Pharmacognosy : study the Sources of drug and the physical and chemical Properties of drug of vegetable and animal origin.

Therapeutics : treatment of disease in general and includes surgery, radiation, behavioral modification and other modalities.

chemotherapy : branch of Pharmacology dealing with drug that selectively inhibit or destroy specific agents of disease such as bacteria, viruses, fungi and other Parasites.

Toxicology : study of Poisoning of therapeutic agents administered in excess and of substance having only a toxic action.

Drug : is derived from old french drogue which meant herb (عشب)

Drug : Any substance and all chemical except foods that are used to Promote or Protect health of human beings or animals.

Posology: Is a study of medicine dosage, which varies with the species of animal

Dose: The amount of a drug necessary to elicit the desired therapeutic response in the patient.

The student should differentiate between the terms dose and dosage

A dose: is the d quantity of medication to be administered at one time.

whereas dosage: refers to determination and regulation of doses.

metrology: study of weight and measures as applied to preparation and administration of drugs.

Pharmacokinetics:

The aim of drug therapy is to prevent, cure, or control various disease states.
to achieve this goal, adequate drug doses must be delivered to the target tissues so that therapeutic yet nontoxic levels are obtained.

and must be recognize that:

1- The speed of onset of drug action.

2- Intensity of the drug's effect.

3- The duration of drug action

This are controlled by (4) fundamental Pathways of drug movement and modification in the body.

First: (absorption) drug absorption from the site of administration into blood circulation.

second: (distribution) drug leave the bloodstream and distribute into the interstitial and intracellular fluids.

Third: (metabolism) drug may be metabolized by the liver, kidney or other tissues.

Four: (excretion) drug may be eliminated from the body in urin, bile or feces.

Routes of drug administration:

The route of administration is determined by:

1- Properties of the drug (water or lipid solubility, ionization, non ionization etc)

2- therapeutic objective (rapid onest of action, need for long-term administration, restriction to alocal site)

therefore (2) two major routes of drug administratio

1- Enteral
2- Parenteral

Enteral:

1- oral
2- sublingual
3- Rectal

oral: 1- The most common route.
2- giving the drug by mouth
3- drug are absorbed from the stomach, however the duodenum is the major site of entry to the blood circulation because of its largen absorptive surface.

2 - Sublingual:

1- Placement under the tongue allows a drug to diffuse into the capillary network and enter the systemic circulation directly.

2- drug avoids first pass metabolism.

3- Rectal:

1- prevent the destruction of the drug by intestinal enzymes or by low PH in the stomach.

2- rectal route useful if the drug induce vomiting or if the patient is already vomiting.

Parenteral:

- used for drug poorly absorbed from the GI tract.
- for drug are unstable in the GI tract
- used for treatment of unconscious patients
- for rapid onset of action.

1- intravenous (IV) injection

2- intramuscular (IM)

3- Subcutaneous (SC)

1- intravenous:

1- the most common Parenteral route.
2- drug that are not absorbed orally.
3- The drug avoids the GI tract and therefore first-pass metabolism by the liver

4- rapid effect and a maximal degree in circulation
5- contamination with bacteria at the site of injection.
6. IV injection may also induce hemolysis.
7- IV injection may be causes adverse reaction by too-rapid delivery of high concentration of drug to the plasma & tissue. therefore the rate of infusion must be carefully controlled.

2- Intramuscular :

1- Drugs can be aqueous solutions or nonaqueous vehicle such as polyethylene glycol.

2- drug in aqueous solution fast absorption but other is slow.

3. Subcutaneous :

1- This route like IM injection but requires long time for absorption.

2- minimizes risks.

3- Some time minute amounts of epinephrine combined with adrug to restict its area of action

epinephrine acts as vasoconstrictor and decrease removal of adrug

3- other route

1- inhalation
2- intranasal
3- intrathecal (intraventricular) → direct to cerebrospinal fluid
4- Topical
5- Transdermal

I- Absorption of drugs :

absorption is the transfer of a drug from its site of administration to the bloodstream.

The rate and efficiency of absorption depend on the route of administration.

- for IV injection absorption is complete, the total dose of drug reaches the systemic circulation. but other route partial absorption and lower bioavailability

For example, the oral route requires that a drug dissolve in the GI fluid and penetrate the epithelial cell of the intestinal mucosa, disease states or the presence of food may affect.

A- Transport of a drug from the GI tract.

depending on chemical properties of drugs may be absorbed from GI tract by

- passive diffusion.
- active transport.

1- Passive diffusion:

1- The drug moves from a region of high concentration to lower concentration.

2- no need Carrier.

3- not saturable.

4- Lipid-soluble drugs readily move across most biological membranes.

5- Water soluble drugs Penetrate the cell membrane through aqueous channels.

2- Active transport:

1- need specific Carrier Proteins

2- energy dependent (by hydrolysis of ~~adno~~ adenosine triphosphate)

3- moving the drugs against a concentration (from low conc to higher drug conc)

4- saturation for the carrier.

