Drugs and Chemotherapy

In general the drug may be defined as the substances used in the prevention, diagnosis, treatment or cure of disease in man or animals.

"The use of chemicals to destroy infectious micro organisms without causing any injury to the host is called as chemotherapy".

1. Classification of drugs

(a) On the basis of pharmacological effect

It is useful for doctors because it provides them the whole range of drugs available for the treatment of a particular type of problem. For example, analgesics have pain killing effect, antiseptics kill or arrest the growth of microorganisms.

(b) On the basis of drug action

It is based on the action of a drug on a particular biochemical process. For example, all antihistamines inhibit the action of the compound, histamine which causes inflammation in the body.

(c) On the basis of chemical structure

Drugs classified in this way share common structural features and often have similar pharmacological activity.

(d) On the basis of molecular targets

Drugs usually interact with biomolecules such as carbohydrates, lipids, proteins and nucleic acids. These are called target molecules or drug targets. Drugs possessing some common structural features may have the same mechanism of action on targets.

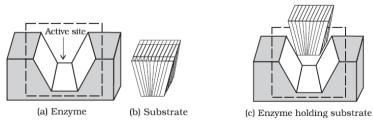
2. Drug target interaction

Macromolecules of biological origin perform various functions in the body for example proteins which perform the role of biological catalysts in the body are called **enzymes**, and those which are crucial to communication system in the body are called **receptors**.

2.1 Enzymes as drug targets

(a) Catalystic action of enzymes

In catalytic activity, enzymes perform two major functions as follows (i) To hold the substrate for chemical reaction :



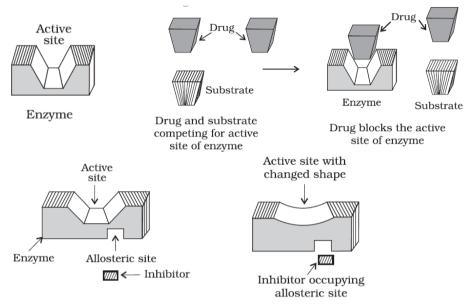
(ii) The second function of the enzyme is to provide functional group which will attacks the substrate to carry out chemical reaction.

(b) Drug enzyme interaction

Drugs inhibit any of the above mentioned activities of enzymes. These can block the binding site of the enzyme and prevent the binding of substrate, or can inhibit the catalytic activity of the enzyme. Such drugs are called **enzyme inhibitors**.

(i) Drugs compete with the natural substrate for their attachment on the active sites of enzymes. Such drugs are called **competitive inhibitors**.

(ii) Some drugs do not bind to the enzyme's active site. These bind to a different site of enzyme which is called **allosteric site**.



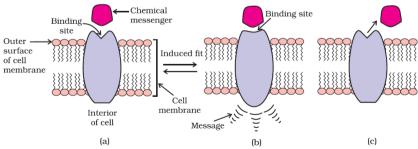
2.2 Receptors as drug targets

Receptors are proteins that are crucial to body's communication process.

There are two types of chemical messengers :

(i) Hormones (ii) Neurotransmitters.

In the body, message between two neurons and that between neurons to muscles is communicated through certain chemicals. These chemicals, known as **chemical messengers** are received at the binding sites of receptor proteins. To accommodate a messenger, shape of the receptor site changes. This brings about the transfer of message into the cell. Thus, chemical messenger gives message to the cell without entering the cell.



(a) Receptor receiving chemical messenger

(b) Shape of the receptor changed after attachment of messenger

(c) Receptor regains structure after removal of chemical messenger.

Drugs that bind to the receptor site and inhibit its natural function are called **antagonists**. These are useful when blocking of message is required. There are other types of drugs that mimic the natural

messenger by switching on the receptor, these are called **agonists**. These are useful when there is lack of natural chemical messenger.

