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RAJASTHAN

PHARMACIST

Rajasthan Subordinate & Ministerial Services Selection Board

Part – B

Volume – 5

Pharmaceutical Chemistry, Jurisprudence and Drug Store Management

SIERRA INNOVATIONS

RAJASTHAN PHARMACIST

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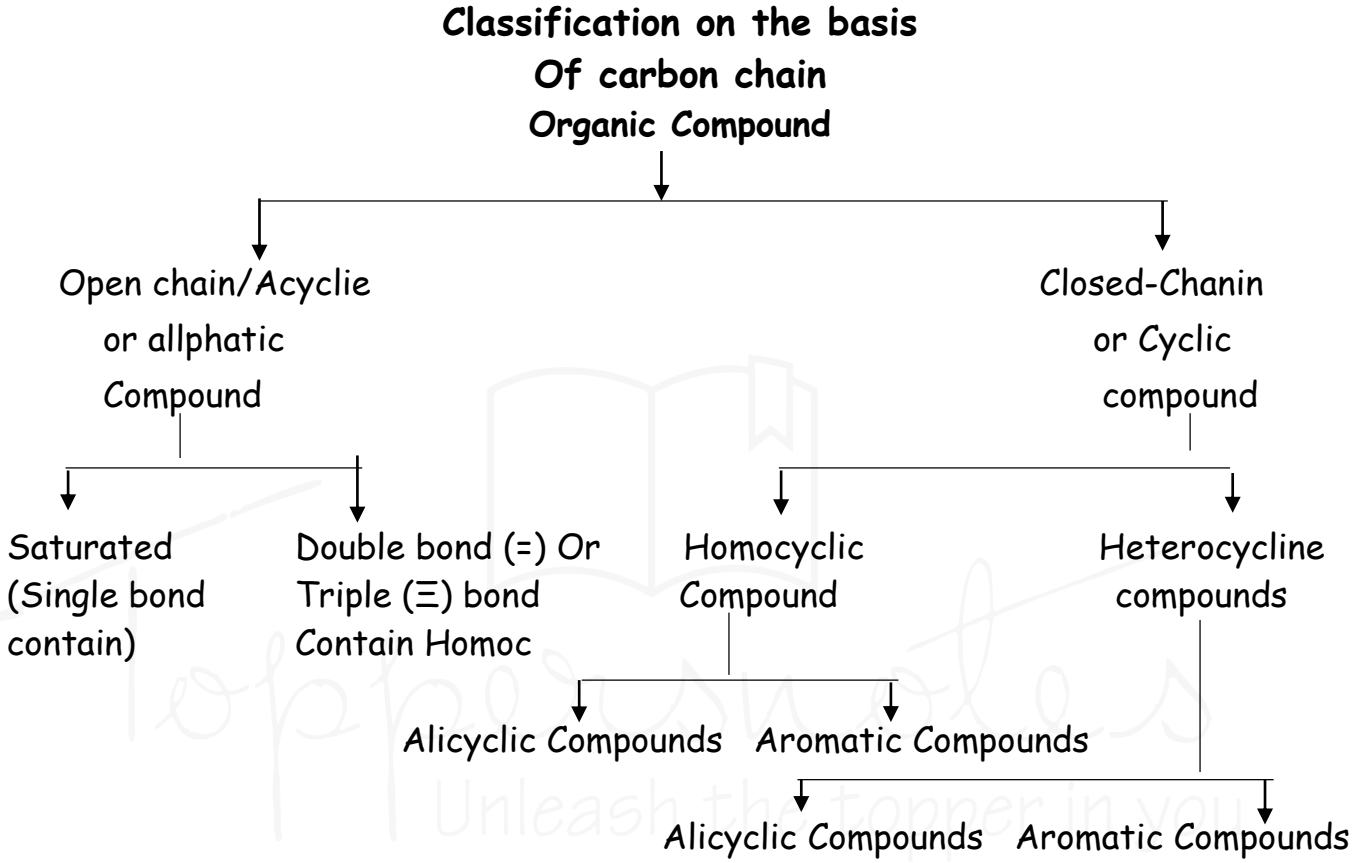
Introduction to the Nomenclature of Organic Chemicals

Mainly two nomenclature system are proposed for the naming of organic compounds.
Classification on the basis of carbon chain



1. Common Naming System

(a) On the basis of source

Example

Chemical	**Source**
CH_4	Marsh gas (marshy place)
CH_3COOH	Acetic acid (vinegar)
$HCOOH$	Formic acid (Red ant)
CH_3OH	Methyl alcohol (wood spirit)

(b) On the basis of hydrocarbons (Radical independent).

