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सर्वश्रेष्ठ परीक्षा पथ-प्रदर्शक

B.Sc. *First Year* (Certificate Course) Semester-II

ZOOLOGY

Biochemistry and Physiology

SYLLABUS

UNIT-I **Structure and Function of Biomolecules :** Structure and Biological importance of carbohydrates (Monosaccharides, Disaccharides, Polysaccharides and Glycoconjugates); Lipids (saturated and unsaturated fatty acids, Tri-acylglycerols, Phospholipids, Glycolipids, Steroids); Structure, Classification and General properties of α-amino acids; Essential and non-essential α-amino acids, Levels of organization in proteins; Simple and conjugate proteins.

UNIT-II **Enzyme Action and Regulation :** Nomenclature and classification of enzymes; Cofactors; Specificity of enzyme action; Isozymes; Mechanism of enzyme action; Enzyme kinetics; Factors affecting rate of enzyme-catalysed reactions; Equation of Michaelis-Menton, Concept of K_m and $V_{max,}$ Enzyme inhibition; Allosteric enzymes and their kinetics; Regulation of enzyme action.

UNIT-III **Metabolism of Carbohydrates and Lipids :** Metabolism of Carbohydrates: glycolysis, citric acid cycle, gluconeogenesis, phosphate pentose pathway; Glycogenolysis and Glycogenesis; Lipids — Biosynthesis of palmitic acid; Ketogenesis, β-oxidation and omega-oxidation of saturated fatty acids with even and odd number of carbon atoms.

UNIT-IV **Metabolism of Protein and Nucleotides :** Catabolism of amino acids : Transamination, Deamination, Urea cycle; Nucleotides and vitamins, Peptide linkages.

UNIT-V **Digestion and Respiration in Humans :** Structural organization and functions of gastrointestinal tract and associated glands; Mechanical and chemical digestion of food; Absorptions of carbohydrates, lipids, proteins, water, minerals and vimtains; Histology of trachea and lung; Mechanism of respiration, Pulmonary ventilation; Respiratory volumes and capacities; Transport of oxygen and carbon dioxide in blood Respiratory pigments, Dissociation curves and the factors influencing it; control of respiration.

UNIT-VI **Circulation and Excretion in Humans :** Components of blood and their functions; hemopoiesis; Blood clotting : Blood clotting system, Blood groups : Rh factor, ABO and MN; Structure of mammalian heart; Cardiac cycle; Cardiac output and its regulation, Electrocardiogram, Blood pressure and its regulation; Structure of kidney and its functional unit; Mechanism of urine formation.

UNIT-VII **Nervous System and Endocrinology in Humans :** Structure of neuron, resting membrane potential; Origin of action potential and its propagation across the myelinated and unmyelinated nerve fibers; Types of synapse; Endocrine glands : pineal, pituitary, thyroid, parathyroid, pancreas, adrenal; hormones secreted by them; Classification of hormones; Mechanism of Hormone action.

UNIT-VIII **Muscular System in Humans :** Histology of different types of muscle; Ultra structure of skeletal muscle; Molecular and chemical basis of muscle contraction; Characteristics of muscle twitch; Motor unit, summation and tetanus.

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UNIT-I

Structure and Function of Biomolecules

SECTION-A VERY SHORT ANSWER TYPE QUESTIONS

Q.1. What are monosaccharides?

Ans. The monosaccharides are polyhydroxy aldehydes or ketone which cannot be hydrolysed to simpler sugar, *e.g.,* glucose.

Q.2. Are carbohydrates hydrophobic?

Ans. Carbohydrates are generally considered as hydrophilic molecule, but indeed they exhibit relatively hydrophobic regions due to their CH_2 group.

Q.3. Which carbohydrate is used in animals?

Ans. Starch and glycogen each serve a similar purpose in storing energy for later use, but starch is used for plants whereas glycogen is used by animals. Examine these two types of complex carbohydrates to understand their structure and function.

Q.4. Write two functions of oligosaccharides.

Ans. (i) It is used in the formation of transport soap.