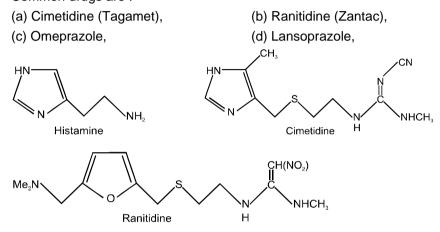
3. Therapeutic action of different class of drugs

3.1 Antacids

The chemicals which are used to reduce the acidity of the stomach are called antacids.

*Antacids are basic in nature. Their pH value is in the range of 7.0 to 8.0. Example sodium hydrogencarbonate or a mixture of **aluminium and magnesium hydroxide**.

Excess of acidity leads to formation of excess of histamine. Therefore modern synthetic drugs are antihistamines for the treatment of gastic ulcers by blocking the acid release action of histamine. Common drugs are :

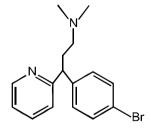


3.2 Antihistamines or Antiallergic drugs

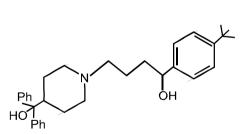
Histamine is a potent vasodilator. It has various functions. It contracts the smooth muscles in the bronchi and gut and relaxes other muscles, such as those in the walls of fine blood vessels. Histamine is also responsible for the nasal congestion associated with common cold and allergic response to pollen.

*Antihistamines are the drugs which diminish or abolish the effects of histamine.

Synthetic drugs, brompheniramine (Dimetapp) and terfenadine (Seldane) act as antihistamines.



Brompheniramine (Dimetapp. Dimetane)



Terfenadine (Seldane)

Allergy : Allergy may be defined as the hypersensitive reponse of the body of certain persons to the external stimulus (such as some drugs, foods, dust, pollen grains, catfur fabrics etc.) *The substances which cause allergy are called allergens. *Most commonly used anti-histamine under the trade name **avil (Pheniramine maleate) and zeet.**

3.3 Neurologically active drugs

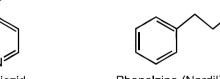
(a) Tranquilizers (Antidepressant drugs)

*The chemicals which are used to reduce mental tension, relieve anxiety and mental stress are called Tranquilizer. They act on central nervous system and are hypnotics.

*Tranquilizers are effective in such mental disorder when ordinary hypnotics or sedatives fail. These are called as psychotherapeutic drugs.

Noradrenaline is a mood change neurotransmitter. Iproniazid and phenelzine are anti depressent drugs. These drugs inhibits the enzyme which catalyse the degradation of noradrenaline.

 $O_{\text{NHNHCH}(CH_3)_2}$



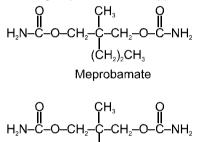
Iproniazid

Phenelzine (Nardil)

Note : * Reserpine, an alkanoid, is a powerful tranquillizer. It is obtained from a plant Rauwolfia serpentina (common name - Sarpagandha) which grows in india.

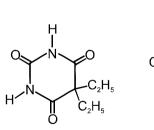
Tranquillizer namely chlordiazepoxide and meprobamate are relatively mild suitable for relieving tension. Equanil is used in controlling depression and hypertension.



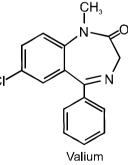


Equanil

Barbituric acid and their derivatives (Barbiturates) as **veronal**, **amytal**, **nembutal**, **seconal** and **luminal** are hypnotic and sleep producing agents. Some other substances used as tranquillizers are valium and serotonin.



Veronal



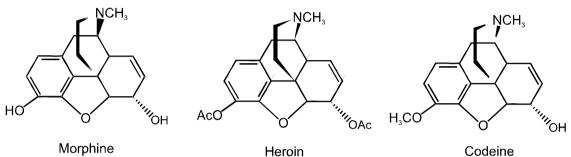
(b) Analgesics

The chemicals which are used for relieving pain are called Analgesics.

(i) Non-narcotic analgesics (Non addictive) : Aspirin (acetyl salicylic acid), Paracetamol (4-acidamido phenol), Ibuprofen belong to this class. These drugs also act as antipyretic (reducing fever), and preventing platelet coagulation.

