Pharmaceutical Chemistry

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Introduction to pharmaceutical Chemistry

Medicinal chemistry and pharmaceutical chemistry are disciplines at the intersection of chemistry, especially synthetic organic chemistry, and pharmacology and various other biological specialties, where they are involved with design, chemical synthesis and development for market of pharmaceutical agents, or bio-active molecules (drugs).

Definition:-

Pharmaceutical chemistry is the study of drugs, and it involves drug development. This includes drug discovery, delivery, absorption, metabolism, and more. There are elements of biomedical analysis, pharmacology, pharmacokinetics, and pharmacodynamics.

Generally Medicinal Chemists can:

- Make new compounds
- Determine their effect on biological processes.
- Alter the structure of the compound for optimum effect and minimum side effects.
- Study uptake, distribution, metabolism and excretion of drugs.

Medicinal chemistry covers the following stages:

(i) In the first stage new active substances or drugs are identified and prepared from natural sources, organic chemical reactions or biotechnological processes. They are known as lead molecules.
(ii) The second stage is optimization of lead structure to improve potency, selectivity and to reduce toxicity.
(iii) Third stage is development stage, which involves optimization of synthetic route for bulk production and modification of pharmacokinetic and pharmaceutical Properties of active substance to render it clinically useful.

A **drug** is, in the broadest of terms, a chemical substance that has known biological effects on humans or other animals.

In **pharmacology**, a drug is "a chemical substance used in the treatment, cure, prevention, or diagnosis of disease ." Pharmaceutical drugs may be used for a limited duration, or on a regular basis for chronic disorders.

Psychoactive drugs:

are chemical substances that affect the function of the nervous system. Alcohol, nicotine, and caffeine are the most widely consumed psychoactive drugs worldwide.

Recreational drugs:

Are drugs that are not used for medicinal purposes, but are instead used for pleasure. Common recreational drugs include alcohol, nicotine and caffeine, as well as other substances such as opiates anesthesia.

Some drugs can cause addiction and all drugs can cause side effects..

CLASSIFICATION OF DRUGS:-

Drugs can be classified according to various criteria:

1. By origin—sources of drugs

Drugs may be obtained from 1. Plants 2. Animals 3. Minerals or 4. Microorganisms. The drugs may also be semi synthetic or synthetic compounds. The sources of drugs are summarized as follows:

A. Synthetic. Most of the drugs in use today are synthetic in origin. Such drugs are chemically pure and it is easy to maintain supply line. Ex. : Aspirin, Paracetamol.

B. Natural. There are number of natural sources. They are:

(i) **Plants.** A number of plant based drugs such as taxol, digoxin, quinine, reserpine, ergotamine, ephedrine, colchicine etc. are still a part of standard therapy.

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(ii) **Animal.** Some modern drugs continue to be derived from animal sources because the synthesis of such
chemicals is very expensive. Ex. :heparin, insulin, thyroid extracts and enzymes.

(iii) **Microorganisms.** Following the accidental discovery of penicillin from a mold in 1928 and its successful use in chemotherapy in 1940, a large number of antibiotics have been discovered from a variety of soil fungi and some bacteria. These drugs form the most important group of chemotherapeutic agents used against infective diseases.
Ex. : Penicillin, Streptomycin, Tetracycline.

(iv) **Minerals.** Minerals of medicinal value are iron, calcium, magnesium, aluminium, sodium, potassium etc.

C. Semi-synthetic. In some cases, especially with complex molecules, the synthesis of a drug may be
very difficult or expensive and uneconomical. At the same time, the ones derived from natural sources may be impure. In these cases semi synthetic processes are used.
Ex. : 6-Aminopenicillanic acid is obtained from the fungus *Penicillium chrysogenum.*

2. By Action

According to similarity of drug effects: Ex: marijuana and atropine both increase heart rate and cause
dryness of the mouth. Thus, marijuana would be classified as atropine-like drug.

3. By therapeutic use

These drugs mainly affect the normal dynamic processes of the body. They are;
(i) Anti-arrhythmics
(iv) Anti-hypertensives
(v) Antiallergic agents
(vi) Drugs acting on GIT
(vii) Drugs influence renal function
(viii) Drugs acting on central nervous system
(xi) Drugs acting on peripheral nervous system

4. By site of drug action

Ex: Alcohol is a depressant drug because of its depressant CNS action. This system is limited when a drug has an effect at several body sites (e.g., the CNS stimulant cocaine also has local anesthetic (pain reducing) effects.

5. By Chemical Structure

Drugs are classified according to the chemical structure or functional group. They may be further sub classified as:

(i) Hydrocarbons
(ii) Halogenated compounds
(iii) Alcohols
(iv) Carboxylic acids
(v) Phenols
(vi) Nitro compounds
(vii) Amides
(viii) Amines
(ix) Sulphonamides, sulphones etc.

CHARACTERISTICS OF DIFFERENT ROUTES OF DRUG ADMINISTRATION:-

Most drugs can be administered by a variety of routes. The choice of appropriate route in a given situation depends both on drug as well as patient related factors. Drugs my be administered locally or systemically. The drugs administered through systemic routes are intended to be absorbed into blood and distributed all over the body.

1. Oral/swallowed.

Oral ingestion is the oldest and commonest mode of drug administration. Most drugs in this route of administration are absorbed in small intestine. Full stomach delays absorption (e.g. alcohol). Several drugs may subject to first-pass metabolism by liver.

