Definitions

Pharmacology: The study or science of drugs. Or the study of the effects of chemical substances upon living tissues.

Drug: Chemical substance. Capable of modifying a biological system. Used for the treatment, diagnosis or prevention of a condition.

Pharmacodynamics: Study of the biological activity a drug has on a living system. Mechanism of action. Structure- activity relationship of the drug.

Pharmacokinetics: Study of the processes of absorption, distribution, transformation and excretion of drugs in the body in function of the time. Study of effects the body has on a drug.

Sources of Drugs

Natrual:

1: Insulin: Obtained from the pancreas of bovine or pigs

2: Digitalis: Extracted from species of the foxglove plant

3: Iron (ferrous/Sulfate): Obtained mineral sources

Synthetic:

1: Synthesized by chemists - Majority of today's drugs

Routes of Adminitration:

Inhalation:

Used as gas: volatile anaesthesia

Used as an areosol: bronchodialtors

Routes of Administration

Local routes of admistration:

- topical	- intrathecal
- intra-conjuctival	- vaginal
- intradermal	- intra-nasal
- intra-oral	- intra-articular

Locally administered drugs may result in production of systemic effects

Routes of Adminitration

Systemic:

Enternal Administration:

- sublingual

- gastrointersinal: oral

-rectal

Parenteral Administration:

- subcutaneous (sc)
- intramuscular (im)
- intravenous (iv)

General Principles of Drug Action:

*see picture in Powerpoint

Mechanisms involved in passage of drugs across cell membranes:

1. Pharmaceutical formulation

2. Lipid diffusion: A lipid-soluble , non-electrolyte is readily absorbed. A lipid insoluble non-electrolyte is absorbed very slowly. Most drugs are weak organic substances. Most drugs exist partly un-ionized and partly ionized

Most common mechanism by which drugs cross cell membranes: To enter the body, To be distributed To be reabsorbed

General Principles of Drug Action: (cont)

3. Aqueous Diffusion: Filtration through pores. Water-soluble drugs: MW < 100 Daltons, Cross the cell membranes through the polar pores and the spaces between membranes of adjacent cells.

4. Active transport: Specific carrier-mediated transport sysytem. For substances which are: Lipid insoluble to dissolve in the cell membrane and too large to flow through pores.

Features for active transport system: -Ability to workagainst concentration, osmotic ,electrical or hydrostatic gradiants. -Specificity. -Need for energy source (usually ATP) -Site for competition of drugs/substances. -Saturable

5. Facillitated Diffusion: Passive process. Involves a specific and saturable carrier system. More rapid than simple diffusion.

6. Pinocytosis: Extracellular fluid taken into a cell. The membrane develops a saccular indentation fillled with extracellular fluid. The indentation is pinched off forming a vesicle or vacuole of fluid within the cell.

Factors of the Fate of a Drug in the Body:

Physical and Chemical profile of the drug:

> 1. molecular Weight. 2. Chemical stabilty. 3. Lipid solubility.

Degree of ionization.

Absorption:

Transfer of a drug from its site of administration to the blood stream.

Its rate & efficiency depend on the route of administration.

Complete (100%) after IV administration.

Factors Influencing Absorption of Drugs:

1. Blood flow to the absorption site

2. Total surface area available for absorption

3. Contact time at the absorption site

4. Presence of food and gastric emptying

5. Binding of drugs to food constituents

pH , pKa and Ionization of a Weak Basic Drug:

When a weak basic drug is in a medium where the pH is **alkaline** , it dissociates into ionized and un-ionized particles. The fraction (%) of un-ionized particles is higher than the fraction of ionized particles. Therefore the absorption rate of the drug is higher. The higher the alkalinity of the medium the higher the absorption rate of a weak basic drug.

When a weak basic drug is in a medium where the pH is **acidic** , it dissociates into ionized and un-ionized particles. The fraction (%) of un-ionized particles is lower than the fraction of ionized particles. Therefore the absorption rate of the drug is lower. The higher the acidity of the medium the lower the absorption rate of the weak basic drug.

Drug Distribution:

Process by which a drug leaves the blood stream and enters the interstitium (extracellular fluid) or the cells of the tissues

Principle factors involved in drug distribution:

1.Blood flow

2.Capillary permeability

3.Degree of binding of the drug to plasma and tissue proteins

Drug Displacement:

Warfarin and other highly bound coumarin-type anticogaulants

Clofibrate Phenylbutazone, Ethacrynic acid, Mefenamic acid, Nalidixic acid, Oxyphebutazone , Chloral hydrate

Tolbutamide

Phenylbutazone, Salicylates, Sulfafurzole

Bioavailibilty:

Extent of absorption ofa drug following its administration by routes other than iv injection.

*factors that infuence bioavailibity:**

-First pass effect

-Solubility of drug

-Chemical stability

-Nature of drug formation

Therapeutic Equivalance:

Two similar drugs that have comparable efficancy and safety.

Bioequivalance:

Two related drugs that show comparable bioavailibity

Bioinequivalant: Two related drugs with a significant difference in bioavailability.

Inactivation of Drugs:

-Drug metabolism

-Drugs are eliminated from body by 2 principle mechanisms:

1. Liver metabolism

2. Renal excretion

> Water- soluble drugs are generally excreted unchanged by the kidney.
> Lipid- soluble drugs are not easily excreted by the kidney because they are *largely reabsorbed from the proximal tube*

Effects of Drug Metabolism:

> To form *inactive metabolite from an active drug*, thereby terminating the action of the drug. (eg. asprin, paracetamol)

> To form an *active metabolite from an inactive or less active drug.* (eg. dopamine)

>To form a *toxic metabolite from an initially less toxic drug.* (eg. hydroxylamine)