Anti-Hypertensives

The arterial blood pressure of a normal healthy adult is 100-120 mm Hg systolic and 70-80 mm Hg diastolic. A condition where persistant raise in blood pressure above 140/90 mm Hg is known as hypertension. There are two types of hypertension:

1. Primary or essential hypertension.
2. Secondary hypertension.

CLASSIFICATION

1.	Angiotensin-converting enzyme inhibitor (ACE inhibitor)	:	Captopril, Enalapril, Lisinopril
2.	Calcium channel blockers	:	Verapamil, Diltiazem Nifedipine, Amlodipine
3.	Diuretics	:	Hydrochlorthiazide Chlorthalidone, Frusemide Spironolactone
4.	B-adrenergic blockers	:	Propranolol, Atenolol Metaprolol
5.	Adrenergic blockers	:	Prazosin, Phentolamine
6.	Central sympatholytics	:	Clonidine, Methyldopa
7.	Vasodilators	:	Hydralazine
8	Adrenergic neuron blockers	:	Reserpine, Guanethidine

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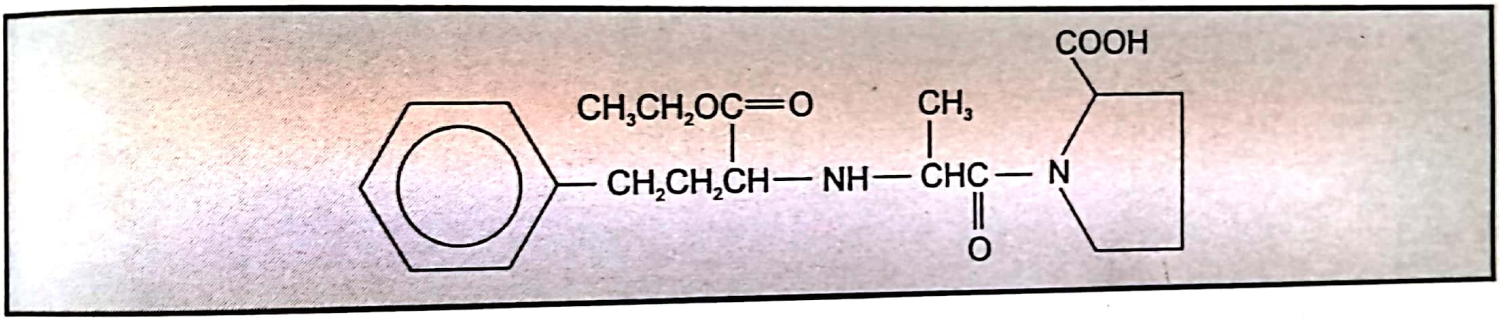
ENALAPRIL MALEATE

Enalapril is a derivative of proline and alanine.

Brand name: Envas.

Chemical name: Enalpril is N-(N (1-ethoxy carbonyl-3-phenyl propyl)-L-alanyl) L-proline.

Structure:



Physical Properties

Nature: Off-white crystalline powder.

Solubility: Freely soluble in methanol, slightly soluble in acetone. Insoluble in ether.

Melting point: 144°C.

Stability: Stable at room temperature.

Storage: Well closed container.

Use: It is used as an antihypertensive.

Formulation: Enalapril tablets.

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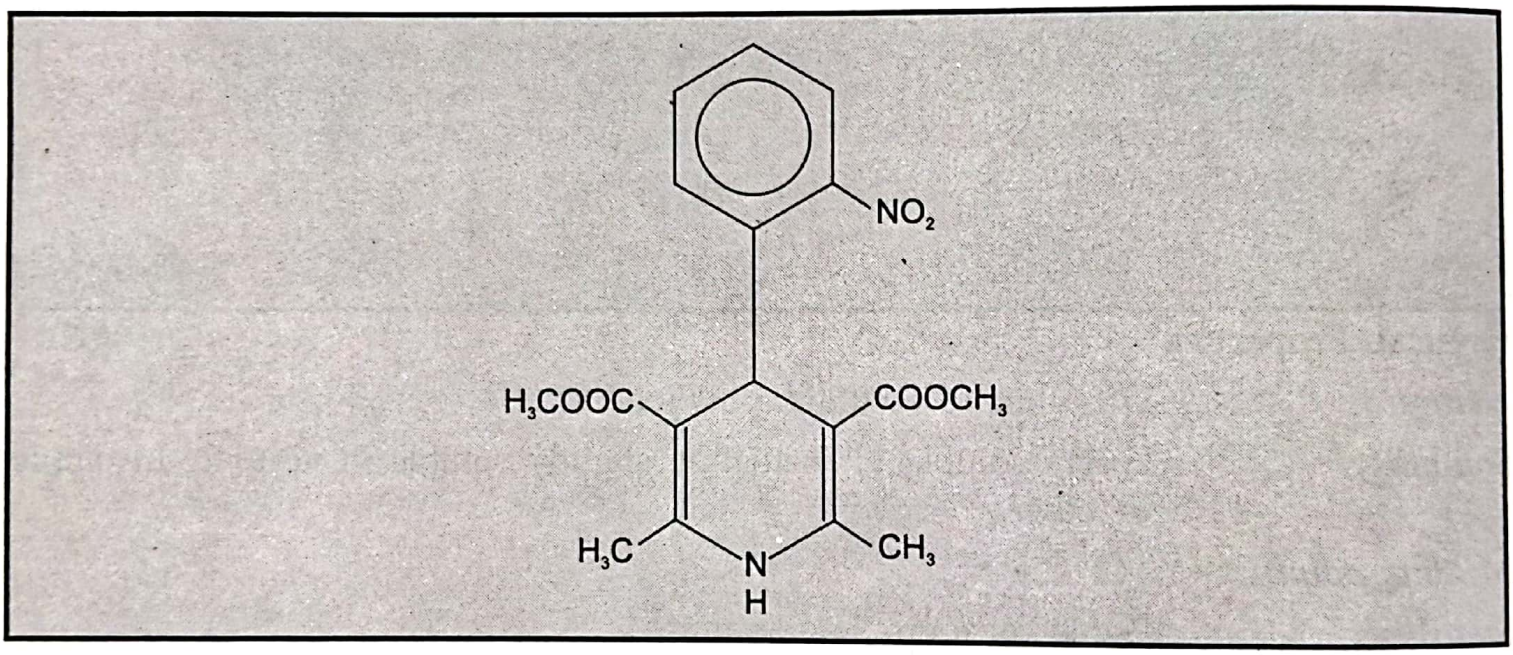
NIFEDIPINE

Niferipine is a pyridine derivative.

Brand name: Depin.

Chemical name: Nifedipine is dimethyl–1, 4-dihydro-2, 6-dimethyl-4-(2 nitro phenyl) pyridine-3, 5-dicarboxylate.

Structure:



Physical Properties

Nature: Yellow, crystalline powder.

Solubility: Freely soluble in ethanol. Insoluble in water.

Melting point: 171 and 175°C.

Chemical Properties

Nifedipine can be reduced to amino compound. The amino compound can be diazotized by nitrous acid and coupled with N (1-Naphthyl ethylene diamine to produce a red colour dye.

Stability: On exposure to sunlight nifedipine is converted into nitrosophenyl derivative.

Storage: Light-resistant container.

Uses: It is used as

- Coronary vasodilator.
- Antihypertensive agent.