No. of Carbon Atoms	Prefix
1C	form
2C	acet
3C	propion
4C	butyr
5C	valer

- Three carbon with one double bond— Acryl.
- Four carbon with one double bond— croton.

Functional groups	Suffix
-CHO	aldehyde
-COOH	IC acid
-COOR	alkyl-ate
-COX	alkyl halide
$-CONH_2$	alkyl halide
-CN	Onitrile

Radical dependent-

Sr.No.	Number of Bond	Suffix
1.	Single bond (-)	ane suffix
2.	Double bond (=)	ene suffix
3.	Triple(≡) bond	yne suffix

For saturated hydrocarbon—$CnH_{2n^{+2}}$-

Suffix used as -ane.

- If unbranched hydrocarbon then use prefix (n)
- When one methyl group is attached to the second C-atom of the continuous chainthen iso prefix is used.
- When Two methyl group is attached to the second C-atom of the continuous chain then neo prefix is used.

  Note — when one hydrogen group are removed from the alkane then radical is form and called monovalent radical or alkyl. $-CH_3$—methyl $-C_2H_5$—ethyl For unsaturated hydrocarbon…
- Double bond(CnH_{2n})—suffix — ene
- Triple bond($CnH_{2n^{-2}}$)—suffix — yne Note—unsaturated radical.

Ex.$-CH_2=CH$--- vinyl. $-CH_2-CH=CH_2$ — Allyl.

If any functional group are attached to the radical then direct functional suffix are used to radical. Name= prefix of R + Suffix of

Functional groups	Suffix
-OH	alcohol
$-NH_2$	Amine
-O-	ether
-S-	thio ether
-X-	halide
-CN-	Cyanide
-CO-	ketone.

Iupac Naming System

Rule—

(A.) Selection of longest continuous parent carbon chain.

(B.) Numbering in selected parent carbon chain.

Priority order for selection of carbon chain

(Functional group > multiple bond>number of carbon atom>substituents)

Functional group-

S.No.	Functional Group	Prefix	Suffix
1.	-(C) OOH (carboxylic acid) -COOH	x carboxy	oic acid carboxylic acid
2.	$-SO_3H$ (sulphoric acid)	sulpho	sulphonic acid
3.	-(C)OOR(ester) -COOR	x alkoxy carbonyl or carbalkoxy	alkyl-oate alkyl-carboxylate
4.	-(C)OX(acid halide) -COX	X halo formyl	oyl halide carbonyl halide
5.	$-(C)ONH_2$(amide) $-CONH_2$	x carbamoyl	amide carbonitrile
6.	-(C)N (cyanide) –CN	x cyano	Nitrile carboxamide
7.	-(C)HO (aldehyde) –CHO	oxo formyl	al carbaldehyde
8.	-OH (alcohol)	hydroxy	ol
9.	-SH (thio alcohol)	mercapto	thiol
10.	$-NH_2$ (amine)	amino	amine

Multiple Bond

Sr.no	Number of Bond	Suffix
1.	Single bond (-)	ane suffix
2.	Double bond (=)	ene suffix
3.	Triple(≡) bond	yne suffix

No of Carbon Atom

Number of Carbons	Root Word
1C	Meth
2C	Eth
3C	Prop
4C	But
5C	Pent
6C	Hex
7C	Hept
8C	oct

Substituents Means

Substituents	Prefix
-R	alkyl
$-NH_2$	amino
-o-N=O	Nitrite
$-OCH_2CH_3$	ethoxy
$-CH_2-Cl$	Chloro methyl
-S-	Thio
-X	Halo

Numbering of selected carbon chain---
Priority order.
Functional group>multiple bond>substituents.

