	First pass effect (Slow bioavailability)
	Not suitable for : vomiting , unconscious patients, emergency and bad taste drugs

Notes: ^Safe means; the number of systemic infections is limited.

^The duodenum is a major site of entry to the systemic circulation because of its large absorptive surface, but there some by the stomach also.

^ Sterilization means; it has to be clear and clean.

^ Expected time for oral administration to work is from 1 up to 3 hours .

--- long time---- needs more time for absorption --- slow effect

^ Protein in nature drugs get destructed by the enzymes in the intestines--- example is insulin can't be given orally

Sublingual advantages and disadvantages :

Adv.	Dis Adv.
Rapid effect	Not for irritant drugs
Used in emergency	Not for frequent use
High bioavailability	
No first pass metabolism	
No GIT irritation	
No food-drug interactions	

Notes : ^ Sublingual is Place the drug under the tongue..

^There is abundant supply of vessels under the tongue (the drug will go to the blood directly)---- sublingual drugs have rapid effect

^Example of sublingual drugs = angina

Rectal administration advantages and disadvantages :

Adv.	Dis Adv.
Suitable for : Children , vomiting and unconscious patients , irritant and bad taste drugs	Irritation of rectal mucosa
Less first pass metabolism than oral by 50%	Irregular absorption and bioavailablility

I.V. administration advantages and disadvantages :

Adv.	Dis Adv.
Rapid effect (emergency)	Only for water soluble drugs
High bioavailability	Infections
No first pass metabolism	Sterilization
No food-drug interaction	Expensive
No gastric irritation	pain
Suitable for : vomiting and unconscious patients , Irritant and bad taste drugs	Need skill
	Anaphylaxis
	Not suitable for : oily solutions , poorly soluble substance

Notes : ^I.V. administration is the Most common.

^ **Anaphylaxis** is a serious allergic reaction that is rapid in onset and may cause death.

Inhalation administration advantages and disadvantages :

Adv.	Dis Adv.
Mucous membrane of respiratory system	Not suitable for : irritant drugs
low bioavailability	Only for some drugs as inhalation anesthetics and bronchodilators
No first pass metabolism	
Less side effects	
Rapid absorption (due to large surface)	
Provide local action	
Limited systematic effect	

Notes: ^ Inhalation administration Produce an effect almost as rapidly as with IV injection.

Factors affecting absorption from GIT :