(ii) In the form of lactose it is the mainly used as food for child and parents.

Q.5. What is fatty acid?

Ans. Fatty acids are organic compounds consisting of a hydrocarbon chain and terminal carboxyl group. General formula of fatty acid is $CH_3(CH_2)_nCOOH$. The chain length generally ranges from one hydrogen atom to nearly thirty carbon atoms.

Q.6. Write the name of two saturated fatty acid.

Ans. (i) Butyric acid, (ii) Stearic acid.

Q.7. Write the name of two unsaturated fatty acid.

Ans. (i) Oleic acid, (ii) Linoleic acid.

Q.8. What are amino acids?

Ans. Amino acids constitute a group of neutral products clearly distinguished from other natural compounds chemically, mainly because of their ampholytic properties, and biochemically, mainly because of their role as protein constituents. An amino acid is a carboxylic acid-containing an aliphatic primary amino group in the α position to the carboxyl group and with a characteristic stereochemistry.

Q.9. Write the physical properties of amino acids.

Ans. Some physical properties of amino acids are as follows :

1. Amino acids are colourless, crystalline solid.
2. All amino acids have a high melting point greater than 200°.

3. **Solubility :** They are soluble in water, slightly soluble in alcohol, and dissolve with difficulty in methanol, ethanol, and propanol. *R*-group of amino acids and pH of the solvent play important role in solubility.
4. On heating to high temperatures, they decompose.
5. All amino acids (except glycine) are optically active.
6. Peptide bond formation : Amino acids can connect with a peptide bond involving their amino and carboxylate groups. A covalent bond formed between the alpha-amino group of one amino acid and an alpha-carboxyl group of other forming —CO—NH—linkage. Peptide bonds are planar and partially ionic.

Q.10. What do you mean by glycogen?

Ans. Glycogen is called as animal starch as it serves as the chief reserve of glucose in them. It is mainly stored in liver and muscles of animals in the form of small granules. Glycogen is a highly branched polysaccharide and structurally similar to amylopectin, but it has comparatively more number of glucose residues and branch points compared to amylopectin.

Q.11. What is peptide bond?

Ans. A peptide bond is a chemical formed between two molecules when the corboxyl group of one molecule reacts with the amino group of the other molecule, releasing a molecule of water.

Q.12. What is the quaternary structure of proteins?

Ans. Some proteins have more polypeptide chain and the orientation of such type of protein is known as quaternary proteins structure.

Q.13. Which disease is caused due to deficiency of protein?

Ans. Kwashiorkor disease is caused due to deficiency of protein.

Q.14. What are nucleoproteins?

Ans. They are complexes of one or more protein molecules with nucleic acids. The nucleic acid of the cell nucleus is chiefly deoxyribonucleic acid (DNA) which combines with the protamines, histones and other proteins of the cell nucleus. The nucleoprotein of the cytoplasm contains ribonucleic acid (RNA). The principal ribonucleoproteins are in the ribosomes, which have the capacity for protein synthesis.

Q.15. What are the exceptions of amino acid?

Ans. The exceptions of amino acids are as follows :

1. Glycine, which does not have a side chain. Its α-carbon contains two hydrogens.
2. Proline, in which the nitrogen is part of a ring.
3. Thus, each amino acid has an amine group at one end and an acid group at the other, and a distinctive side chain. The backbone is the same for all amino acids while the side chain differs from one amino acid to the next.
4. All of the 20 amino acids except glycine are of the *L*-configuration, as for all but one amino acid the α-carbon is an asymmetric carbon. Because glycine does not contain an asymmetric carbon atom, it is not optically active and, thus, is neither *D* nor *L*.

SECTION-B SHORT ANSWER TYPE QUESTIONS

Q.1. Write a short note on structure and properties of maltose.

Ans. **Maltose**

The structure and properties of maltose are given as follows :

Structure

Maltose is composed of 2 molecules of glucose and is obtained by the hydrolysis of starch as an intermediate product either by amylase or by diastase. It contains a free sugar group. Maltose is a reducing sugar and gives the reactions of hemiacetal. On hydrolysis, it yields two molecules of glucose. So, it is a glucose a-glucoside and generally crystallizes as the β-form. It structural formula is as follows which shows an α-1, 4 glucoside linkage in between the two glucose units.