Procedure of naming

(Secondary prefix----- primary prefix----- word)
(root----- primary suffix------- Secondary suffix.)

- Secondary prefix means — substituents with locants
- Primary prefix means—cyclic group(cyclo).
- Word root means—number of carbon chain.
- Primary suffix means-- - ane, -ene, - yne.
- Secondary suffix means—principle fuctional groups.
- umber and alphabets are seperated by hyphen(-).Di,tri,iso,neo and cyclo are niether seperated by comma nor by hyphen .
- First latter of naming is always capital letter and space required between naming.
- If more than one substituents then use alphabetical order of substituent names.

Examples

Heterocyclic rings which are used during the naming…

Antimycobacterial Agents

Antitubercular And Antileprotic Agents

Mycobacteria are transition forms between bacteria and fungi. They are characterised by non-motile, non-sporulating rods and are not decolourised by acidified organic solvents. Hence, they are called 'acid-fast' bacteria. Some species of mycobacteria are pathogenic for man and are responsible for two important human chronic diseases namely tuberculosis and leprosy (Hansen disease).

Tuberculosis (TB) is an acute or chronic communicable disease. It is caused in humans by mycobacterium tuberculosis of homonis type, but can also be caused by bovine type. It is characterised by inflammatory infiltrations, tubercle formation, fibrosis and calcification. It affects the respiratory tract. Extrapulmonary TB is more common in patients suffering from AIDS (i.e. HIV infected patients). The primary tuberculosis spreads through blood stream to mainly meninges, bones and genitourinary tract. Post primary tuberculosis leads to necrosis, ulceration and cavitation to give extensive lesions.

Leprosy is a chronic disease caused by mycobacterium leprae, the organisms identified by Hansen in 1871. It is characterised by lesions of skin and peripheral nerves. The two forms of disease are:

(i) **Tuberculoid leprosy:** In this, skin and peripheral nerves are involved resulting in motor and sensory changes in affected area.

(ii) **Lepromatous leprosy:** Skin gets thickened and oedematous and painless nodular lessions occur in it, which may become necrotic and ulcerate, releasing large number of mycobacteria.

The development of antimycobacterial agents started when it was observed that sulphonamides are only slightly effective on tuberculosis. A slight structural modification of sulphonamides results in development of dapsone. It has feeble antitubercular activity but is most effective in the treatment of leprosy.

The major advances in the development of antitubercular agents started when streptomycin was discovered in 1944 by Waksman and his associates.

The observations that salicylic acid increase the oxygen consumption of tubercle bacilli, leads to development of p-amino salicylic acid as antitubercular agent. Later on isoniazid was developed by structural modification of nicotinamide, a component of Vitamin B-complex. Later on the first synthetic compound, ethambutol, and the semisynthetic antibiotic, rifampin (rifampicin), having antitubercular activity, were developed.

The antileprotic drugs, viz. thioacetazone and thiambutasine were developed by a chemical modification of thiosemicarbazone of p-acetamido benzaldehyde. Clofazimine, a diaminophenazine derivative, is now extensively used in the treatment of leprosy. Although leprosy is scarcely infectious, its victims are cast out from society.

(A) Classification of antitubercular agents:

(i) p-amino salicylic acid and analogues:
e.g. p-aminosalicylic acid (PAS)
(ii) Pyridine derivatives e.g. Isoniazid, ethionamide
(iii) Pyrazine derivatives e.g. pyrazinamide
(iv) Ethylene diamine derivatives e.g. ethambutol
Antibiotics e.g. cycloserine, streptomycin, rifampicin.

(B) Classification of antileprotic agents:

The antileprotic agents used therapeutically can be placed under the following categories:

(i) Sulphones e.g. Dapsone
(ii) Thiosemicarbazone derivatives
(iii) Phenazine (diaminophenazine) derivatives e.g. clofazimine
The other drugs which exhibit activity against M. leprae are:
(a) Long acting sulphonamides
(b) Thloacetazone
(c) Ethionamide
(d) Antibiotics like rifampicin.