Formulation: Nifedipine capsules/Tablets

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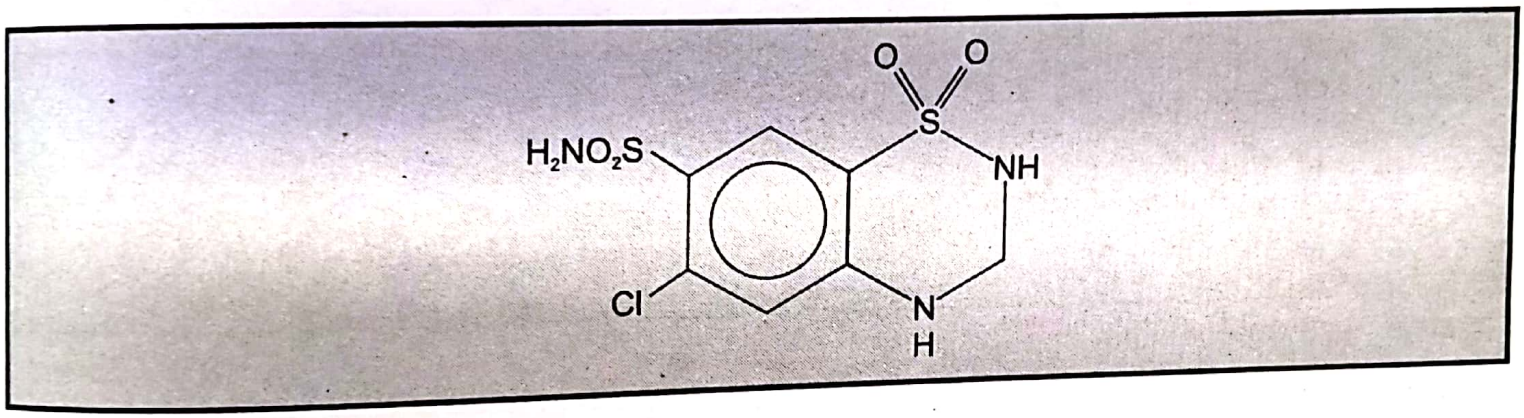
HYDROCHLORTHIAZIDE

Hydrochlorthiazide is the reduced form of chlorthiazide. It is a diuretic and antihypertensive.

Brand name: Hydrodiuril.

Chemical name: 6-chloro-3, 4-dihydro-2H-1, 2, 4-benzo thiadiazide-7-sulphonamide-1, 1-dioxide.

Structure:



Physical Properties

Nature: It is a white crystalline odourless powder with slightly bitter taste.

Solubility: Insoluble in water, chloroform, ether and freely soluble in alkaline solutions.

Chemical Properties

Hydrochlorthiazide produces violet colour when warmed with sodium salt of chromotropic acid and sulphuric acid.

Stability: Stable at room temperature.

Storage: Well closed container.

Uses: It is used in the

- Treatment of oedema.
- Hypertension.

Formulation: Hydrochlorthiazide Tablets.

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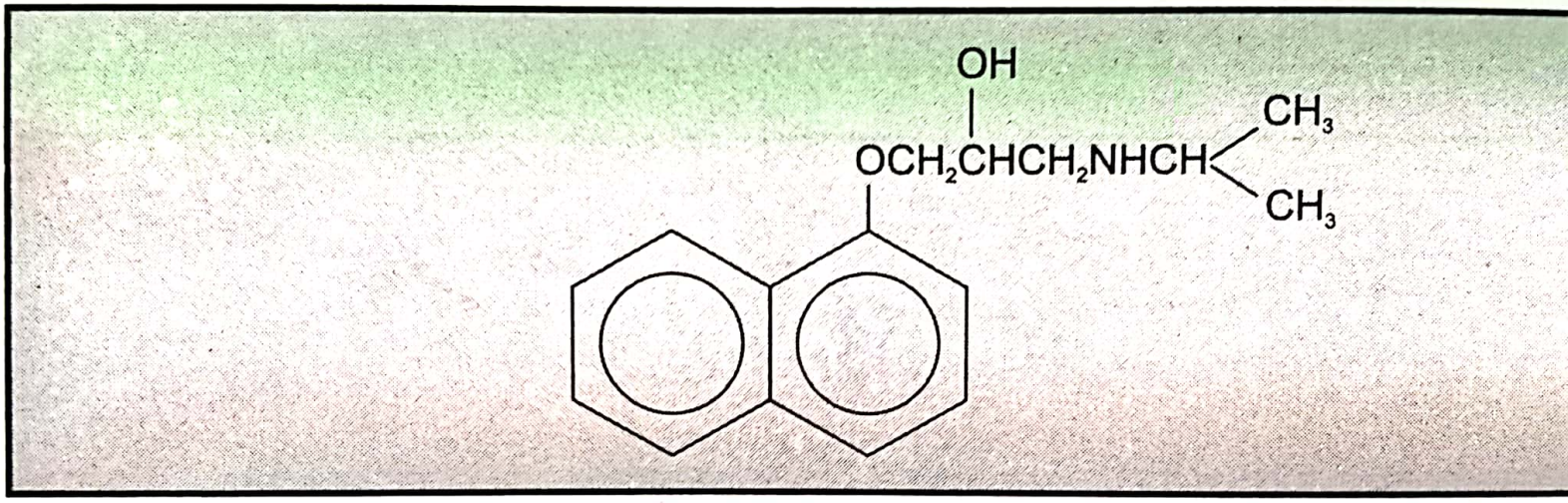
PROPRANOLOL

It is a naphthalene derivative.

Synonym: Inderal.

Chemical name: 1-(Isopropylamino)-3-(1-napthyloxy)-2-propanol.

Structure:



Physical Properties

Nature: White crystalline powder.

Solubility: Soluble in water.

Melting point: 163–166°C.

Uses:

- To treat hypertension.
- Cardiac arrhythmias.
- Myocardial infarction.

Formulation: Propranolol Tablets/Injection.

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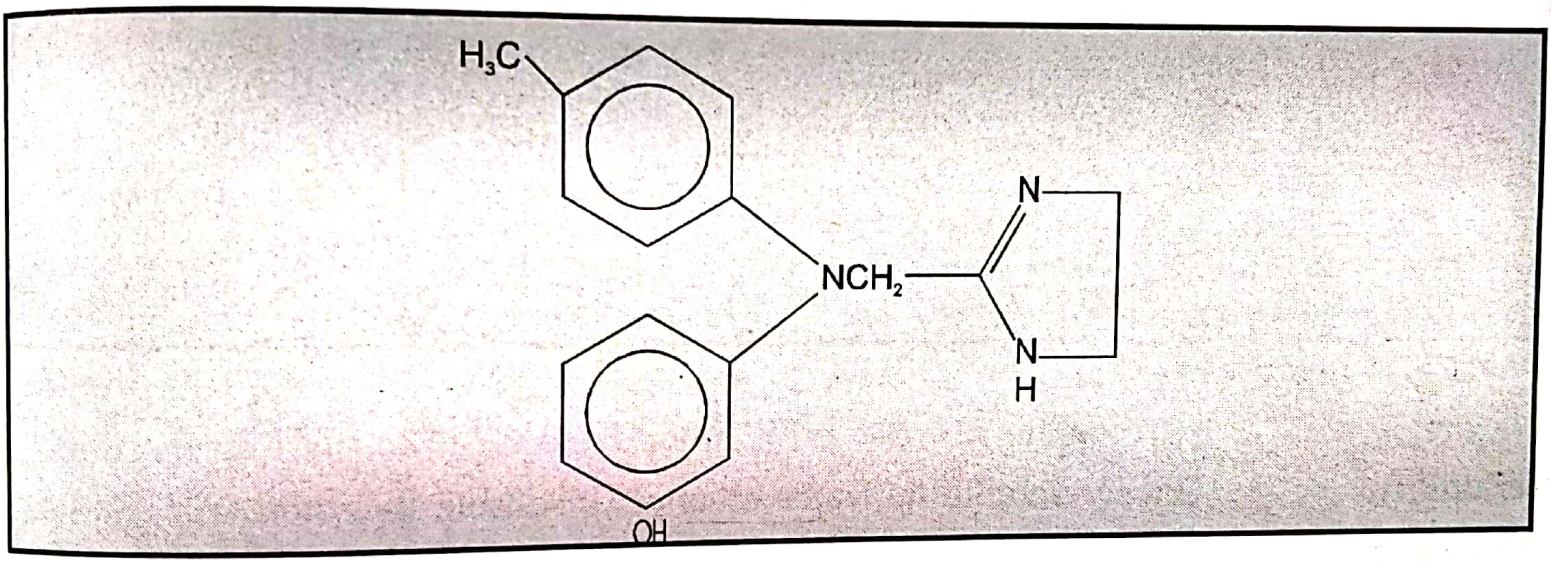
PHENTOLAMINE MESYLATE