(ii) Narcotic Analgesics

Morphine, Heroin, Codeine and its homolgues in medicinal doses, relieve pain and produce sleep. In higher doses these produce STUPOR, COMA, CONVULSIONS and ultimately death. The narcotics are mainly used for the relief of postoperative pain, cardiac pain and pain of terminal cancer, and in child birth.



3.4 Antimicrobials

*The chemicals which stop the growth or kill the micro organism such as bacteria, virus, fungi, molds etc are called antimicrobials.

* Antibiotics, antiseptics and disinfectants are antimicrobial drugs.

(a) Antibiotics

*The chemicals produced by micro organisms like bacteria, fungi and molds that inhibit the growth or destory other micro organism causing infectious diseases in men or animal's body are called antibiotics. The range of bacteria or other microorganisms that are affected by a certain antibiotic is expressed as its spectrum of action.

Antibiotics which kill or inhibit a wide range of Gram-positive and Gram-negative bacteria are said to be **broad spectrum antibiotics**. Those effective mainly against Gram-positive or Gram-negative bacteria are **narrow spectrum antibiotics**.

Bactericidal	Bacteriostatic
Penicillin	Erythromycin
Aminoglycosides	Tetracycline
ofloxacin	Chloramphenicol

(I) **Penicillin :** *Six types of penicillines have been isolated so far. Among them penicillin-G is most widely used and is narrow spectrum.

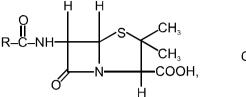
*Ampicillin and amoxicilline are synthetic modification of penicilline and these have broad spectrum effect.

Penicillin is used for the treatment of pneumonia bronchitis bounds etc.

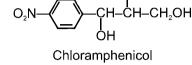
(II) Streptomycin : It is an effective broad spectrum antibiotic. It is used for the treatment of tuberculosis, meningitis and pneumonia

(III) Tetracyclin : Teramycin and oriomycin are important examples of this class of antibiotics. Teramycin is used for the treatment of typhoid and oriomycin is used for the treatment of eyes.

(IV) Chloramphenicol : It is marketed as chloromycetin and is used for the treatement of typhoid, dysentery pneumonia, meningitis etc.



General Sturcture of Pencillin



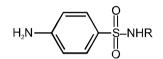
NHCOCHCl₂

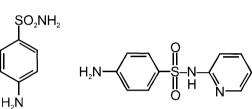
Sulphapyridine

(V) Sulpha Drugs

A group of drugs (Sulphonamides) which are derivatives of sulphanilamide are known as sulpha drugs.

eg. Sulphadiazine, Sulphapyridine.

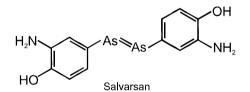


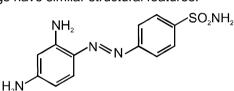


Structural features of sulphonamides

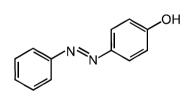
Sulphanilamide

Structure of some other antibacterial drugs have similar structural features.





Prontosil



Azodye

(b) Antiseptic and Disinfectants

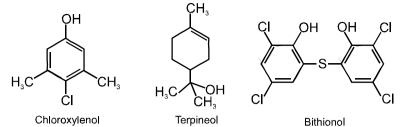
Antiseptics and disinfectants are also the chemicals which either kill or prevent the growth of microorganisms.

*Antiseptics are applied to the living tissues such as wounds, cuts ulcers and diseased skin surface. Examples are furacin, soframycin etc.

* These are not ingested like antibiotics.

*Commonly used antiseptic is **dettol**, it is a mixture of chloroxylenol and terpineol.

*Bithional is added to soaps to impart antiseptic properties.



lodine is a powerful antiseptic. Its 2-3 percent solution in alcohol water mixture is known as tincture of iodine

*lodoform is also used as antiseptic for wounds, boric acid in dilute aqueous solution is weak antiseptic for eyes.

Disinfactants are the substances which applied to inanimate objects such as floor, drainage system, instruments etc.