Antitubercular Agents

First line agents: They are well tolerated or have less incidence of side effects. e.g. Isoniazid, Rifampin, Pyrazinamide, Ethambutol, Streptomycin.

Second line agents: They are less well-tolerated or have higher incidence of adverse effects. They are used if resistance or intolerance to first line agent develops.

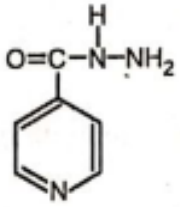
Isoniazid

Other names

INH, isonicotinic acid hydrazide, Isonicotino hydrazide, isonicotinyl hydrazide.

Chemical name

Pyridine - 4 - carbohydrazide.

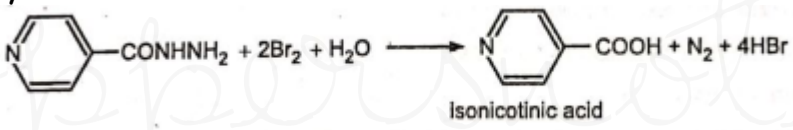


Physical properties

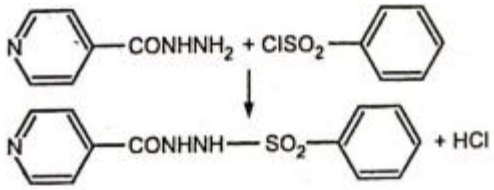
It occurs as colourless crystals or white crystalline powder. It is odourless and has sweet taste followed by bitter taste. It is soluble in water.

Chemical properties

When isoniazid is treated with bromine water, in presence of hydrochloric acid, it is quantitatively converted into isonicotinic acid with liberation of N_2 gas.

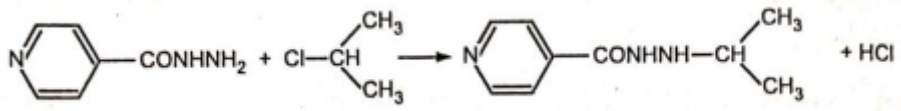


When isoniazid is treated with benzene sulphonyl chloride, it is converted to its benzene sulphonyl derivative.



The compound formed is an intermediate for the synthesis of gamma nicotinaldehyde thiosemicarbazone.

When isoniazid is treated with isopropyl chloride, it is converted to N-isonicotinyl, N-Isopropyl hydrazine which also possess antitubercular activity but is more toxic.



Stability and Storage

It is affected by light and hence it is stored in tightly-closed light-resistant containers.

Uses

It is used in the treatment of:

(i) pulmonary tuberculosis
(ii) extrapulmonary lesions, including meningeal and genito-urinary infections.
(iii) lupus vulgaris.

As isoniazid develops resistance within a few weeks, it is given in conjunction with ethambutol or rifampicin or streptomycin.

Pharmaceutical Preparations:

1. Isoniazid elixir (syrup)
2. Isoniazid tablets
3. Sodium aminosalicylate and Isoniazid granules
4. Sodium aminosalicylate and Isoniazid powder
5. Isoniazid and ethambutol tablets
6. Isoniazid and rifampicin tablets
7. Isoniazid injection.

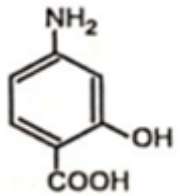
Brand names:

Cadizide, Isonex, Rimpazid, Isocadipas.

1. P-Amino Salicylic Acid (PAS)

Chemical name

4-amino, 2-hydroxy, benzoic acid.

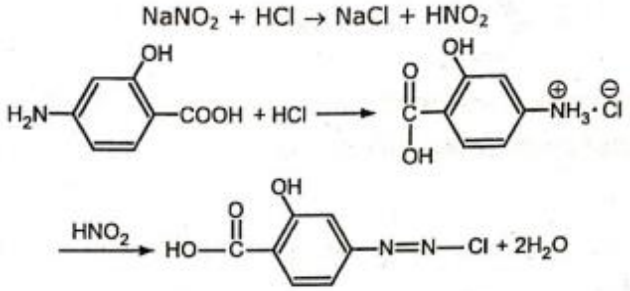


Physical properties

It occurs as white or yellowish white crystals. It is odourless and has slightly acid taste. It is slightly soluble in water but soluble in alkalies and in dilute nitric acid. Its hydrochloride and sulphate salts are soluble in water. Its sodium salt is very soluble in water.

