UNIT I

BIOPHARMACEUTICS

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Introduction to biopharmaceutics:

- **Biopharmaceutics**: the study of how the physicochemical properties of drugs, dosage forms and routes of administration affect the rate and extent of the drug absorption.

- Thus, biopharmaceutics involves factors that influence the:
  1. Protection and stability of the drug within the product;
  2. The rate of drug release from the product;
  3. The rate of dissolution of the drug at the absorption site; and
  4. The availability of the drug at its site of action.
Introduction to biopharmaceutics (Cont.):

Scheme demonstrating the dynamic relationships among the drug, the product, and pharmacologic effect.
Introduction to bipharmaceutics (Cont.):

- **ADME**: is an acronym in pharmacokinetics and pharmacology for absorption, distribution, metabolism, and excretion, and describes the disposition of a pharmaceutical compound within an organism.

- **Pharmacokinetics**: The study and characterization of the time course (kinetics) of drug absorption, distribution, metabolism and excretion (ADME) and their relationship with its therapeutic and toxic effects of the drug.
• Absorption: is the process of a movement of a drug from its site of administration to systemic circulation.

• Distribution: is the dispersion of substances throughout the fluids and tissues of the body i.e. the movement of drug between one compartment and the other.

• Elimination: a process that tends to remove the drug from the body and terminates its action.

• Metabolism: is the irreversible transformation of parent compounds into daughter metabolites.

• Excretion: is the elimination of the substances from the body.
The use of pharmacokinetic principles in optimizing the dosage to suit individual patient needs and achieving maximum therapeutic utility.

To achieve optimal therapy with a drug, the drug product must be designed to deliver the active principle at an optimal rate and amount, depending upon patient’s needs.

The therapeutic objective can only be achieved through a better understanding of pharmacokinetics which helps in designing a proper dosage form.
Drug administration and therapy can now be divided into 4 phases:

1. **The Pharmaceutical Phase**: It is concerned with-
   - Physicochemical properties of drug
   - Design and manufacture of an effective drug product for administration by a suitable route.

2. **The Pharmacokinetic phase**: It is concerned with the ADME of drugs as elicited by the plasma drug-time profile.

3. **The Pharmacodynamic Phase**: It is concerned with the biochemical and physiological effects of the drug and its mechanism of action. It is characterized by the concentration of drug at the site of action and its relation to the magnitude of effects observed.
Thus in comparison-
- **Pharmacokinetics** is a study of what the body does to the drug, whereas
- **Pharmacodynamics** is a study of what the drug does to the body.
- **Pharmacokinetics** relates changes in concentration of drug within the body with time after its administration, whereas
- **Pharmacodynamics** relates response to concentration of drug in the body.

4. **The Therapeutic Phase**: It is concerned with the translation of pharmacological effect of drug in the body.
Pharmacodynamics is the study of the biochemical and physiological effects of drugs on the body or within the body and the mechanisms of drug action and the relationship between drug concentration and effect. One dominant example is drug-receptor interactions as modeled by

\[ L + R \rightleftharpoons L \cdot R \]

where \( L \) = ligand (drug), \( R \) = receptor (attachment site), reaction dynamics that can be studied mathematically through tools such as free energy maps. Pharmacodynamics is often summarized as the study of what a drug does to the body.
The terms **pharmacogenomics** and pharmaco genetics tend to be used interchangeably.

- Pharmacogenetics is generally regarded as the study or clinical testing of genetic variation that gives rise to differing response to drugs, while **pharmacogenomics** is the broader application of genomic technologies to new drug discovery and further characterization of older drugs.
- Pharmacogenetics refers to genetic differences in metabolic pathways which can affect individual responses to drugs, both in terms of therapeutic effect as well as adverse effects.
PHARMACOTHERAPEUTICS
The study of the therapeutic uses and effects of drugs.

CELL MEMBRANE STRUCTURE AND PHYSIOLOGY
- Also called the plasma membrane, plasmalemma or phospholipid bilayer.
- The plasma membrane is a flexible yet sturdy barrier that surrounds & contains the cytoplasm of a cell.
- Cell membrane mainly consists of:
  1. Lipid bilayer-
     - phospholipid
     - Cholesterol
     - Glycolipids.
  2. Proteins-
     - Integral membrane protein
     - Lipid anchored proteins,
     - Peripheral Proteins
For a drug to be absorbed and distributed into organs and tissues and eliminated from the body, it must pass through 1 or more biological membranes at various locations. Such a movement of drug across the membrane is called as drug transport.

The basic structure of cell membrane is shown below;
PHOSPHOLIPID

The phospholipids belayed is arranged in such a fashion that the hydrocarbon chains of the amphiphilic phospholipid molecules are oriented to form the lipophilic phase, and their polar heads oriented to form the outer and inner hydrophilic boundaries.

CHOLESTEROL

- Amount in membrane is 20%.
- Insert in membrane with same orientation as phospholipids molecules.
- Polar head of cholesterol is aligned with polar head of phospholipids.
FUNCTION:
- Immobilize first few hydrocarbons groups phospholipids molecules.
- Prevents crystallization of hydrocarbons & phase shift in membrane.

GLYCOLIPIDS
- Another component of membrane lipids present about 5%.
- Carbohydrate groups form polar “head”.
- Fatty acids “tails” are non polar.
- Present in membrane layer that faces the extracellular fluid.
- This is one reason due to which bilayer is asymmetric.
FUNCTIONS:
- Protective
- Insulator
- Site of receptor binding

INTEGRAL PROTEINS
- Also known as “Transmembrane protein”.
- Have hydrophilic and hydrophobic domain.
- Hydrophobic domain anchores within the cell membrane and hydrophilic domain interacts with external molecules.
- Hydrophobic domain consists of one, multiple or combination of $\alpha$–helices and $\beta$–sheets protein units.
- Eg. – Ion Channels, Proton pump, GPCR
LIPID ANCHORED PROTEIN

- Covalently bound to single or multiple lipid molecules.
- Hydrophobically inert into cell membrane & anchor the protein.
- The protein itself is not in contact with membrane.
- **Eg.** – G Proteins.
PERIPHERAL PROTEINS

- Attached to integral membrane proteins OR associated with peripheral regions of lipid bilayer.
- Have only temporary interaction with biological membrane.
- Once reacted with molecule, dissociates to carry on its work in cytoplasm.
- **Eg.** – Some Enzyme, Some Hormone
Membrane is a mayonnaise sandwich where a bimolecular layer of lipids is contained between two parallel monomolecular layers of proteins.

The hydrophobic core is responsible for the relative impermeability of polar molecules.

Aqueous filled pores or perforations of 4-10Å in diameter are also present in membrane structure through which inorganic ions and small organic water soluble molecules like urea can pass.
In general, the biomembrane acts like a semipermeable barrier permitting rapid and limited passage of some compounds while restricting that of others.

The GI lining constituting the absorption barrier allows most nutrients like glucose, amino acids, fatty acids, vitamins, etc to pass rapidly through it into the systemic circulation but prevents the entry of certain toxins and medicaments.

Thus for a drug to get absorbed after oral administration it must pass through this biological barrier.
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