Phentolamine is an imidazole derivative.

Brand name: Regitin.

Chemical name: 3-(N-(2-imidazolin-2yl methyl)-4-toluidino) phenol methane sulphonate.

Structure:



Physical Properties

Nature: White, hygroscopic powder with bitter taste.

Solubility: It is soluble in water, ethanol and slightly soluble in chloroform.

Melting point: 177 to 181°C.

Chemical Properties

It gives a light green precipitate with ammonium meta vanadate in acid medium.

Stability: Stable at room temperature.

Storage: Air-tight, light-resistant containers.

Use: It is used as an anti-hypertensive.

Formulation: Phentolamine mesylate Injection.

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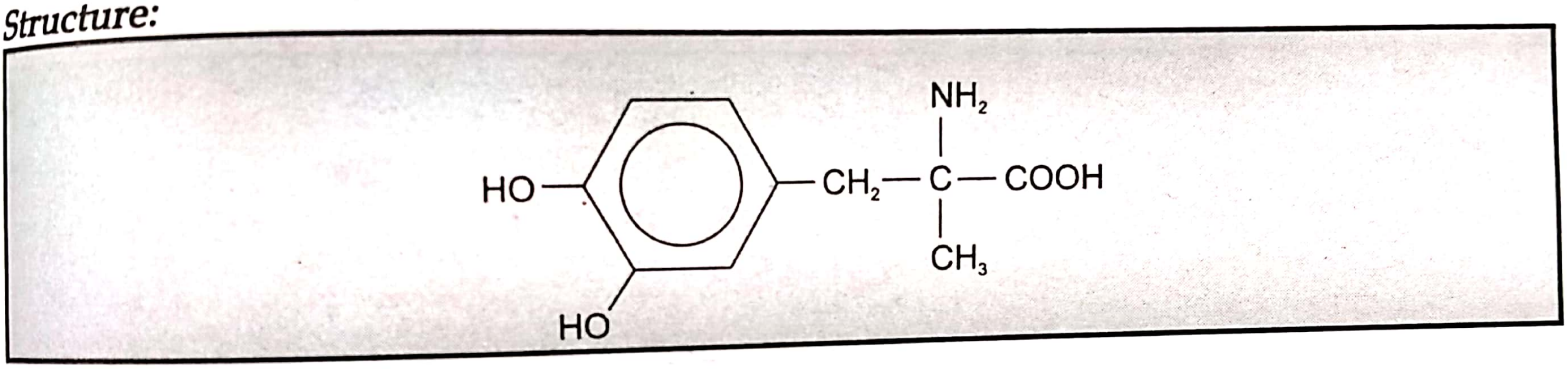
METHYLDOPA

Methyl dopa is an alanine derivative.

Brand name: Dopamet.

Chemical name: 3(3, 4-dihydroxyphenyl)-2 methyl-L-alanine).

Structure:



Physical Properties

Nature: White or yellowish white crystalline powder.

Solubility: Slightly soluble in water and freely soluble in hydrochloric acid.

Melting point: 310°C.

Chemical Properties

It gives dark purple colour with ninhydrin reagent.

Storage: Well closed, light resistant containers.

Use: It is used as an antihypertensive.

Formulation: Methyl dopa Tablet.

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24 Cardiac Glycosides
(Cardiotonic Agents, Cardiac Steroids)

Glycosides are found in plants. Most of them are bitter in taste.

CHEMISTRY

Glycosides are substances which contain a sugar residue linkes from C_1 through oxygen, nitrogen, sulphur or carbon to a non-sugar moiety.

They are named according to the linkage, as O, N, S or C glycoside respectively. The sugar portion is called glycone and the non-sugar portion is called aglycone. The carditonic activity is due to the aglycone only.

The aglycones of cardiac glycoside are of two types:

1. Cadenolide
2. Bufadienolide.

Both of them contain steroid nucleus.

The most important cardiac glycosides and their sources are

Glycosides	*Sources*
Cardenolide	
Digitoxin, Gigoxin	Digitalis purpurea leaf
Digoxin, lanatoside C	Digitalis lanata leaf
Deslanoside	
Strophanthin K	Strophanthus komb (seed)
Strophanthin G or Ouabin	Strophanthus gratus (seed)
Bufadienolides	
Scillaridin A	Squill
Bufotoxin	Bufovulgaris (toad skin)

DIGOXIN, DIGITOXIN, LANATOSIDE C AND DESLANOSIDE

The difference between digitoxin and digoxin in the structure is the presence of —OH group at C_{12} of digoxin which is absent in digitoxin.

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Brand name: Digoxin – Cardioxin, Lanoxin
Digitoxin – Digimerck
Lanatoside C – Lanocide

Physical Properties of Cardiac Glycosides

Nature: All are white, colourless powders.

Solubility: Insoluble in water, sparingly soluble in chloroform and freely soluble in pyridine.

Chemical Properties

A mixture of digoxin and digitoxin with a mixture of acetic anhydride, acetyl chloride and trifluoroacetic acid produces characteristic fluorescence.
Cardiac glycosides answer the following tests.

Keller Killiani Reaction

Substance is dissolved in glacial acetic acid and treated with few drops of ferric chloride. Concentrated sulphuric acid is added slowly. A brown colour develops at the junction of the liquids.

Kedde's Reaction:

When a suspension of the substance is treated with dinitrobenzoic acid in alkaline medium, a violet colour is produced.

Stability and Storage

All cardiac glycosides should be stored in well closed light resistant container.

Formulation

1. Digoxin tablets/Injection/Pediatric solution.
2. Digitoxin tablet/Lanatoside C tablet.
3. Deslanoside Injection.

Use: It is used as cardiotonic agent to improve the cardiac activity.

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30 Vitamins

Vitamins are organic substances found in food. They are essential for normal metabolism, growth and development of the animal and human body. They play a vital role in energy transportation. They act as coenzymes in enzyme system. Most of the vitamins are isolated from animal or plant sources, some are synthesized and a very few are formed in our body *viz.* Vitamin A from carotene, Vitamin D by U.V. light on skin, Vitamin K from symbiotic bacteria of the intestine.