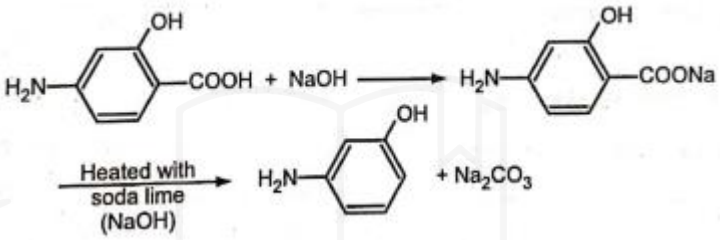
Chemical properties

1. Diazotisation reaction: When PAS is treated with sodium nitrite in presence of hydrochloric acid at 0°C to 10°C, the primary amino group is converted to diazo group.



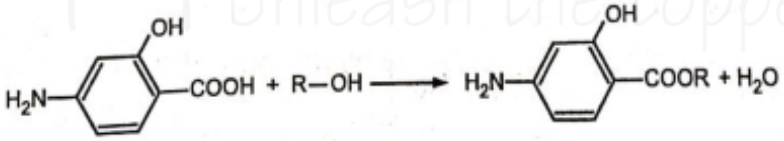
This reaction is the basis for assay of PAS.

2. When PAS is heated with soda lime, the decarboxylation reaction occurs giving m-amino phenol.

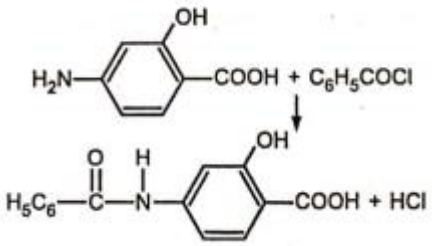


3. In order to reduce gastric irritation produced by PAS when given orally, it is converted to:
   (a) esters by treating with alcohol in presence of dil. sulphuric acid or
   (b) N-acyl derivative e.g. N-benzoyl derivative by treating with benzoyl chloride.

   (a)



   (b)



The esters and acyl derivatives can be hydrolysed in the body to PAS.

4. It is oxidised by air or oxygen with the formation of brown or black pigments.

Stability and storage

It darkens on exposure to air and light. Hence, it is stored in tightly-closed, light-resistant containers.

Uses

It is used in the treatment of tuberculosis.

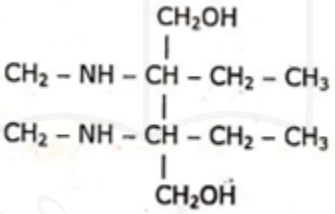
It is generally given in combination with isoniazid and streptomycin. It is now replaced by more effective and well tolerated antitubercular agents like rifampicin, ethambutol etc.

Pharmaceutical formulations :

(i) Amino salicylic acid tablets
(ii) Amino salicylate sodium tablets
(iii) Amino salicylate potassium tablets
(iv) Amino salicylate calcium capsules
(v) Amino salicylate calcium tablets
(vi) Benzoyl PAS calcium tablets.

Brand names: Idipas, Isopar, Benzapas.

3. Ethambutol



Chemical name

(+) N, N' - Bis [(R)' - 1 -hydroxy methyl propyl] ethylenediamine.

Physical properties

It is official as its hydrochloride salt which is a white crystalline powder. It is odourless and freely soluble in water. Its dextro rotatory isomer is more potent than laevo rotatory isomer. Chemical properties:

When aqueous solution of ethambutol hydrochloride is treated with copper sulphate and the solution is made alkaline with NaOH, a distinct blue colour is produced. This property is used for its identification.

Storage: It is stored in tightly-closed containers.

Uses

It is used in the treatment of tuberculosis.