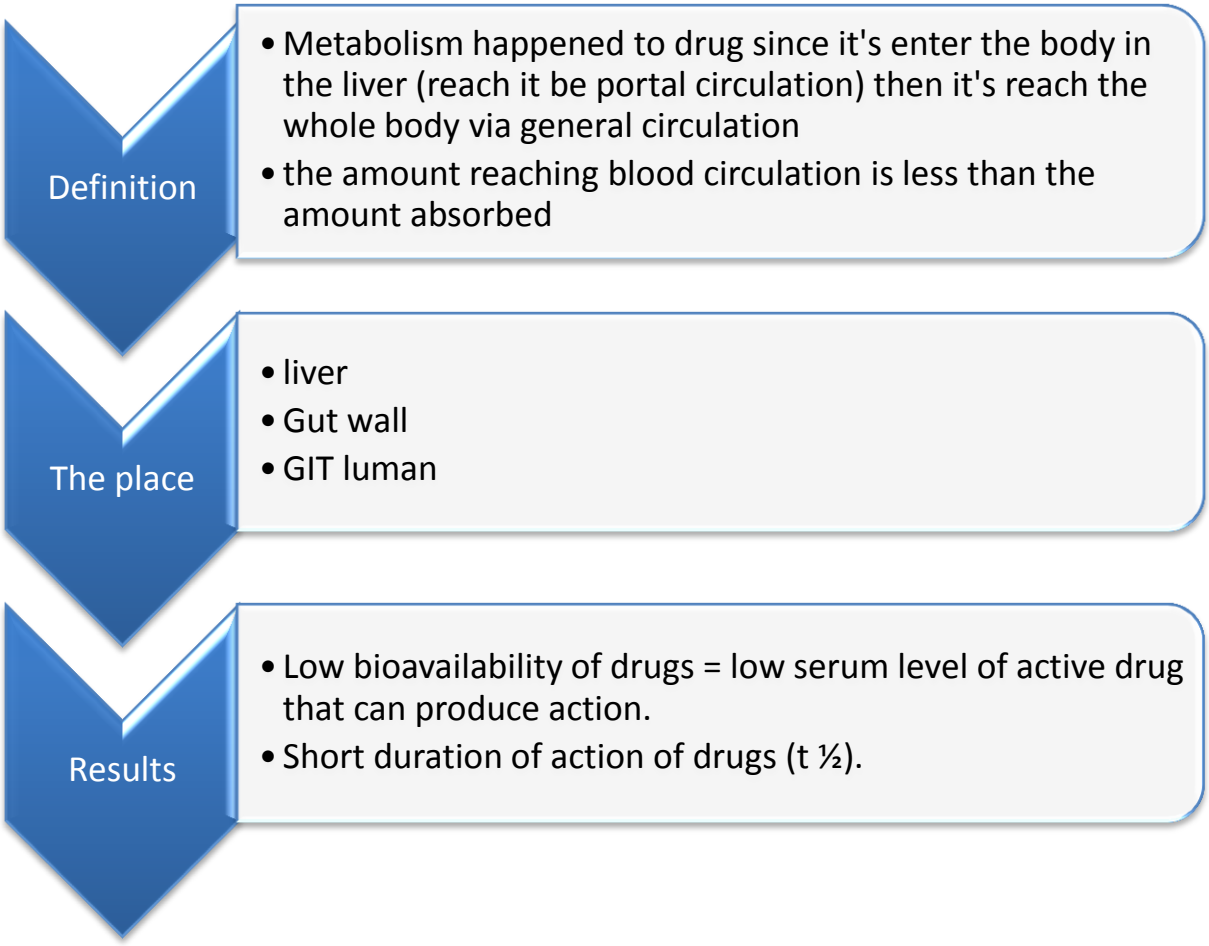
- ✓ GIT motility changed by drug / diseases
- ✓ Presence of food
- ✓ Blood flow/surface area
- ✓ GIT juices
- ✓ pH of GIT fluids
- ✓ Chemical/drug interactions
- ✓ dosage form of a drug

Most of the drug is absorbed within 1-3 hours, mostly it occurs in small intestine ,rate of absorption depends on lipid solubility ,ionization and PH.

Factors Modifying drug absorption :

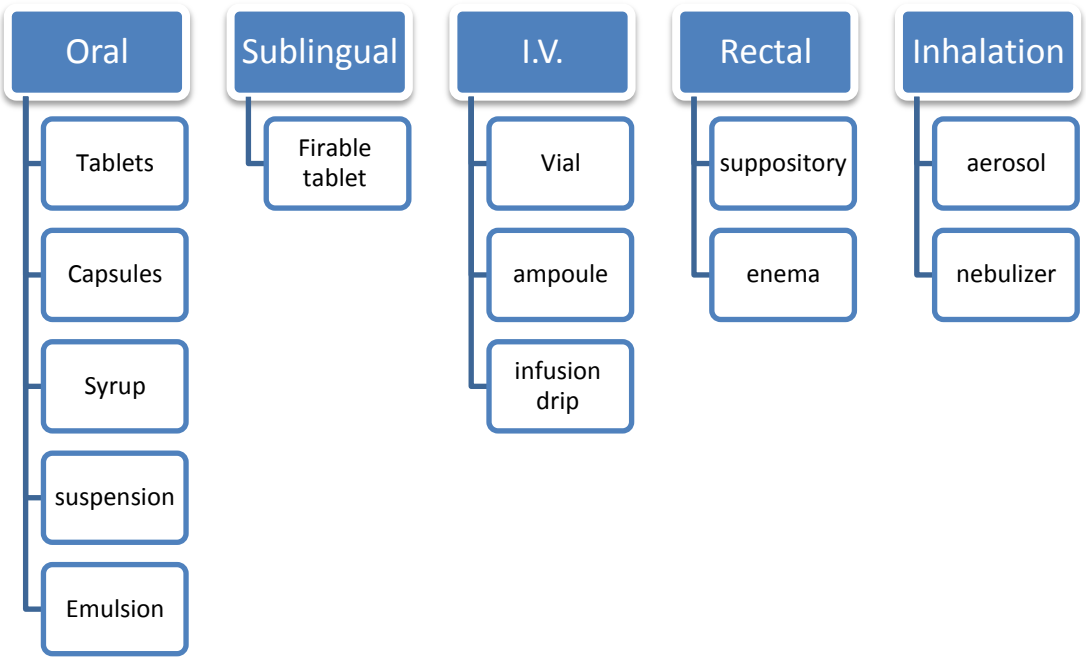
- ✓ Lipid solubility
- ✓ Degree of ionization
- ✓ Drug solubility (aqueous sol better than oily, suspension, solution)
- ✓ Dosage forms (depending on particle size and disintegration)
- ✓ Concentration of drugs
- ✓ Circulation at site of absorption
- ✓ Area of absorbing surface
- ✓ Route of administration.

