INTRODUCTION TO PHARMACEUTICAL AND MEDICINAL CHEMİSTRY

PHARMACEUTICAL CHEMISTRY I

PHA385

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Pharmaceutical chemistry and **Medicinal chemistry**

- **chemistry-based disciplines,**
- **also involving aspects of biological, medical and pharmaceutical sciences.**

Treatment of disease:

- **Radical treatment** is vigorous treatment that aims at the **complete cure** of a disease.

- **Symptomatic treatment** is any medical therapy of a disease that only **affects its symptoms**.

PROPERTIES OF IDEAL DRUG

the most potent
the least toxic
the least side effects

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ADME

ADME is an abbreviation in pharmacokinetics and pharmacology for "Absorption, Distribution, Metabolism, and Excretion," and describes the disposition of a pharmaceutical compound within an organism.

Absorption

For a compound to reach a tissue, it usually must be taken into the bloodstream - often via mucous surfaces like the digestive tract (intestinal absorption) - before being taken up by the target cells.

Distribution

The compound needs to be carried to its effector site, most often via the bloodstream. From there, the compound may distribute into muscle and organs, usually to differing extents.

Metabolism

Compounds begin to break down as soon as they enter the body. The majority of drug metabolism is carried out in the liver by cytochrome P450 enzymes.

As metabolism occurs, the initial (parent) compound is converted to new compounds called metabolites.

Excretion

Compounds and their metabolites need to be removed from the body via excretion, usually through the kidneys (urine) or in the feces.

Drug Transport (Diffusion) Systems

- Active Transpot
- Passive Transport
- Facilitated Diffusion
- Pinocytosis

Drug Design

Drug design, often referred to as **rational drug design** or simply rational design, is the inventive process of finding new drugs based on the knowledge of a biological target.

computer-aided drug design

structure-based drug design

Drug Targets

A biomolecular target (most commonly a protein or nucleic acid) is a key molecule involved in a particular metabolic or signaling pathway that is associated with a specific disease condition or pathology or to the infectivity or survival of a microbial pathogen.

Molecular Modification

Molecular modification is chemical alteration of a known and previously characterized lead compound for the purpose of enhancing its usefulness as a drug.

Isosteres

Bioisosteres

In 1970, Alfred Burger classified and subdivided bioisoteres into two broad categories:

1. Classic Bioisoteres
2. Non Classic Bioisoteres

Classical bioisosteres

Classical bioisosterism was originally formulated by James Moir and refined by Irving Langmuir as a response to the observation that different atoms with the same valence electron structure had similar biological properties.

Non-classical bioisosteres

Non-classical bioisosteres may differ in a multitude of ways from classical bioisosteres, but retain the focus on providing similar sterics and electronic profile to the original functional group.

The Significance of Acid/Base Properties in Drug Discovery

Medicinal chemists have been actively involved in understanding drug failures by examining and defining the **physicochemical properties** of compounds that predict successful outcomes.

There is clear evidence that working with large and lipophilic molecules is related to problems concerning promiscuity, **metabolism, bioavailability, efflux, solubility and plasma protein binding**.

An **acid** has been simply classified as a species **HA** which at a **pH above** the **pK_a** will dissociate into the **anionic A- form** and a **proton** (for a simple monoprotic case).

Similarly a **basic** substance can be depicted as species **B** that will accept a proton **below** the **pK_a** value to generate the **cationic** species.