Vitamins are readily destroyed by oxidation, heat light and aging. Deficiency of vitamins causes certain diseases.

CLASSIFICATION

1. **Water soluble vitamins**
   - Vitamin B Complex
   - Vitamin B_1 (Thiamine)
   - Vitamin B_2 (Riboflavin)
   - Vitamin B_3 (Nicotinic acid)
   - Vitamin B_6 (Pyridoxine)
   - Vitamin B_{12} (Cyanocobalamine)
   - Folic acid
   - Vitamin C (Ascorbic acid)
2. **Fat soluble vitamins**
   - Vitamin A (Retinol)
   - Vitamin D (Calciferol)
   - Vitamin E (Tocoferol)
   - Vitamin K (Phytomenadione)

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THIAMINE HYDROCHLORIDE

It contains pyrimidine and thiazole ring linked by a methylene group.

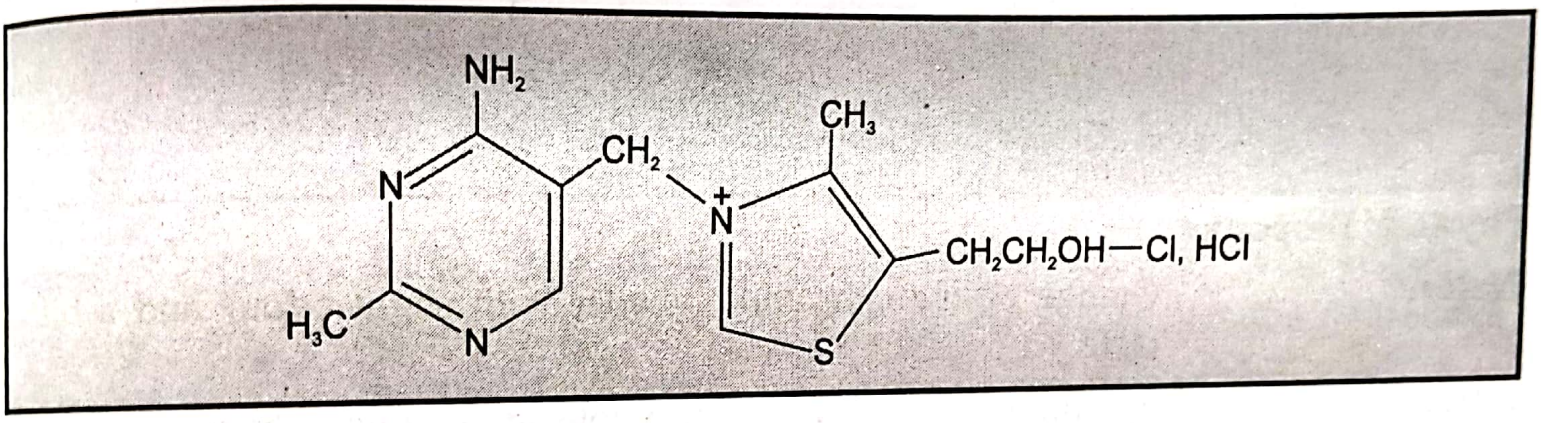
Source: Rice polishing, liver, yeast, pork and synthetic route.

Deficiency disease: Beri-beri.

Brand name: Berin.

Chemical name: 3-((4-amino-2-methyl) pyrimidin-5-yl)-5-(2-hydroxy ethyl)-4-methyl thiazolium chloride.

Structure:



Physical Properties

Nature: White crystalline powder with meat-like odour and a bitter taste.

Solubility: Soluble in water, methylalcohol, and glycerol. Insoluble in acetone.

Melting point: 248°C.

Chemical Properties

1. Thiamine hydrochloride is oxidized by alkaline potassium ferricyanide to thiochrome, which exhibits a blue fluorescence.
2. Thiamine is precipitated by silicotungstic acid.

Stability: Unstable in aqueous solution of pH greater than 5.

Storage: Air tight non–metallic container to prevent atmospheric oxidation.

Uses: It is used in the treatment of

- Beri-beri, pellagra, *i.e,* Vit. B complex deficiency.
- Neuritis.

Formulation:

- Thiamine hydrochloride Tablets
- Thiamine hydrochloride Injection.

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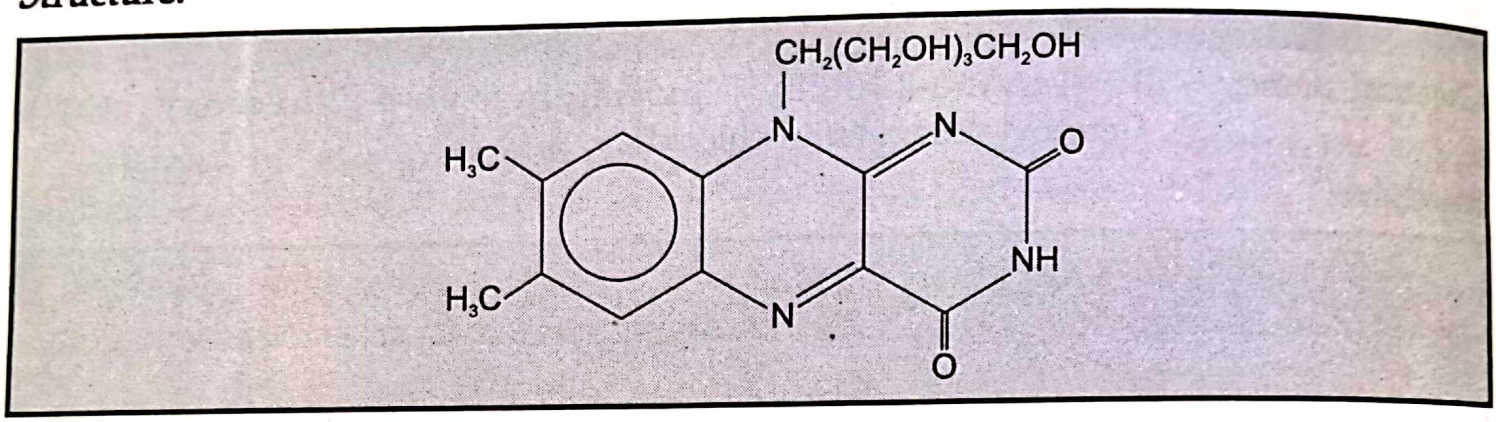
RIBOFLAVIN (VITAMIN B_2)

Riboflavin contains isoalloxazine ring system.

Chemical name: 7, 8-Dimethyl-10(1-D-ribityl) is isoalloxazine.

Structure:



Physical Properties

Nature: Orange yellow crystalline powder with slight odour and a bitter taste.

Solubility: Sparingly soluble water, insoluble in organic solvents and very soluble in alkaline solutions.

Melting point: 280°C.

Chemical Properties:

1. Aqueous solution of riboflavin, in presence of alkali or light deteriorates rapidly.
2. Aqueous solution gives a pale greenish yellow colour and yellowish green fluorescence which disappears on addition of acid or alkali.

Storage: Air tight light resistant container.

Uses: It is used in

1. Angular steatites (ulcer in mouth).
2. Glossitis (ulcer in tongue).

Formulation:

- Riboflavin Tablets.