B- Effect of PH on drug absorption:

Most drugs are either weak acids or weak bases.

Acidic drugs (HA) release a H^+ causing a charge anion (A^-)

$$HA \rightleftharpoons H^+ + A^-$$

non-ionized ionized

weak base (BH^+) relase a H^+, the Protonated from of basic drugs is usually charged, and loss of Proton produce the uncharged base (B)

$$\underset{\text{ionized}}{BH^+} \rightleftharpoons \underset{\text{nonionized}}{B} + H^+$$

all nonionized drugs are lipid soluble and the ionized drug are water soluble.

The cell membrane is PhosPholipid in nature sothat the nonionized drug cane be diffusion through the lipid membrane by simple diffusion without energy.

$PH = -Log[H^+]$ اللوغاريتم السالب لتركيز ايون الهيدروجين

↑
PH for medium → متغير unconstant

$PKa = -Log\ Ka$ اللوغاريتم السالب لثابت التأين

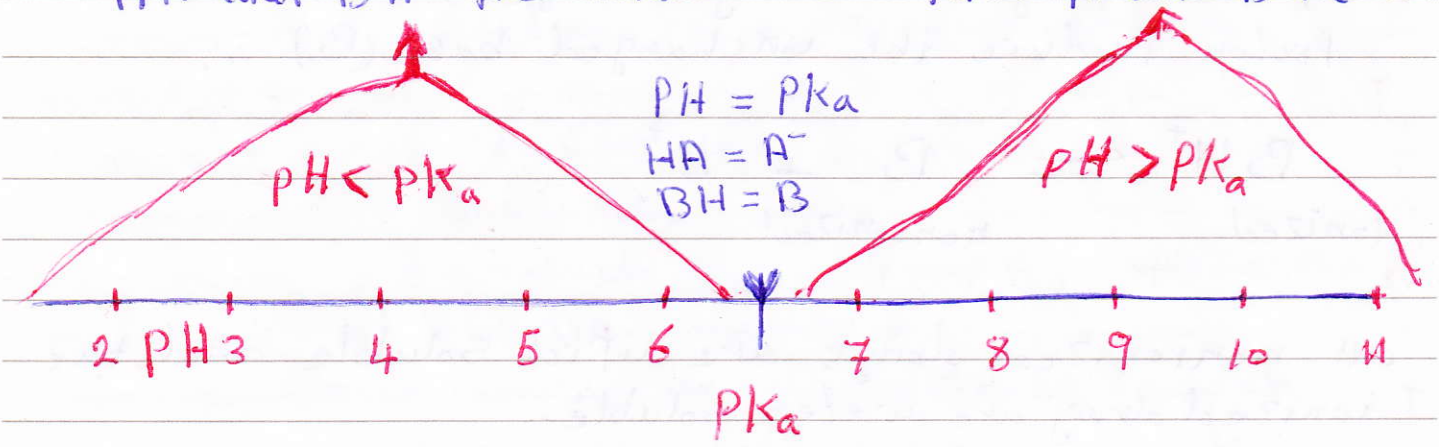
↑
for drug → ثابت constant

The distribution of a drug between its ionized and nonionized forms depends on the pH ~~and~~ and pKa of the drug.

Pka for drug 6.5 = ثابت

when pH is less than pKa the protonated form HA and BH predominate

when pH is greater than pKa the deprotonated form A^- and B predom-



drug weak base in pH (medium) acidic in stomach ionized form greater than unionized → low absorption

weak base in pH (medium) alkalin in intestin non ionized greater than ionized → high absorption.

- Determination of how much drug will be found on either side of a membrane:

The relationship of pKa and the ratio of acid-base concentrations to pH is expressed by the (Henderson-Hasselbalch) equation.

for acids: $pH = pK_a + \text{Log} \frac{[A^-]}{[HA]}$ ← non

for base: $pH = pK_a + \text{Log} \frac{[B]}{[BH^+]}$ ← non

This equation is useful in determintion how much drug will be found on either side of a membrane that separate two compartment that differ in pH for example

Stomach = PH 1.0 – 1.5

blood plasma = pH 7.4

- Physical factors influencing absorption:

1- Blood flow to the absorption site:

blood flow to the intestine is much greater than the flow to the stomach, thus absorption from intestine over that from the stomach.

2- Total surface area available for absorption:

because the intestine has a surface rich in microvilli and surface area is about 1,000 fold that of the stomach, thus absorption of drug across the intestine is more efficient.

3- Contact time at the absorption surface:

- drug moves through the GI tract very quickly as in severe diarrhea, it is not well absorbed.
- The Presence of food in the stomach both dilutes the drug and slow gastric emptying, therefore a drug taken with a meal absorbed more slowly.