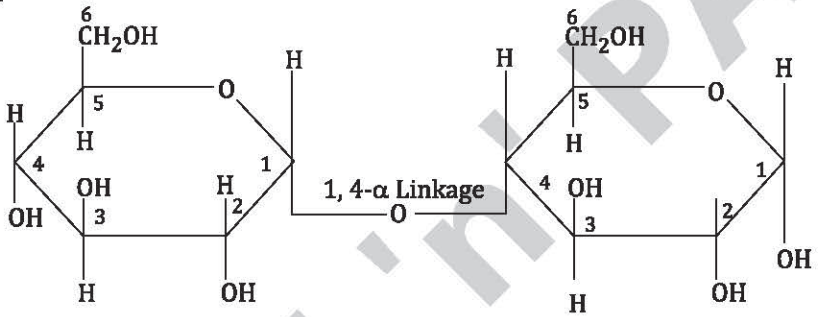


Fig. : Maltose

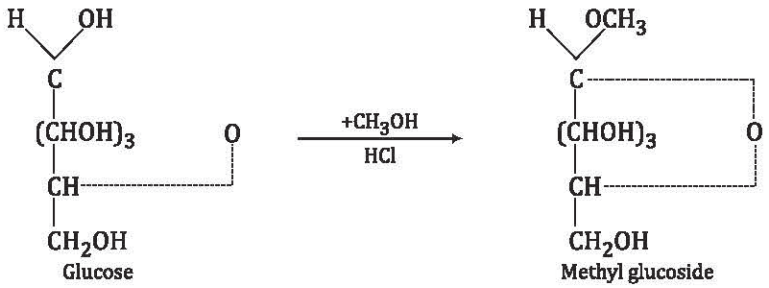
Properties

1. Maltose is colourless, crystalline, soluble in water and insoluble in ether.
2. It forms slender and white needles on crystallization.
3. It is fermentable by yeast directly.
4. Maltose is dextrorotatory with specific rotation +137°.
5. It reduces Fehling solution, Benedict's solution and Nylander's reagent.

Q.2. Write about the chemical properties of monosaccharides.

Ans. **Chemical Properties of Monosaccharides**

1. **Glucoside Formation :** When glucose is heated with alcohols in the presence of HCl, monosaccharides form ethers known as glucosides. Thus, with methyl alcohol, glucose forms methyl glucoside and fructose forms methyl fructoside.



2. **Reduction** : When reduced with, sodium amalgam in aqueous solution, monosaccharides form polyhydric alcohols.

$$\underset{\text{Glucose}}{CH_2OH(CHOH)_4 \cdot CHO} + 2[H] \longrightarrow \underset{\text{Sorbitol}}{CH_2OH \cdot (CHOH)_4 \cdot CH_2OH}$$

With stronger reducing agent like—Red P + Conc. HI, glucose forms ***n*-hexane**

$$CH_2OH(CHOH)_4 \cdot CHO \xrightarrow[HI]{\text{Red P}} \underset{n\text{-hexane}}{CH_3(CH_2)_4CH_2}$$

3. **Oxidation :** (a) With mild oxidising agent like, Br_2 Water, fehling solution and Tollen's reagent forms gluconic acid.

$$\underset{\text{Glucose}}{CH_2OH(CHOH)_4CHO} + O \xrightarrow{Br_2 \text{ Water}} \underset{\text{Gluconic acid}}{CH_2OH(CHOH)_4COOH}$$

(b) With strong oxidising agent like HNO_3 forms saccharic acids.

$$\underset{\text{Glucose}}{CH_3OH(CHOH)_4CHO} \xrightarrow{HNO_3} \underset{\text{Saccharic acid}}{COOH(CHOH)_4COOH}$$

4. **Action of HCN :** Form addition products with HCN.