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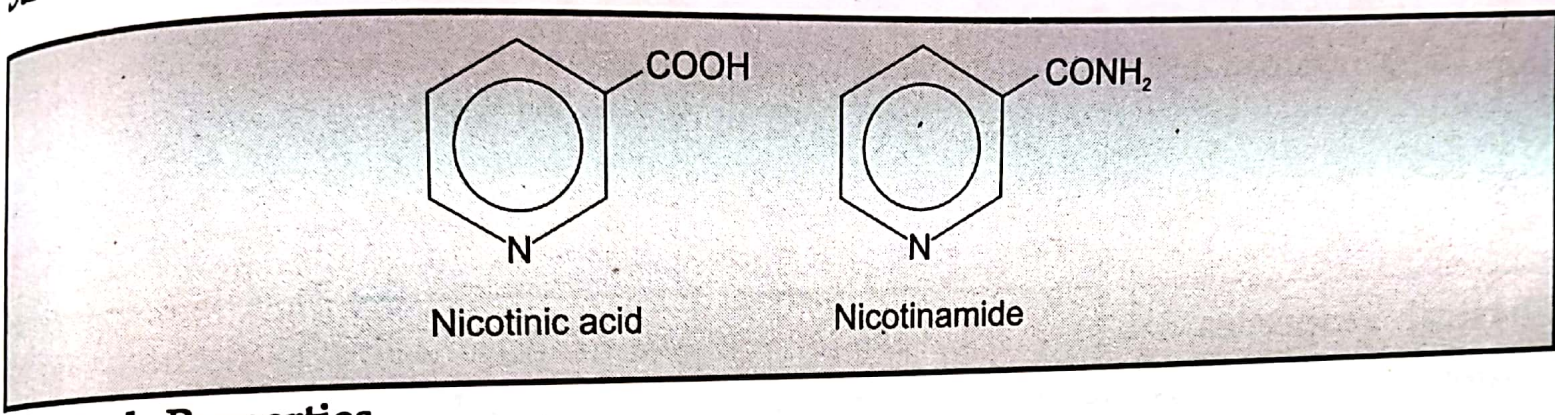
NICOTINIC ACID (VITAMIN B_3, NIACIN, NICOTINAMIDE)

Source: Rice polishing, yeast, liver, meat and synthetic route.

Chemical name: Pyridine-3-carboxylic acid.

Structure:



Nicotinic acid Nicotinamide

Physical Properties

Nature: White, odourless, crystalline powder with acid taste.

Solubility: Soluble in water, alcohol and aqueous solution of alkali. Insoluble in organic solvents.

Melting point: 234–237°C.

Chemical Properties

1. Nicotinic acid gives blue precipitate with copper sulphate solution.
2. It gives golden yellow colour with cyanogen bromide and aniline.

Storage: Well closed, light resistant container.

Uses:

- It is used in the treatment of pellagra
- It is used as vasodilator
- It is used as lipid lowering agent.

Formulation: Nicotinic acid Tablets.

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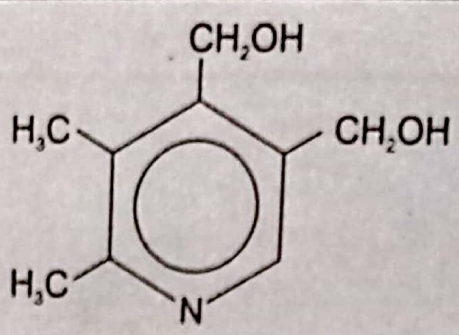
PYRIDOXIN (VITAMIN B_6)

Chemical name: 3-hydroxy-4, 5-bis(hydroxyl methyl)-2-methyl pyridine.

Structure:



Physical Properties

Nature: White crystalline powder with slightly bitter taste.

Solubility: Soluble in water and alcohol and insoluble in organic solvents.

Melting point: 202 – 206°.

Chemical Properties

Pyridoxine is oxidized by hydrogen peroxide and other oxidizing agents.

Storage: Well closed, light resistant container.

Uses: It is used in

- Treatment of Neuritis.
- Megaloblastic anemia.
- Nausea and vomiting during pregnancy.

Formulation: Pyridoxine Tablets.

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CYANOCOBALAMIN (VITAMIN B_{12})

Cyanocobalamin is organo cobalt compound obtained from liver or culture medium of certain species of streptomyces.

Physical Properties

Nature: Dark-red, odourless, tasteless, hygroscopic crystalline powder.

Solubility: Soluble in water and alcohol and insoluble in organic solvents. Hydrocobalamin is the related compound in which the cyano group of cyanocobalamin is replaced by hydroxyl group.

Chemical Properties

Decomposition of vitamin B_{12} with potassium sulphate and sulphuric acid results in blue coloured complex with ammonium thiocyanate.

Stability: Stable in neutral aqueous solution. Decomposed in alkaline acid or medium.

Storage: Well closed light resistant container.

Use: It is used in the treatment of megaloblastic anemia.

Formulation: Cyanocobalamin Injection.

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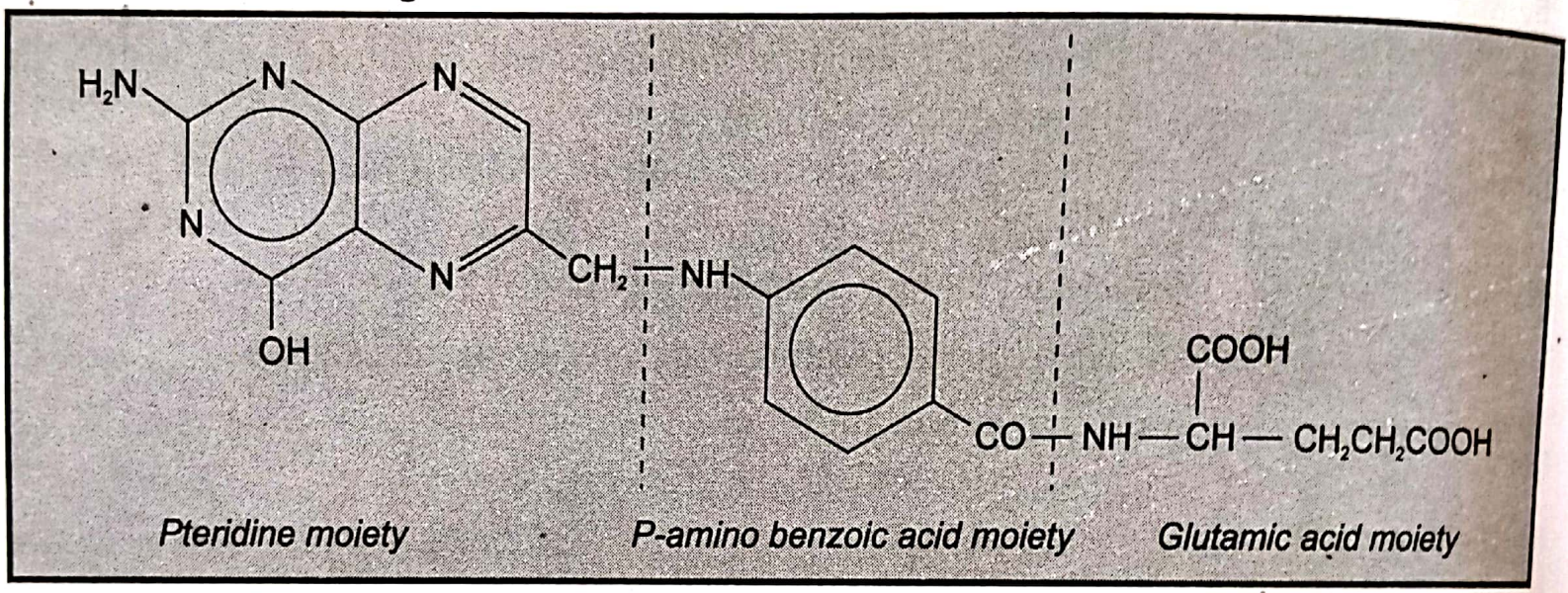
FOLIC ACID (PTEROYL GLUTAMIC ACID)

Source: Green plant tissue, liver and yeast. The chemical structure of fol acid is composed of three moieties.