First pass Metabolism :



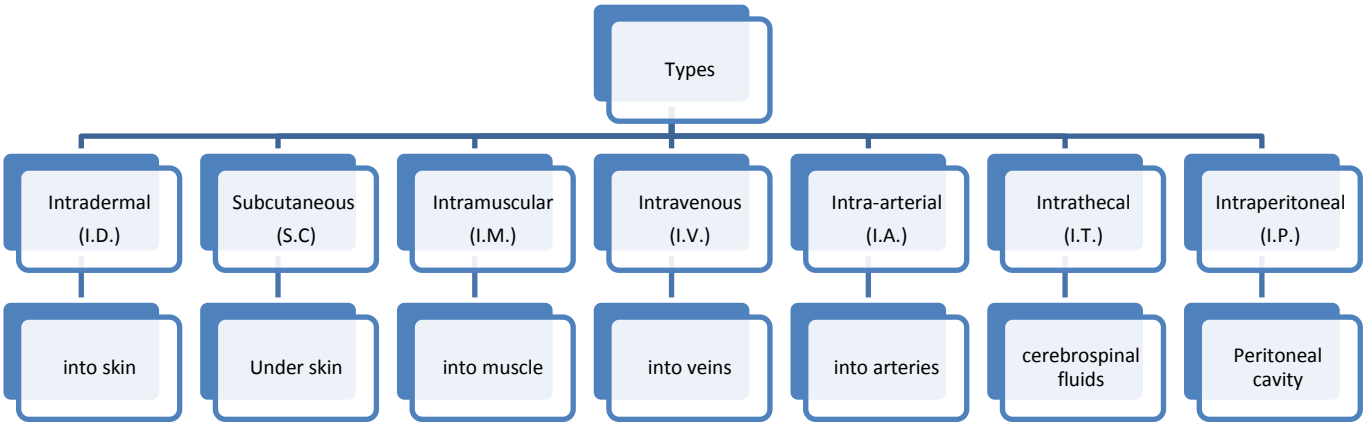
Notes : The liver is the main place to metabolize food and drugs

Dosage Forms :



Notes: ^Friable tablet = dissolve rapidly

Parenteral Administration :



Notes : ^Insulin is given by subcutaneous

^If irritant drug is given by intramuscular--- muscles will get irritated and tissue necrosis will occur

^Most suitable way to introduce irritant drug ---- intravenous

^The drug given by intravenous must be water clear solution, if not it will cause blood clotting.

^Oily solution drug is given by intramuscular

Topical application:

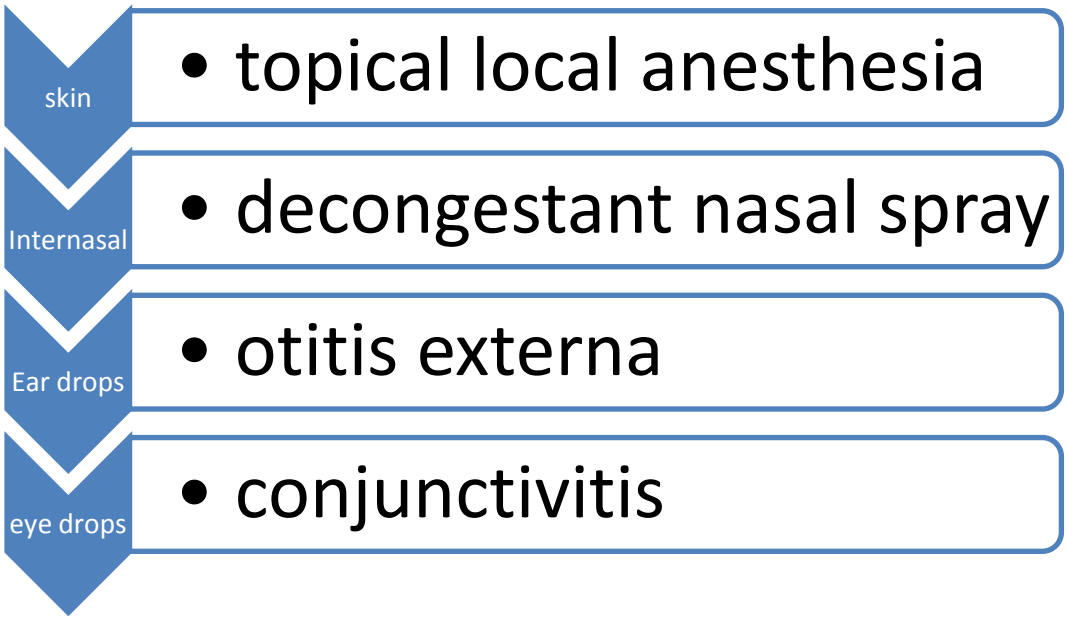
^ Used to provide a local action and for lipid soluble drugs