It is given in conjunction with other antitubercular drugs.

t is also active against the strains which are resistant to other antitubercular drugs.

Pharmaceutical formulations

Chemical name

(+) N, N' - Bis ((R)' - 1 -hydroxy methyl propyl) ethylenediamine.

Physical properties:

It is official as its hydrochloride salt which is a white crystalline powder. It is odourless and freely soluble in water. Its dextro rotatory isomer is more potent than laevo rotatory isomer.

Chemical properties

When aqueous solution of ethambutol hydrochloride is treated with copper sulphate and the solution is made alkaline with NaOH, a distinct blue colour is produced. This property is used for its identification.

Storage: It is stored in tightly-closed containers.

Uses: It is used in the treatment of tuberculosis.

It is given in conjunction with other antitubercular drugs.
It is also active against the strains which are resistant to other antitubercular drugs.

Pharmaceutical formulations:

(i) Ethambutol tablets
(ii) Ethambutol powder
(iii) Isoniazid and ethambutol tablets.

Brand names: Myambutol, Albutol, Ly-Butol.

4. Thiacetazone or Thioacetazone

It is thiosemicarbazone of p-acetamido benzaldehyde.

Physical properties

It occurs as pale yellow crystals or crystalline powder. It is odourless and very slightly soluble in water.

Chemical properties

1. When its solution in N NaOH is boiled with lead acetate solution for1 minute, a black ppt. of lead sulphide is obtained.
2. Hydrolysis and diazotisation reaction: When it is boiled with 1 N HCI, the acetamido group is hydrolysed to get primary amino group which on treatment with $NaNO_2$, and HCI gives diazo compound. This on coupling with2-naphthol in alkaline medium gives red dye.

Stability and storage

It is affected by light and hence it is stored in air-tight, light-resistant containers,

Uses

It is used in the treatment of:

(i) tuberculosis

(ii) leprosy.

It is used in conjunction with streptomycin and isoniazid.

Pharmaceutical preparation: Thiacetazone tablets.

Brand names: Thiopramizone, Thioce Vit., Decetazone.

5. Ethionamide

Physical properties

It occurs as a bright yellow crystalline powder with a slight odour and has an unpleasant sulphurous taste. It is practically insoluble in water.

Chemical properties

1. When it is heated with sodium hydroxide, ammonia gas evolves.
2. When it is heated with hydrochloric acid, H_2S gas is evolved. Both these properties are useful for its identification.

Stability and storage

It is affected by light and hence it is stored in well-closed light resistant containers.

Uses

It is used to treat pulmonary tuberculosis, which is resistant to isoniazid or intolerant to other drugs.

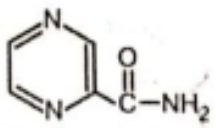
Pharmaceutical formulation: Ethionamide tablets.

Brand names: Ethinex, Trescalyl.

6. Pyrazinamide

Chemical name

Pyrazine - 2 - Carboxamide.



Physical properties

It occurs as a white crystalline powder. It is odourless and has slightly bitter taste. It is sparingly soluble in water but soluble in ether and in chloroform.

Storage

It is stored in tightly-closed containers.

Uses

It is used as a tuberculostatic agent.
It is active against the strains which are resistant to other antitubercular agents.

Pharmaceutical formulations: Pyrazinamide tablets
Brand names: Zinamide, Pyride, Pyrina - 500.

7. Cycloserine or Seromycin

Chemistry

It is a low molecular weight hydrophilic antibiotic obtained from streptomyces orchidaceus or s. garyphatus. It is obtained by synthesis also. It contains isoxazolidine heterocycle and the two groups viz. oxo and amino groups are present at 3 and 4 positions respectively.

It is a structural analogue of D-alanine and hence it is competitive inhibitor of the enzymes, alanine racemase and synthatase. It exists in equilibrium with its enol form (due to lactum - lactim tautomerisation). Hence, it can form monosodium salt with aq. sodium hydroxide.

It also forms salts with strong acids. In aqueous solution, it forms a dipolar ion which on standing dimerises to 2-5-bis (aminoxymethyl)-3, 6-diketopiperazine. It exists as zwitterion.

