MEDICINAL CHEMISTRY 1

UNIT – 1

Introduction to Medicinal Chemistry:

Definition: Medicinal chemistry is a multidisciplinary field that integrates knowledge from chemistry, biology, and pharmacology to discover, develop, and design bioactive compounds with therapeutic potential.

History and Development:

- Ancient civilizations, such as the Greeks, Egyptians, and Chinese, used natural substances for medicinal purposes.
- In the 19th century, advancements in organic chemistry led to the isolation of active compounds from plants.
- The 20th century saw the development of synthetic drugs, penicillin being a landmark discovery.
- Modern medicinal chemistry involves molecular design, computer-aided drug design, and the study of molecular mechanisms.

Physicochemical Properties in Relation to Biological Action:

1. **Ionization:** pH-dependent ionization affects drug absorption, distribution, and elimination. Weak acids or bases change ionization states in different pH environments.
2. **Solubility:** Affects drug absorption. Poorly soluble drugs may have low bioavailability.
3. **Partition Coefficient:** Determines the distribution of a drug between lipid and water phases. Important for drug absorption.
4. **Hydrogen Bonding:** Interactions with biological molecules. Hydrogen bonds influence drug-receptor interactions.
5. **Protein Binding:** Influences drug distribution and duration of action. Only unbound drug is pharmacologically active.
6. **Chelation:** Metal ion binding can affect drug stability and activity.
7. **Bioisosterism:** Replacement of one atom or functional group with another having similar properties. Used to optimize drug properties.
8. **Optical and Geometrical Isomerism:** Stereochemistry affects drug activity. Enantiomers can have different biological effects.

Drug Metabolism:

Principles:

- **Phase I Metabolism:** Converts lipophilic compounds to more polar compounds through reactions like oxidation, reduction, or hydrolysis. Often introduces or unmasks functional groups.
- **Phase II Metabolism:** Involves conjugation reactions (e.g., glucuronidation, sulfation) to increase water solubility for excretion.

Factors Affecting Drug Metabolism:

1. **Enzyme Induction/Inhibition:** Drugs can induce or inhibit metabolic enzymes, altering the metabolism of other drugs.
2. **Genetic Factors:** Genetic polymorphisms can affect enzyme activity, leading to interindividual variability in drug metabolism.
3. **Stereochemical Aspects:** Stereoisomers may be metabolized differently. Enzymes may show stereoselectivity.
4. **Age:** Metabolic capacity can vary with age.
5. **Disease States:** Conditions affecting liver function or enzyme activity can influence drug metabolism.

Understanding these principles is crucial for medicinal chemists to design drugs with optimal pharmacokinetic properties and therapeutic efficacy.