- Pteridine
- P-amino benzoic acid
- Glutamic acid.

Brand name: Folvite.

Chemical name: 4-(2-amino-4-hydroxy pteridin-6-yl) methyl amino benzoyl-L-glutamic acid.



Physical Properties

Nature: Yellow, odourless, tasteless, microcrystalline powder.

Solubility: Insoluble in cold water and organic solvents, slightly soluble in boiling water and soluble in acid and alkali solution.

A major part of the vitamin is destroyed during cooking.

Chemical Properties

When heated with zinc and hydrochloric acid, the pteridine and benzoic acid moieties are cleaved with formation of primary amino group. This can be diazotized with nitrous acid and coupled with N-(1-naphthyl) ethylene diamine to a magenta colour dye.

Storage: Stored in tightly closed light resistant container.

Uses:

1. It is used in the treatment of Sprue (a disease characteristed by weakness anaemia and loss of weight due to malabsorption of essential nutrients).
2. It is used in the treatment of megalobalstic anaemia.

Formulation: Folic acid Tablets/Multivitamin liquid formulations of folic acid are formulated with 20% of sugar which prevents deterioration.

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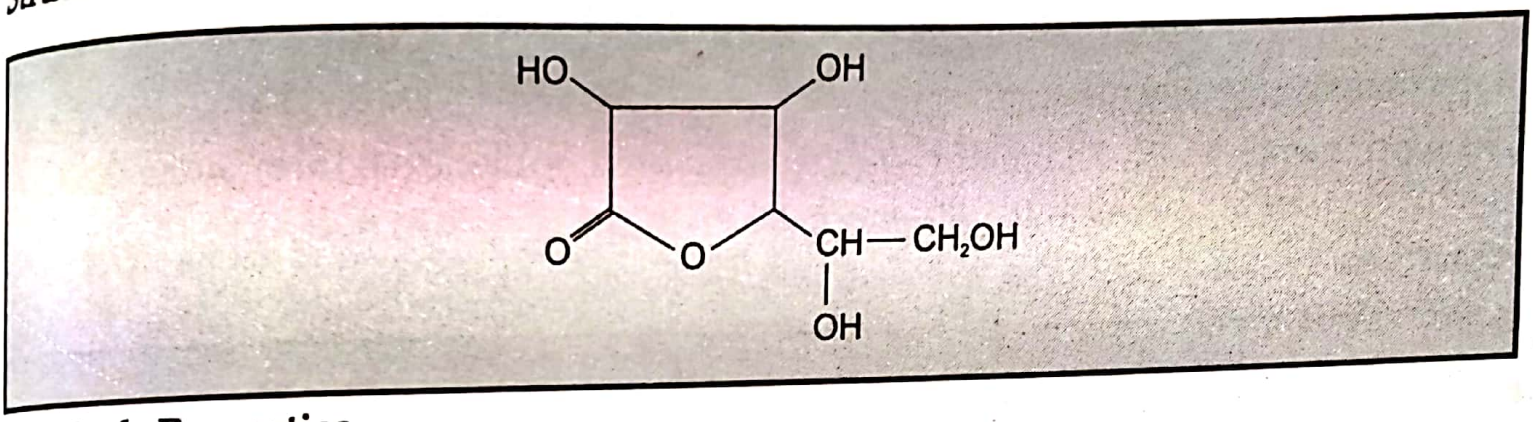
ASCORBIC ACID (VITAMIN C)

Brand name: Celin, Limcee.

Chemical name: 5-(1,2-dihydroxy ethyl)-3, 4-dihydroxy-5 (H) furan-2-one.

Structure:



Physical Properties

Nature: Colourless or pale yellow crystalline powder.

Solubility: Soluble in water, alcohol and acetone and insoluble in chloroform and ether.

Stability: Darkens on exposure to air light and heat.

Melting point: 190°C.

Chemical Properties

1. The acidic property of ascorbic acid is due to the existence of keto enol tautomerism.
2. It can be oxidized to dehydroascorbic acid, which can be reduced to ascorbic acid.
3. Ascorbic acid decolourises the blue coloured 2, 6-dichloropheneol indophenol (Tillmann's reagent).
4. It gives yellow colour with sodium nitroprusside in alkaline medium and blue colour in acid medium.
5. The enolic hydroxyl group gives violet coloured iron (II) ascorbate salt.
6. It reduces oxidizing agent viz. iodine, ceric ammonium sulphate and methylene blue.

Storage: Air-tight, light-resistant non-metallic container in a cool place. The liquid preparations should be prepared with antioxidant.

Uses:

- It is used in the treatment of Scurvy.
- It is used as antioxidant in pharmaceutical formulations.

Formulation: Ascorbic acid Tablets/Injection.

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VITAMIN A (RETINOL)

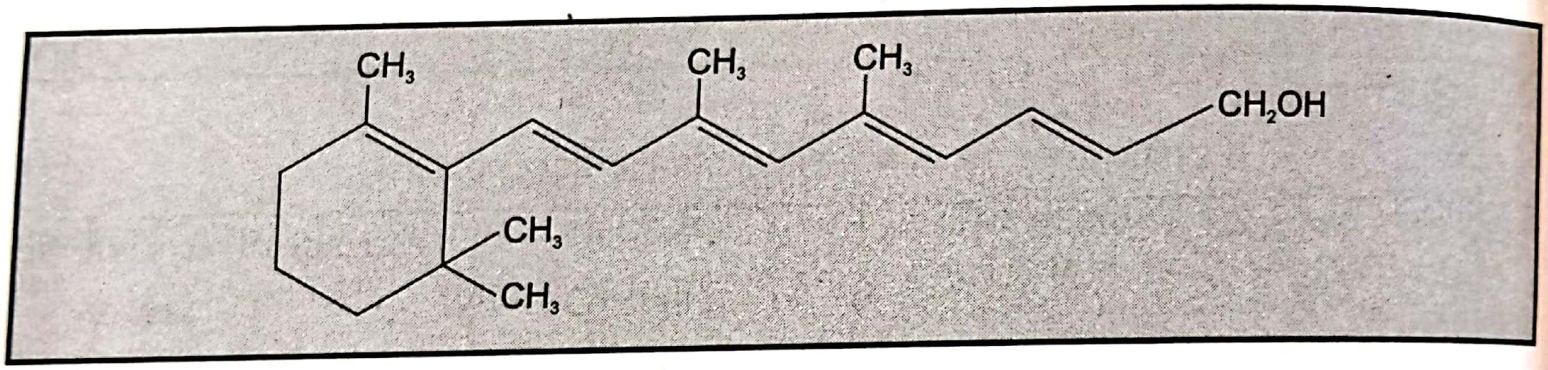
Source: Vitamin A is biosynthesized in animals from carotene.

Each molecule of Carotene produces two molecules of retinol, which contains alcoholic group. Retinal is vitamin A aldehyde and retinoic acid is an acid.