Bioavailability :

~~bioavailabi~~ bioavailability is the fraction of administered drug that reaches the systemic circulation (fraction of drug as chemically unchanged form).

ex: if 100 mg of drug are administered orally and 70 mg of this drug absorbed unchanged,

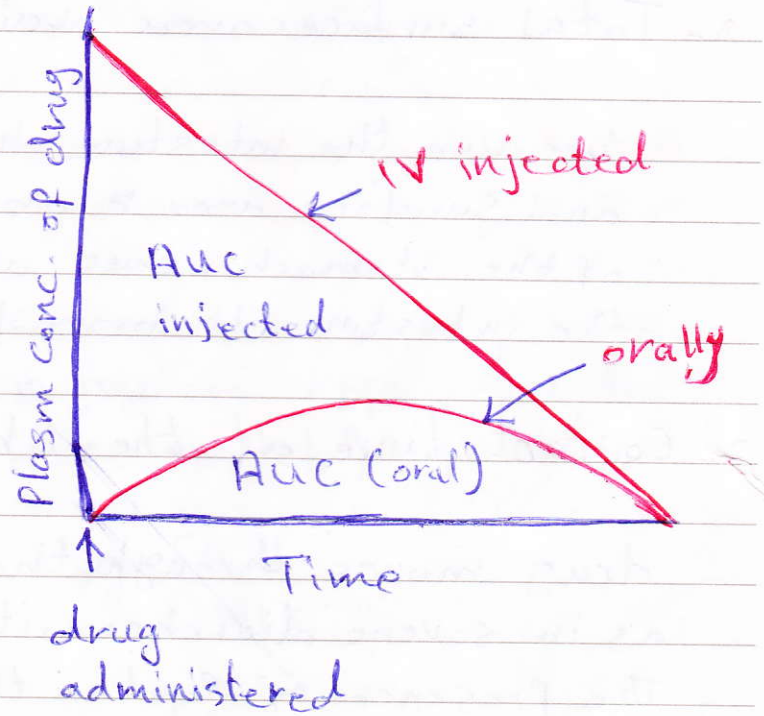
the bioavailability is 70 % (seventy Percent).

A- Determination of bioavailability :

bioavailability is determined by comparing plasma levels of a drug after oral administration with plasma drug levels by IV injection.

AUC = area under the curve

Bio availability $= \frac{\text{AUC oral}}{\text{AUC injected}} \times 100$



B- factors that influence bioavailability:

1- first-pass hepatic metabolism:

when drug is absorbed across the GI tract. it enters the portal circulation before entering the systemic circulation

if the drug is rapidly metabolized by the liver, the amount of unchanged reach ~~to~~ systemic circulation is decreased. (Lidocaine, Propranolol)

2- solubility of the drug:

hydrophilic drug are poorly absorbed because of their inability to cross the lipid-rich cell membrane

3- Chemical instability:

Some drug such as Penicillin G, are unstable in the pH of the gastric contents, other insulin are destroyed in the GI tract by digestive enzymes.

4- Nature of the drug formulation:

Durg absorption may be altered by factors unrelated to the chemistry of the drug, but for example:

- particle size.
- salt form.
- crystal, dispersing agent) can influence on the dissolution and therefore alter the rate of absorptio

- Drug Distribution

drug distribution is the process by which adrug reversibly leaves the bloodstream and enter the interstitium (fluid, extracellular) and or the cell of the tissues.

this process depend on:

1- Blood flow
2- Capillary Permeability.
3- Binding of drug to proteins (Plasma Protein)

1- blood flow:

The rate of blood flow to the tissue capillaries varies widely as result of the unequal distribution of Cardiac output to the varies organs.
blood flow to the brain, liver, kidney is greater than to the skeletal muscles, adipose tissue is still lower rate of blood flow.

2- Capillary Permeability: is determined by:

1- Capillary structure
2- Chemical nature of the drug.

1- Capillary structure in the brain is continuous, and no slit junction (Pore between the endothelial cell) in the basement membrane but in liver and spleen discontinuous capillaries and large plasma protein can pass.

General Pharmacology

Pharmacy:- Science which concened with collection, Preparation, standarization and dispensing of drugs.

Pharmacology: experimental science dealing(give) with the properties of drugs and their effects on living systems.

The knowledge of the history sources (Physical and chemical properties compound, biochemical and physiological effect, mechanism of action, absorption, distribution, biotransformation and excretion and therapeutic and other uses of drugs

Pharmacokinetics: study the fate of drug and effect of body on the drugs at the time course

1. absorption 2. distribution 3. metabolism
4. excretion

Pharmacodynamics: study the action and fate of drugs in the body.

its study of physiologic and biochemical effects of drugs and how these effects relate to a drugs mechanism of action.

Pharmacodynamics focuses on the action and effects of drugs within the body.

3- Binding of drug to Proteins:

Reversible binding to Plasma Protein, the drug bind non diffusible and slow transfer out of the vascular compartment.

Plasma albumin is the major drug binding Protein and may act as a drug reservoir, the free drug concentration is decrease.

Volume distribution:

The volume of distribution is a hypothetical volume of fluid into which a drug is disseminated.

A- water compartments in the body.

any drug enters the body, from whatever route of administration it has potential to distribute into any of three functionally distinct:

1- Compartment of body water.
2- Extracellular fluid.
3- Intra Cellular fluid.