*One substance can act as an antiseptic and also act as disinfactant for example :

(i) **0.2 percent solution of phenol** is an antiseptic while its 1% solution is disinfectant.

(ii) Chlorine in 0.2 to 0.4 ppm in aqueous solution is used to disinfect drinking water.

(iii) Hexachlorophen : It is mainly used in soaps creams and emulsions.

(iv) Thymol: It is a natural derivative of phenol and is a powerfull disinfectant.

(v) Amyl meta cresol (5-methyl-2-pentyl phenol) it is used as antiseptic in mouth wash or gargles.

(vi) Gention violet and methylene blue are organic dyes but used as effective antiseptic.

(c) Antimalarials

In earlier days malaria was treated with the bark of cinchona tree.

* The chloroquine and their phosphates are sold in the market as antimalarial drugs under the trade name - resochin, larigo, ciplaquine, nivaquine etc.

Chloroquine

(d) Antifungal drugs : These are drugs used for superfical and deep (systemic) fungal infections. Two important antibiotics used as antifungal drugs, introduced way back in 1960, are **amphotericin-B** and **griseofulvin**.

(e) Antiamoebic drugs : These are drugs useful in infection, caused by the protozoa entamoeba histolytica. Metronidazole, tinidazole and tetracyclines are important antiamoebic drugs, used these days.

(f) Antiviral drugs : Viruses are the ultimate expression of parasitism; they not only take nutrition from the host cell but also direct its metabolic machinery to synthesize new virus particles. Acyclovir, ribavirin, zidovudine, interferons are some of the important antiviral drugs, used these days.

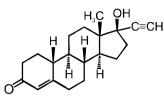
3.5 Antifertility drugs

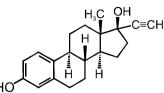
"Chemcial substances which are used to check pregnancy in women are called anti-fertility drugs or birth control pills or oral contraceptives".

*Birth control pills essentially contain a mixture of synthetic estrogen and progesteron derivatives. Both of these compounds are hormones.

eg.: Norethyndron, Ethynylestradiol (novestrol)

*Mifepristone is a synthetic steriod that blocks the effects of progesterone and is used as a "morning after pill" in many countries.





Norethindrone

Ethynylestradiol (novestrol)

4. Chemicals in food

Chemicals are added to food for their preservation, enhancing their appeal and adding nutritive values in them Main catergories of food additives are as follows

- (i) Food colours.
- (iii) Fat emulsifiers and stabilising agents.
- (ii) Flavours and sweeteners.
- (iv) Flour improvers, antistaling agent and bleaches.(vi) Preservatives

(v) Antioxidants

(vii) Nutritional supplements such as minerals

Vitamins and amino acids, except for chemicals of category-(vii) none of the above have nutritive values.

4.1 Food preservatives

*The chemical which are used to stop undesirable change in food caused by microorganism and save them from spoiling are called preservatives. It reduces (stop the growth) rate of reactions occuring due to bacteria in food.

*The following properties must be present in a preservative :

(i) It should not react with food material.

(ii) It's effect should be for longer period.

(iii) It should not decrease the quality of food.

(iv) It should not have harmfull effect on the body.

Improtant preservatives are as follows

(a) Sodium benzoate : It's 0.06% to 0.1% concentration is used for preservation of fruit juice, jam, jelly, pickles etc.

(b) Parabens : These are alkyl p-hydroxy benzoate and used for preservation of tomato sauce etc.

(c) **Sorbates** : These are salt of sorbic acid and used for preservation of milk cheese preparation certain meats and fish products. It inhibit the growth of yeast.

(d) **Propionates :** These are ethyl and phenyl ester of propionic acid and used for the preservation of biscuits and baked product from mold fungi etc.

(e) Sodium or potassium metabisulphite ($Na_2S_2O_5$ or $K_2S_2O_5$): It is used as a preservative for food products such as jams, squashes, pickles etc.

(f) Epoxides : Epoxides are gases and preserves low moisture foods like nuts, dried fruits. Epoxides destroy all type of microorganism including spores and viruses.