Brand name: Arovit.

Chemical name: 3, 7-Dimethyl-9-(2,6,6-trimethyl cyclohex-1-1nly) nona-2, 4, 6, 8-all-trans-tetraen-1-o).

Structure:



Physical Properties

Nature: Pale yellow crystals.

Solubility: Insoluble in water and freely soluble in organic solvents and fixed oils.

Chemical Properties

1. **Carr-Price reaction**. Vitamin A in chloroform gives an intense blue colour with antimony trichloride in chloroform.
2. It also gives blue colour with trufluroacetic acid, with phosphotungstic acid. Violet colour with glycerol and dichlorohydrin.

I.P. gives monograph for three vitamin A preparations.

1. Vitamin A concentrate (oily form).
2. Vitamin A concentrate (powder form).
3. Vitamin A concentrate (water-miscible form).

acetate,

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Water miscible form: By adding suitable solubilisers to the pure vitamin A. It contains not less than 1,00,000 units of vitamin A per gram and stabilizing agents, antioxidant and antimicrobial preservative.

Melting point: 64°C.

Stability: It is deteriorated by air, oxidizing agents, light and acids.

Storage: Well-filled, tightly closed, light-resistant container and kept in cool place.

Uses:

- It is used in the treatment of night blindness.
- It is used in the treatment of dry and rough skin.

Formulation: Vitamin A drops/A and D drops.

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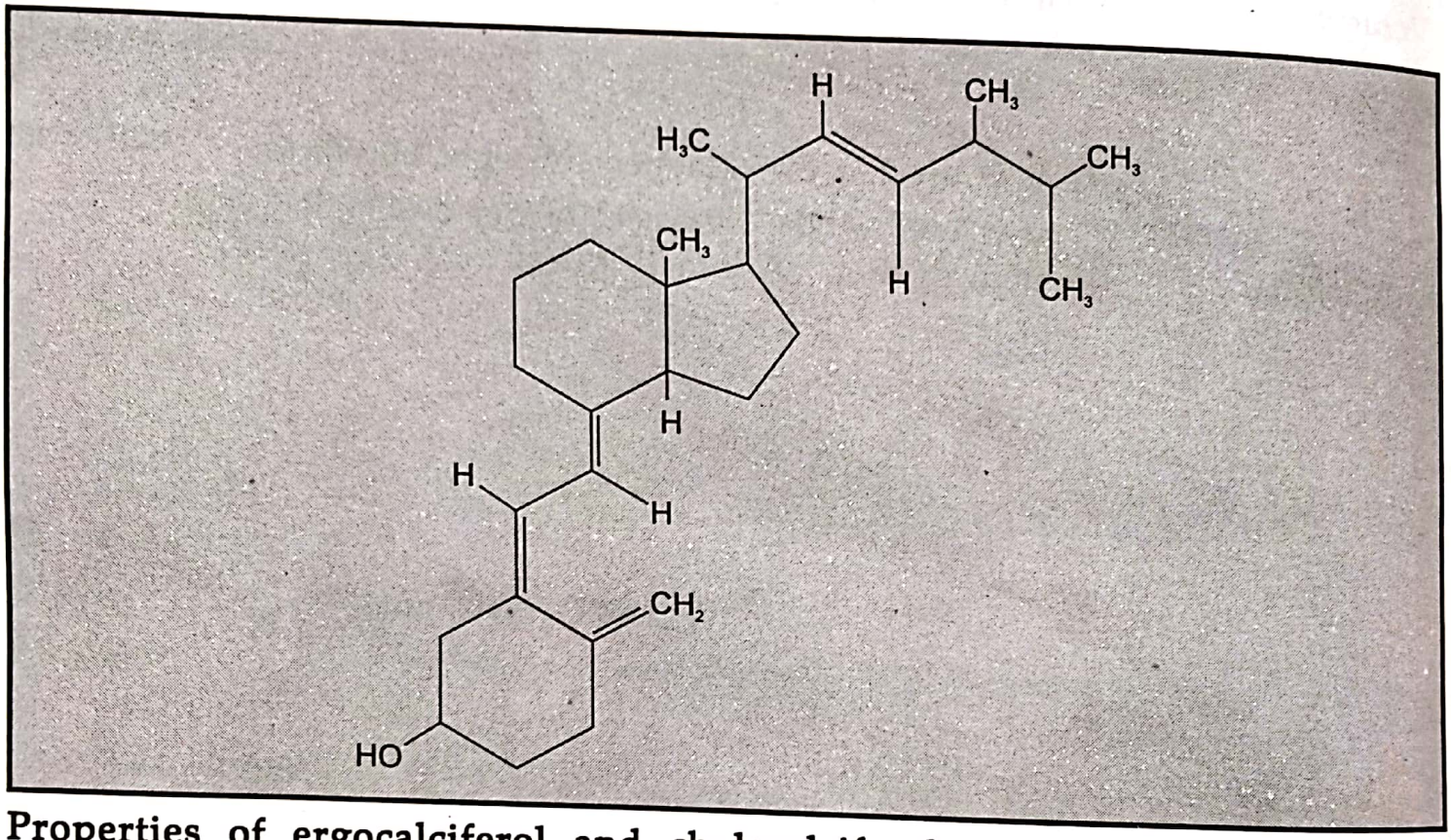
VITAMIN D (ERGOCALCIFEROL AND CHOLECALCIFEROL)

The term vitamin D represents groups of fat soluble compounds. They are ergoclaciferol (vit. D_2), cholecalciferol (vit. D_3), 2,5-hydroxycholecalciferol, 1, 25-dihydroxycholecalciferol and dihydrotachysterol.

Deficiency disease: Rickets.

Structure:



Properties of ergocalciferol and cholecalciferol:

Nature: Both are crystals sensitive to air, light and heat.

Solubility: Freely soluble in ethanol, acetone, chloroform, ether and fixed oils. Insoluble in water.

Melting point: Ergocalciferol 115°C cholecalciferol 84°C.

Chemical Properties

Both the substances give yellowish orange colour with antimony trichloride in chloroform (vitamin A gives blue colour).

Stability: The solutions in volatile solvents are unstable.

Storage: Thermostatically sealed light resistant container filled with nitrogen in cool place.

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Uses:

- It is used in the treatment of Rickets.
- It is used in the treatment of hypoparathyroidism.
- It is used in the treatment of hypocalcaemic tetany.