Physical properties

It occurs as white or pale yellow crystalline powder. It is odourless and has slightly bitter taste. It is hygroscopic. It is soluble in water. It is dextro rotatory.

Stability and storage

It is hygroscopic and is affected by heat and hence it is stored in tightly-closed containers at a temperature not exceeding 25°C.

Category: Antibacterial (tuberculostatic).

Uses

(i) It is used in the treatment of pulmonary tuberculosis.
(ii) It is also used as antibacterial agent (active against gram +ve and –ve bacteria). It is used only if streptomycin is not effective.
(iii) It is also used in the treatment of urinary tract infections.

Pharmaceutical formulations

(i) Cycloserine tablets
(ii) Cycloserine capsules.

Brand names: Cycosin, Themiserine.

8. Streptomycin

Chemistry

Streptomycin was the first aminoglycoside introduced in chemotherapy in 1944 by Wasksman and his associates. It was isolated from streptomyces griseus. Now-a-days it is obtained by synthesis.

It is called as aminoglycoside because its structure consists of amino sugar linked glycosidically. In this, the proportion of oxygen is high which is characteristic of carbohydrate. It contains three basic units namely, (i) streptidine, (ii) L-streptose and (iii) N-methyl-Lglucosamine. Units (i) and (iii) are linked glycosidically with unit (ii).

Streptomycin contains two strongly polar and basic guanidino groups and one weakly basic methyl amino group. Hence, it acts as triacidic base.

As streptomycin is a highly polar compound, it is not absorbed through G.1. tract. Hence, for systemic infections, it is given by parenteral route viz. intramuscularly.

On acid hydrolysis, streptomycin gives streptidine and streptobiosamine.
Streptomycin undergoes degradation in presence of dilute aqueous alkali to give maltol, a gamma pyrone. This degradation is due to presence of aldehyde group in streptose. To prevent this degradation, the aldehyde group of streptomycin is reduced to hydroxy group, giving the product called dihydrostreptomycin.

Physical properties:

It is official as its sulphate which is a white or almost white powder. Its odourless or has slight odour and has slightly bitter taste. It is very soluble in wate but sparingly soluble in alcohol. It is strongly basic.

Stability and storage:

It is affected by moisture and heat and hence it is stored in well-closed containers protected from moisture and at a temperature not exceeding 30°C. If intended for parenteral preparations, the container should be sterile and sealed so as to exclude microorganisms.

Uses

It is a broad-spectrum antibiotic and is antibacterial. It is used:

(i) Orally, to treat intestinal infections of large intestine.
(ii) Intramuscularly, to treat all forms of tuberculosis.
(iii) Sometimes intrathecally in tubercular meningitis. Generally, it is given in conjunction with other antitubercular agents.
(iv) To treat non-tubercular infections like cholecystitis, peritonitis etc.

Pharmaceutical formulations:

(i) Streptomycin tablets.
(ii) Streptomycin injection.

Brand names: Chlorostrep, Enterostrep, Lykastrep, Streptomex.

9. Rifampicin Or Rifampin

Chemistry

Rifampicin is a group of chemically related antibiotics namely Rifampicin A, B, C,D and E, obtained from streptomyces mediterrani. Rifampicin is a semisynthetic analogue of rifamycin B. It belongs to the chemical class ansamycins. It contains a macrocyclic ring bridged across two non adjacent (ansa) positions, viz. 2 and 5 positions, of aromatic (naphthyl) ring. Among the different natural and semisynthetic rifamycins, only the rifampicin is well absorbed when taken orally- However, food markedly reduces its absorption. Hence, it is administered on an empty stomach.

Physical properties

It occurs as a brick-red or reddish brown crystalline powder and is odourless. It is very slightly soluble in water and alcohol but soluble in chloroform. It is unstable in presence of moisture.

Chemical properties:

(i) Rifampicin is oxidized, in alkaline medium, to quinone, in which the two hydroxy groups at 1 and 4 positions of naphthyl ring are converted to oxo group.
(ii) It is hydrolysed in acidic medium to give 3-formyl rifampicin.