(g) p-Hydroxy benzoate ester : The methyl, ethyl propyl and heptyl esters of p-hyroxybenzoic acid are used as preservatives in baked foods, soft drinks, beer and syrups.

(h) Table salt and sugar are also used for food preservatives.

4.2 Artificial sweetening agents

* Saccharine is the first popular artificial sweetening agent used since 1879. It is about 550 times more sweet as cane sugar.

Saccharin

*It's use is of great value to diabetic persons and people who need to control intake calories.

*It is used in pan masala, cheap ice cream, cheap drinks, mouthwash, cheap toffies, toothpaste etc.

Artifical sweeteners	Structural formula	Sweetness value in comparison to cane sugar	Remark
(1) Saccharine (o-sulpha) (insoluble in water)		550	Harmless and excreted from body in urine unchanged. (Sodium salt of saccharine is soluble in water)
(2) Aspartame	HO-C-CH ₂ -CH-C-NH-CH-C-OCH ₃ NH ₂ Aspartic acid part Phenylalanine methyl ester part	100	Widely used artificial sweetner. Use is limited to cold foods and coldrinks because it is unstable at cooking temperature.
(3) Sucralose	$H = CH^{2OH} O + O + H + OH H + OH H + OH OH H + OH OH H + OH OH H + O$	600	Trichloro derivative of sucrose. Stable at cooking temperature and does not provide calories.
(4) Alitame	HO-C-CH ₂ -CH-C-NH-CH-C-NH-CH NH ₂ HO-C-CH ₂ -CH-C-NH-CH-C-NH-CH NH ₂ H ₃ C H ₃ C H ₃ C CH ₃ CC H ₃ CC H ₃ CC H ₃ CC H ₃ CC H ₃ CC S H ₃ CC S S H ₃ CC S S H ₃ CC S S S CC S S S S S S S S S S S S S	2000	It is highly potency sweetener, although it is more stable than aspartame, the control of sweetness is difficult while using it.

4.3 Antioxidants

*The chemical substance which reduce the rate of reaction with oxygen in food, thus help in their preservation are called antioxidants.

*They reduce the rate of formation of free radicals responsible for ageing process 2,6-ditertiary butylhydroxy toluene (p-crysol, BHT) and 2-tertiary butyl hydroxy anisole (BHA) are two most familiar antioxidants used.

5. **Cleansing agents**

5.1 Soaps

Soaps are sodium or potassium salts of long chain fatty acids e.g steric, oleic and palmitic acids. Soap containg sodium salts are formed by heating fat (i.e. glyceryl ester of fatty acid) with aqueous sodium hydroxide solution. This reaction is known as SAPONIFICATION. Generally potassium soaps are soft to the skin.

$CH_{2} - O - C - C_{17}H_{35}$ $CH - O - C - C_{17}H_{35} + O$	· 3NaOH —	→ 3C ₁₇ H ₃₅ COO	
$\dot{C}H_2 - O - \ddot{C} - C_{17}H_{35}$			$\dot{C}H_2 - OH$
Glyceryl ester of stearic acid (Fat)	Sodium hydroxide	Sodium stearate	Glycerol (or Glycerine)

Types of soaps :

•••					
There are so many types of soaps due to the using different raw materials					
(i) Toilet soaps	(ii) Water floating soaps	(iii) Transparent soaps			
(iv) Medicated soap	(v) Shaving soaps	(vi) Loundry soaps			
(vii) Soaps chips	(viii) Soap granules				

Que. Why do soaps not work in hard water ? Ans. Hard water contains calcium and magnesium ions. These ions form insoluble calcium and magnesium soaps respectively when sodium or potassium soaps are dissolved in hard water. These insoluble soaps separate as scum in water and are useless as cleansing agent.

5.2 Detergents

The synthetic products, which like soaps remove dust and grease from a surface are called detergents, since they are not soap but work like a soap so they are also called as soapless soap.