^ No first pass metabolism

^The exception of topical application (give local effect) ------ transdermal patches

(give systemic effect)

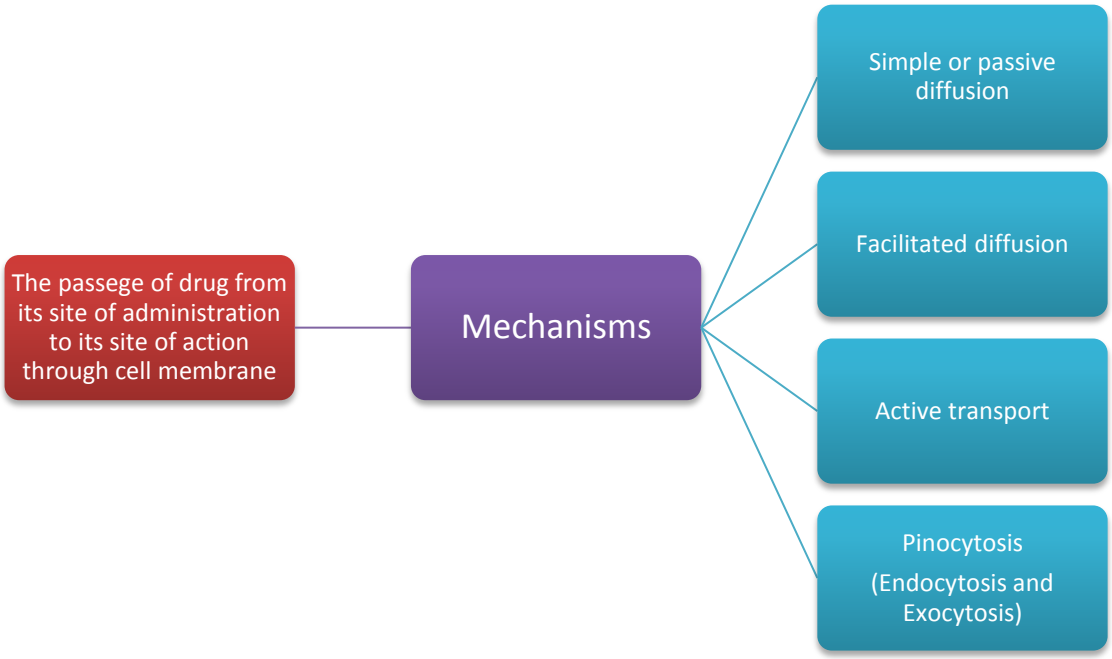
^ applied to:

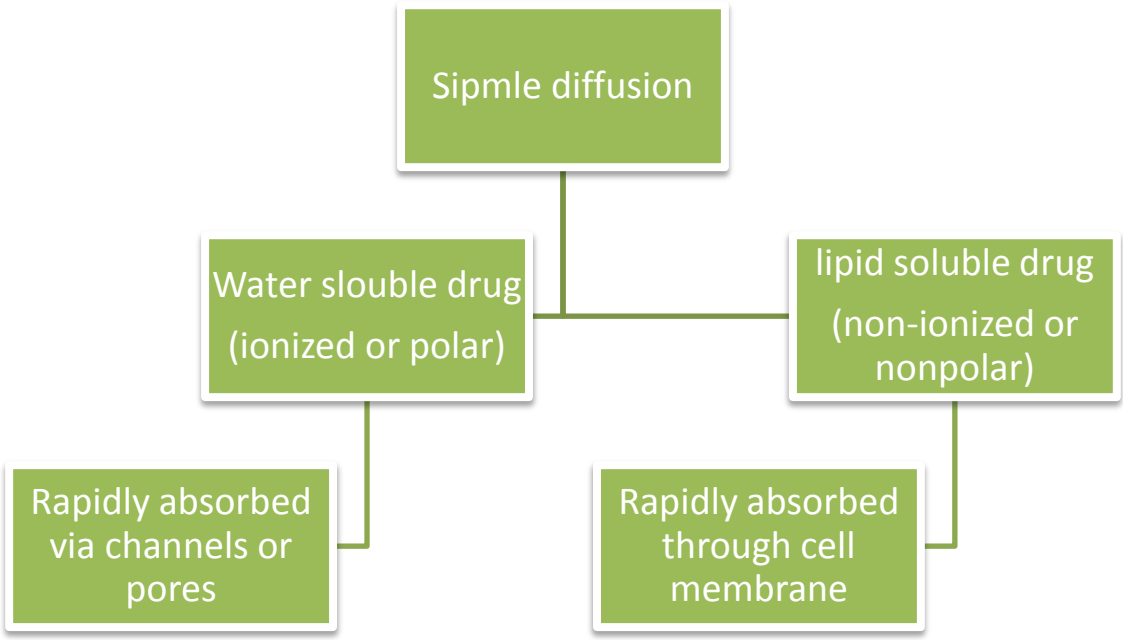


Transdermal patches: applied to skin to provide a systematic effect (prolonged drug action).

Example : nicotine patches

Drug absorption:





Notes : ^ only non-ionized form is absorbed

Characters: Common , no energy required , no carrier required , along concentration gradient **(high-low)** , non-selective , not saturable, Depend on Lipid solubility & pKA of drug – PH of medium

- **Notes :** Not selective --- doesn't matter if acid or base
- Not saturable--- no carrier protein
- low molecular weight drugs pass through the pores
- High molecular weight molecules diffuse through cell membrane (lipid soluble)
- If the PH is changed ---- change for the drug
- Drugs exist in two forms **(ionized and non-ionized)**
- The ratio between ionized and non-ionized is determined by **PH of the medium and pKA of the drug.**

pKA of the drug : pH at which half of the substance is ionized and the other half is non-ionized.

^pKa is the optimal PH for drugs.

^The lower the pKa value (pKa < 6) of the acidic drug the stronger the acid. *e.g aspirin*

^The higher the pK*a value (pKa >8) of a basic drug, the* stronger the base. *e.g propranolol*

PH of the medium : Affects the degree of ionization of drugs.

^Weak acids are best absorbed in stomach.

Weak acids → unionized → slow absorption in intestine → best absorbed in stomach

^Weak bases are best absorbed in intestine.

Weak bases → highly ionized → less absorbed in acidic medium → best absorbed in the intestine

- Acidic drugs are better absorbed in acidic medium---- the drug will be present in non-ionized form
  (it doesn't need to change its form)
- Basic drugs are best adsorbed in basic medium---- the drug will be present in non-ionized form
  (it doesn't need to change its form to ionized)
- The stomach environment has a low PH about 1-2 that's mean is acidic

Active transport Characters : Relatively unusual , against concentration gradient **(low-High)** , requires energy and carries , specific , saturable , Iron absorption , Uptake of levodopa by brain

Facilitated diffusion Characters : along concentration gradient , Requires carries , no energy , saturable , selective

Comparison Between (active transport , passive diffusion , facilitated diffusion) :

A.T	P.D	F.D
Against C.G (low-high)	**Along C.G (high-low)**	
Requires energy	**No energy**	
Carries	**No carries**	**Carries**
Selective	**Not selective**	**selective**
saturable	**Not saturable**	**saturable**

Pinocytosis :

Endocytosis = uptake of membrane bound particles

Exocytosis = Expulsion of membrane bound particles

^ Occurs for high molecular weight drugs or highly lipid insoluble drugs.

Bioavailability: The amount of uncharged drug that enters the systematic circulation after administration and becomes available to produce an action.

- **Bioavailability = the concentration of drug in the blood**
- **I.V. provide 100% Bioavailability**
- **Oral usually has less B.A than I.V.**