Formulation: Vitamin A and B capsule

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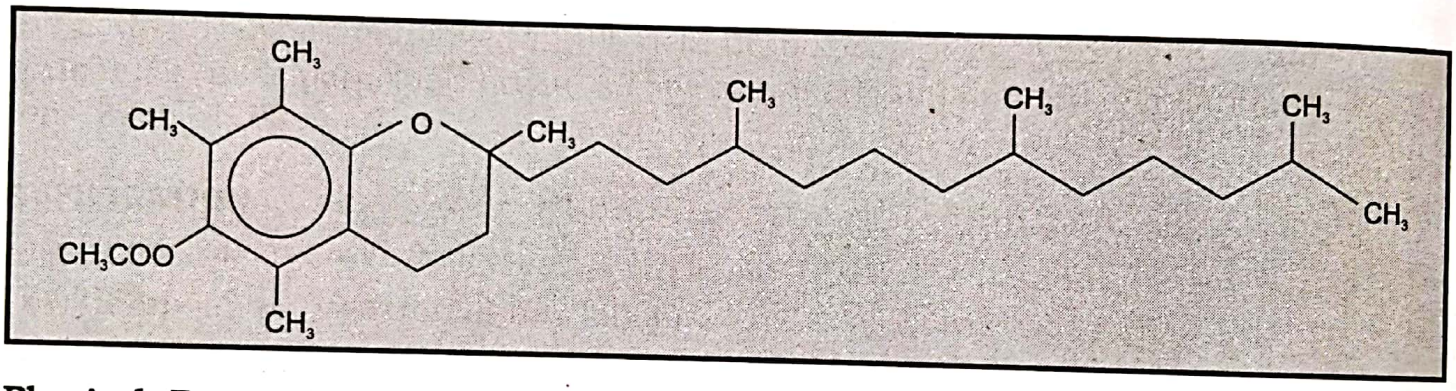
VITAMIN E (ALPHA TOCOPHEROL)

Source: Oil of soyabean, wheat germ, rice germ, cotton seed and green leaves. Not destroyed by cooking. Exists in eight stereo isomers. The most biologically active compound is tocopherol.

Chemical name: 6-acetoxy-2,5,7,8-tetramethyl-2-4, 8,12-trimethyl tridecyl chroman, (tridecyl means (tri+deca 3+10) chain containing 13 carbon atoms).

Structure:



Physical Properties Clear slightly greenish yellow, viscous oily liquid.

Solubility: Freely soluble in acetone, chloroform, ethanol, ether and fixed oils. Insoluble in water.

Chemical Properties

1. Oxidized by nitric acid to give a reddish brown product known as tocopherol red.
2. Gives yellow colour with sulphuric acid and yellowish-green colour with phosphomolybdic acid.

Storage: Well closed light resistant container.

Uses:

- It is used as an antioxidant in pharmaceutical products.
- It is used for protecting lipids in cell membrane from oxidation.

Formulation: Tocopherol Capsules.

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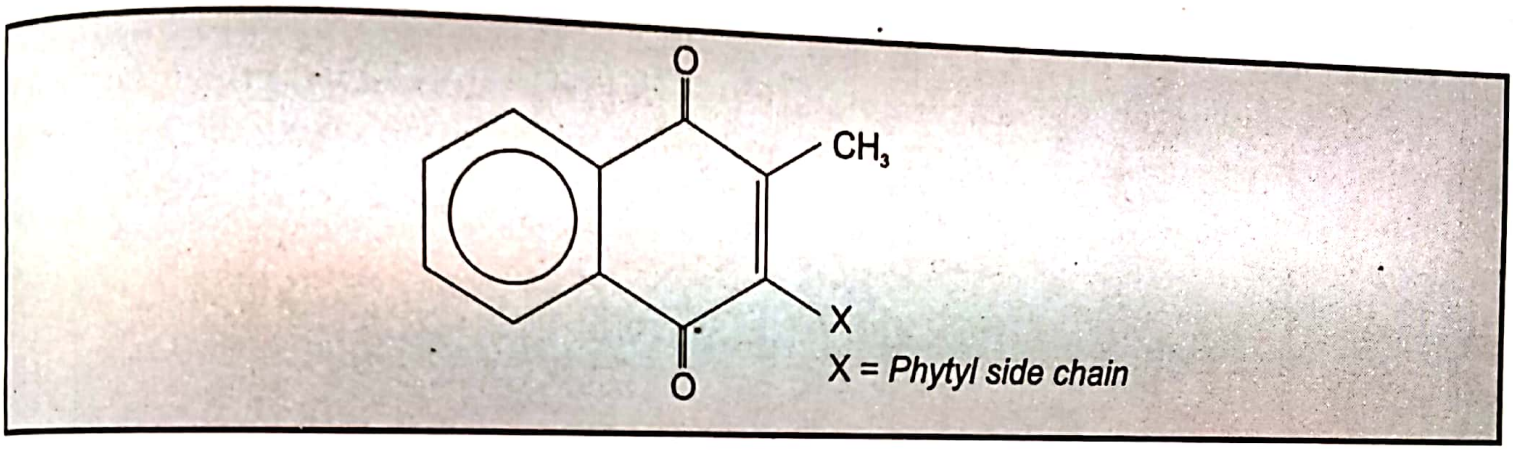
VITAMIN K (PHYTOMENEDIONE)

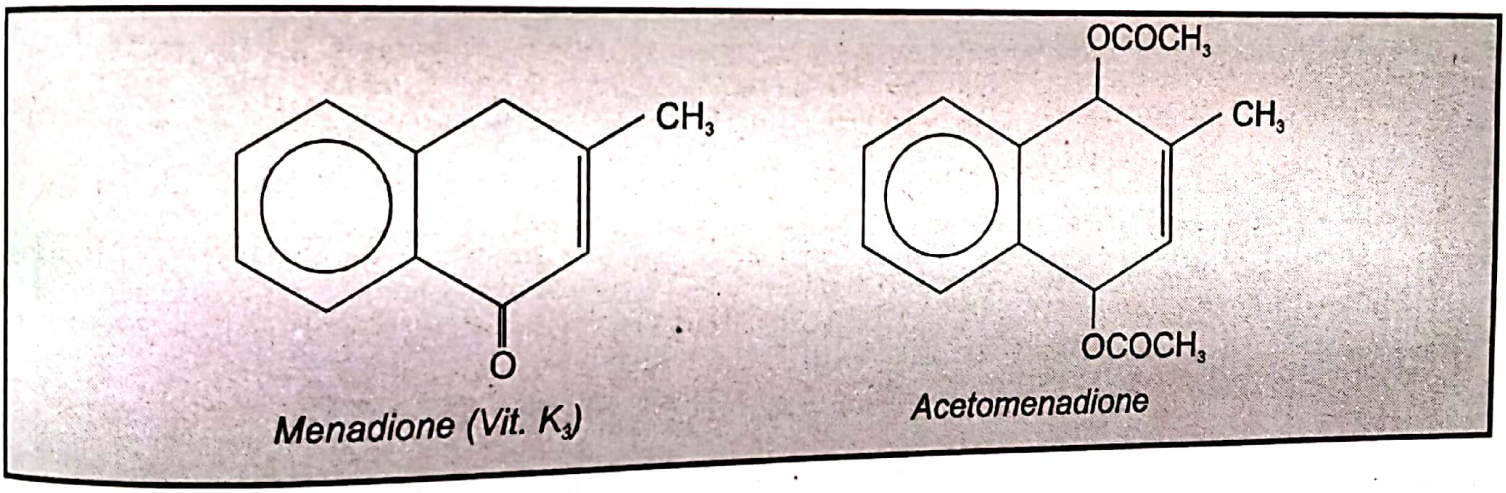
Vitamin K_1 is a naphthoquinone derivative containing phytyl group.

Sources: Fresh green vegetables, fruits and egg-yolk.

Vitamin K_2 is synthesized in intestine by bacteria. Menadione and acetomenadione are synthetic compounds.

Structure:





Physical Properties

Nature: Pale yellow crystalline powder with characteristic odour.

Solubility: Freely soluble in chloroform, toluene, alcohol and ether. Insoluble in water.

Melting point: 105-108°C.

Chemical Properties

It gives bluish-violet colour with ethyl cyanoacetate in slightly alkaline medium.

Stability: It decomposes on exposure to light and darkens to light brown.

Use: It is used in vitamin K deficiency.

Formulation: Vitamin K Tablet/Injection.

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