These can be used both in soft and hard water, as they give foam even in hard water Synthetic detergents are mainly classified into three catagories :

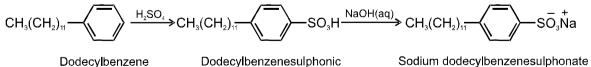
(i) Anionic detergents

These are sodium salt of sulphonated long chain alcohols or hydrocarbons.

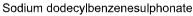
eg. Lauryl alcohol, Lauryl hyrogen sulphate, Sodium lauryl sulphate

$$CH_{3}(CH_{2})_{10}CH_{2}OH \xrightarrow{H_{2}SO_{4}} CH_{3}(CH_{2})_{10}CH_{2}OSO_{3}H \xrightarrow{NaOH(aq)} CH_{3}(CH_{2})_{10}CH_{2}OSO_{3}Na$$
Lauryl alcohol Lauryl hydrogensulphate Sodium laurylsulphate

Sodium alkyl sulphate or Sodium alkyl sulphonate eg. :



Dodecylbenzene



(Anionic detergent)

In anionic detergents, the anionic part of the molecule is involved in the cleansing action. These are smoothly used for household work and are also used in toothpastes.

(ii) Cationic detergents

These are quatenary ammonium salts of amines with acetates, chlorides or bromides as anion. Cetyltrimethylammonium bromide is a popular cationic detergent.

Cationic detergents have germicidal properties and are expensive.

$$\begin{bmatrix} CH_3 \\ I \\ CH_3(CH_2)_{15} - N - CH_3 \\ I \\ CH_3 \end{bmatrix} = \begin{bmatrix} CH_3 \\ Br \end{bmatrix}$$

Cetyltrimethyl ammonium bromide

(iii) Non-ionic detergents

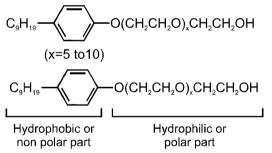
These are moslty esters of poly hydroxy alcohols. They are in liquid form, and do not contain any ion in their constitution. One such detergent is formed when stearic acid reacts with polyethyleneglycol.

Liquid dishwashing detergents are non-ionic type. Mechanism of cleansing action of this type of detergents is the same as that of soaps. These also remove grease and oil by micelle formation. Main problem that appears in the use of detergents is that if their hydrocarbon chain is highly branched, then bacteria cannot degrade this easily. Slow degradation of detergents leads to their accumulation.

 $\begin{array}{c} \mathsf{CH}_3(\mathsf{CH}_2)_{16}\mathsf{COOH} \ + \ \mathsf{HO}(\mathsf{CH}_2\mathsf{CH}_2\mathsf{O})_{\mathsf{n}}\mathsf{CH}_2\mathsf{CH}_2\mathsf{OH} \ \xrightarrow{-\mathsf{H}_2\mathsf{O}} \ \mathsf{CH}_3(\mathsf{CH}_2)_{16}\mathsf{COO}(\mathsf{CH}_2\mathsf{CH}_2\mathsf{O})_{\mathsf{n}}\mathsf{CH}_2\mathsf{CH}_2\mathsf{OH} \\ \xrightarrow{\mathsf{Stearic acid}} \ \mathsf{Poly ethy leegly col} \end{array}$

Effluents containing such detergents reach the rivers, ponds, etc. These persist in water even after sewage treatment and cause foaming in rivers, ponds and streams and their water gets polluted. These days the branching of the hydrocarbon chain is controlled and kept to the minimum. Unbranched chains can be biodegraded more easily and hence pollution is prevented.

Note : Liquid dish washing detergents are non ionic type.



Difference between soap and detergents

(1) Soaps are salts of weak acid and strong base whereas detergents are salts of strong acid and strong base.

(2) Aqueous solution of soap is basic where as aqueous solution of detergents is neutral.

(3) woolen and silk cloths in which soft fibres are present cannot be washed with soap whereas all type of fabrics can be washed with detergents.

(4) Soap cannot work in hard water because soaps are precipitated as insoluble salt by reaction with Ca^{2+} and Mg^{2+} ions.