PHARMACOLOGY
THE HISTORY OF PHARMACOLOGY

Prehistoric people recognized the beneficial or toxic effects of many plant and animal materials. Early written records from Iraq, China and from Egypt list remedies of many types, including a few still recognized as useful drugs today. Most, however, were worthless or actually harmful.

In the 1500 years ago introduced rational methods into medicine, but none was successful owing to the dominance of systems of thought that purported to explain all of biology and disease without the need for experimentation and observation. This idea that disease was caused by excesses of bile or blood in the body, that wounds could be healed by applying a salve to the weapon that caused the wound, and so on.

Around the end of the 17th century, reliance on observation and experimentation began to replace theorizing in medicine. As the value of these methods in the study of disease became clear, physicians began to apply them to the effects of traditional drugs used in their own practices.

In the late 18th and early 19th centuries, began to develop the methods of experimental animal physiology and pharmacology. Advances in chemistry and the further development of physiology therapeutics only about 50 years ago it become possible to accurately evaluate therapeutic claims. Around the same time, a major expansion of research efforts in all areas of biology began. As new concepts and new techniques were introduced, information accumulated about drug action.

Two general principles that the student should always remember are, first, that all substances can under certain circumstances be toxic; and second, that all dietary supplements and all therapies promoted as health-enhancing should meet the same standards of efficacy and safety.
Pharmacology can be defined as the study of substances that interact with living systems through binding to regulatory molecules and activating or inhibiting normal body processes.

Medical pharmacology which is often defined as the science of substances used to prevent, diagnose, and treat disease.

Toxicology is that branch of pharmacology which deals with the undesirable effects of chemicals on living systems, from individual cells to complex system

Pharmacogenetics Which a branch of pharmacology deal with genetic basis for difference drug responsiveness among population

Drug- Drug may be defined as any substance that produce a change in biologic function through its actions.
In the great majority of cases, the drug molecule interact with a specific molecule in the biologic system that plays a regulatory role. This molecules called a receptor. Drugs may be synthesized within the body (e.g., hormones) or may be chemicals not synthesized in the body. Drug to interact chemically with its receptor, a drug molecule must have the appropriate size, electrical charge, shape, and atomic composition.

Classification of drugs
Drugs may be classified by:
1• Body system, e.g. alimentary, cardiovascular
2• Therapeutic use, e.g. receptor blockers, enzyme inhibitors, ion channels
3• Mode or site of action. loop diuretic
4 Molecular structure, e.g. glycoside, alkaloid, steroid
Pharmacodynamics is what drugs do to the body:

**Mechanisms of drug action**

1- Drugs act on the cell membrane by:
   a- Action on specific receptors e.g. histamine receptors
   b- Interference with selective *passage of ions across membranes*, e.g. calcium entry (or channel) blockers
   c- Inhibition of membrane bound enzymes and pumps, e.g. membrane bound ATPase by cardiac glycoside;

2- Drugs act on metabolic processes within the cell by:
   a- *Enzyme inhibition*,
   b- Inhibition of *transport processes*.
   c- *Incorporation into larger molecules*
   d- Altering metabolic processes

3- Drugs act outside the cell by:
   a *Direct chemical interaction*, e.g., antacids
   b *Osmosis*, as with purgatives, e.g. magnesium sulphate, and diuretics, e.g. mannitol,

**RECEPTORS**

Most receptors are protein macro-molecules. When the natural transmitter or hormone (endogenous ligands) binds to the receptor,
the proteins undergo an alteration in conformation which induces changes in systems.

Types of Drug- receptors interaction

1-Agonists.
2-Antagonists
3- Partial agonists.

4-Inverse agonists.

5-Physiological (functional) antagonism

Drug passage across cell membranes
  ● 1-Passive diffusion
  ● 2-Filtration and bulk flow
  ● 3-Endocytosis
  ● 4-Ion-pairing
  ● 5-Active transport

Pharmacokinetics is what the body does to drugs

The individual processes( Absorption, Distribution , (Metabolism (biotransformation), Execration ) Elimination.

Absorption
Considerations of anatomy, physiology, pathology, pharmacology, therapeutics and convenience determine the routes by which drugs are administered. Usually these are:
1- • Internal : by mouth (swallowed) or by sublingual or by rectum
2• Parenteral: by injection to intravenous or, intramuscular, subcutaneous or infusion,
3• Other routes, e.g. inhalation, topical application for local (skin, eye, lung) or for systemic (trans dermal) effect intrathecal, intradermal, intranasal, intratracheal, intrapleural, are used when appropriate.
**Presystemic (first-pass) elimination.**
Drugs are metabolized in a single passage through the gut wall and (principally) the liver.

**Distribution**
If a drug is required to act throughout the body or to reach an organ, it must be go into the blood and into other body compartments. Most drugs distribute widely, in part dissolved in body water, in part bound to plasma proteins, in part to tissues. Drugs may bind selectively to plasma or tissue proteins or be localised within particular organs.

**Metabolism**
Metabolism is a general term for chemical transformations that occur within the body and its processes change drugs by reducing lipid solubility to enhance elimination and alter a biological activity.

1. Conversion of a pharmacologically active to an inactive substance.
2. Conversion of one pharmacologically active to another active
3. Conversion of a pharmacologically inactive to an active substance, i.e. prodrugs

**THE METABOLIC PROCESSES**
The liver is by far the most important drug metabolising organ, although a number of tissues, including the kidney, gut mucosa, lung and skin also contribute.

**Phase 1** metabolism a change in the drug molecule by oxidation, reduction or hydrolysis

**Phase II**
water-soluble conjugate which is readily eliminated by the kidney. Almost invariably terminates biological activity.

**Elimination**
Removed of drug from body by Renal or hepatic or pulmonary elimination.
**Dose:**
Sub Therapeutic dose:
Therapeutic dose:
Minimum dose:
Maximum dose:
Toxic dose:
Fatal dose:

**Median effective dose (ED50):**
the dose at which 50% of individuals exhibit the specified effect.

**Median toxic dose (TD50):**
the dose required to produce a particular toxic effect in 50% of animals

**Median lethal dose (LD50):**
the dose required to produce death in 50% of animals

**Duration of action**: Time from beginning of drug action to end

**Onset of drug action**: Time from drug administration to appearance of action

**T1/2**: Time required to decrease amount of drug in blood to half

**Bioavailability**: Fraction of unchanged drug in blood to dose administered