(Ex: Aldosterone, cortisol, acetyl salicylic acid). *The drug candidates may undergo metabolism before* reaching target receptors.

2. Oral/sublingual.

The tablet containing the drug is placed under the tongue or crushed in the mouth and spread over the buccal mucosa. In this mode of administration fast systemic absorption is observed which, by pass gastrointestinal tract entry.

3. Rectal. Here the drugs are absorbed directly from the rectum. It partially avoids first-pass metabolism by liver and also for those likely to vomit and lose swallowed medication.
Certain irritant and unpleasant drugs can be put into rectum . Ex: Aminophylline, indomethacin, paraldehyde, diazepam, ergotamine.

4. Epithelial. In this technique drugs are absorbed through the skin. This route is useful for those likely
to vomit (e.g. nicotine patch).

5. Inhalation. Volatile oils and gases are given by inhalation ex: genera anesthetic, amyl nitrite.
The drugs enter the bloodstream very rapidly from the lungs. Here no absorption or first-pass metabolism problems occur. This route is potentially dangerous because it is so fast and direct.

6. Parenteral Route. Parenteral administration refers to administration by injection into tissue fluid or blood without having to cross the intestinal mucosa.
The important parenteral routes are subcutancus (SC);
intramuscular (IM); intravenous (IV). The rate of absorption depends on blood flow through injection site.
SC or IM exert effects more quickly than oral
administration. IV is the fastest route and most certain in terms of obtaining desired concentration of drug in blood plasma.

Sites of Drug Action:-

I. Enzyme inhibition.

The prevention of an enzymatic process as a result of the interaction of some substance with an enzyme so as to decrease the rate of the enzymatic reaction.

The substance causing such an effect is termed an inhibitor. Enzyme inhibitors ar e important as Chemotherapeutic agents, as regulators in normal control of enzymatic processes in living organisms, and as useful agents in the study of bioc hemistry.

2. Drug-Receptor interaction. Drugs act on the cell membrane by physical and/or chemical interactions.

This is usually through specific drug receptor sites known to be located on the membrane.

A receptor is the specific chemical constituents of the cell with which a drug interacts to produce its pharmacological effects. Some receptor sites have been identified with specific parts of proteins and nucleic acids.

3. Non-specific interactions.

Drugs act exclusively by physical means outside of cells. These sites include external surfaces of skin and gastrointestinal tract. Drugs also act outside of cell membranes by chemical interactions. Neutralization of stomach acid by antacids is a good example

Mode of Drug action:-

It is important to distinguish between actions of drugs and their effects. Actions of drugs are the biochemicals, physiological mechanisms by which the chemical produces a response in living organisms.

The effect is the observable consequence of a drug action. For example, the action of penicillin is to interfere with cell wall synthesis in bacteria and the effect is the death of bacteria.

One major problem of pharmacology is that no drug produces a single effect. The primary effect is the desired therapeutic effect. Secondary effects are all other effects beside the desired effect which may be either beneficial or harmful. Since the differences may not be very great, drugs may be nonspecific in action and alter normal functions as well as the undesirable ones, this leads to side effects.

The biological effects observed after a drug has been administered are the result of interaction between that chemical and some part of the organism. Mechanisms of drug action can be viewed from different perspectives, namely, the site of action and the general nature of the drug-cell interaction.

I. Killing foreign organisms. Chemotherapeutic agents act by killing or weakening foreign organisms such as bacteria, worms, and viruses. The main principle of action is selective toxicity, i.e. the drug must be more toxic to the parasite than to the host.

2. Stimulation and depression. Drugs act by stimulating or depressing normal physiological functions. Stimulation increases the rate of activity while depression reduces it.

3. Irritation. It is a non-specific action of a drug that can occur in all the body tissues. Certain drugs act by causing irritation. Ex: Drugs like senna and castor oil show their laxative effects by their irritant action on gastrointestinal tract.

MECHANISM OF DRUG ACTION:--

The fundamental mechanisms of drug action can be distinguished into following categories.

1. Physical Properties

A physical property of the drug is responsible for its action.

(*i*) ***Taste.*** Bitter taste drugs increase the flow the hydrochloric acid reflexly in the stomach.

Ex: Quassia, Chirata

(*ii*) ***Mass.*** By increasing the bulk of drug in intestine produce laxative effect. Ex: Isapgol

(*iii*) ***Adsorption.*** Certain drugs like kaolin adsorb water on to its surface.

(*iv*) ***Radioactivity.*** The radioactive substances are commonly used to treat cancer. Ex: 125.

2. Chemical Properties:--

The drugs react extracellularly according to simple chemical reactions like neutralization, chelation, oxidation etc. Ex:

(*i*) *Aluminium hydroxide neutralizes acid in stomach* (*ii*) *Toxic heavy metals can be eliminated by chelating agents like EDTA, BAL,* penicillamine etc.

(*iii*) *Oxidising agents are germicidal.*

3. Through Enzymes

Enzymes are very important targets of drug action because almost all biological reactions are carried out
under the influence of enzymes. Drugs may either increase or decrease enzymatic reactions. Ex:
(*i) Adrenaline stimulates adenyl cyclase*
(*ii) Pyridoxine acts as a cofactor and increases decarboxylase activity.*

4. Through Receptors

A large number of drugs act through specific macromolecular components of the cell, which regulate critical functions like enzymatic activity, permeability, structural features etc.

These macromolecules, which bind and interact with the drugs, are called receptors.