$$\underset{\text{Glucose}}{CH_2OH(CHOH)_4CHO} + HCN \longrightarrow \underset{\text{Glucose (Cyanohydrin)}}{CH_2OH(CHO_4)_4CH(OH)CN}$$

5. **Action of Phenylhydrazine** : When treated with an excess of phenylhydrazine, monosaccharides form Osazones. The reaction takes place in three steps :

(a)
$$\underset{\text{Glucose}}{\begin{array}{l}CH\,[O + H_2]\,N.NHC_6H_5\\ |\\ CHOH\\ |\\ (CHOH)_3\\ |\\ CH_2OH\end{array}} \xrightarrow{\text{Phenylhydrazine}} \underset{\text{Glucose Phenylhydrazine}}{\begin{array}{l}CH{=}N.NHC_6H_5\\ |\\ CHOH\\ |\\ (CHOH)_3 + H_2O\\ |\\ CH_2OH\end{array}}$$

(b)
$$\underset{\text{Glucose Phenylhydrazine}}{\begin{array}{l}CH{=}N.NHC_6O_5\\ |\\ CHOH + C_6H_5NH.NH_2\\ |\\ (CHOH)_3\\ |\\ CH_2OH\end{array}} \longrightarrow \underset{\text{Phenylhydrazine}}{\begin{array}{l}CH{=}N.NHC_6O_5\\ |\\ CO + C_6H_5NH_2 + NH_3\\ |\\ (CHOH)_3\\ |\\ CH_2OH\end{array}}$$

The most important among the monosaccharides from the stand point of occurrence in nature, are the pentose and hexose sugars, with the aldohexoses being the more important of the two.

Q.3. Write a short note on saturated and unsaturated fatty acid.

Ans. (i) **Saturated Fatty Acids :** These are long chain fatty acids in which number of hydrogen atoms in carbon chain is more and more *i.e.,* there is only single bonds. The general formula is $C_nH_{2n}O_2$ or $C_nH_{2n+1}COOH$. Mostly these are present in nature in the form of palmitic (C_{18}) and stearic (C_{15}) fatty acids.

(ii) **Unsaturated Fatty Acids :** These are all fatty acids in which number of hydrogen atom in carbon chain is liest than saturated fatty acids *i.e.,* they have one or more than one double bonds are present. In unsaturated fatty acids, there are two or more double bonds are found. The double bonds are not conjugated (—CH = CH—CH = CH—) but separated by methylene group —CH = CH—CH_2—CH = CH—. Unsaturated fatty acids are further divided into two class :

(a) Monounsaturated fatty acids.

(b) Polyunsaturated fatty acids.

Q.4. Write a short note on hydrolysis of fats.

Or **Describe the physical and chemical properties of fats.**

Ans. **Properties of Fats**

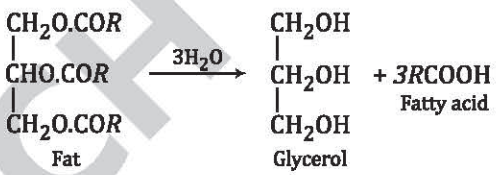
The physical and chemical properties of fats are given as follows :

Physical Properties

1. Most of the pure fats and oils are colourless, odourless tasteless substances. The colour and taste of some of the naturally. Occurring fats is due to the presence of impurities.
2. They are insoluble in water but soluble in organic solvents.
3. They have well defined melting and solidifying points.

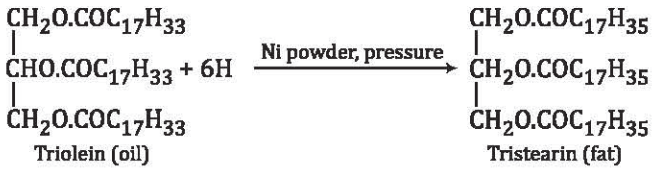
Chemical Properties

1. **Hydrolysis :** Hydrolysis of fats with alkali or enzyme lipase yields fatty acids and glycerol.



When the fats are hydrolysed with alkali (NaOH Or KOH), the free fatty acids react with the alkali to form neutral salts. This salt is a soap and the process of hydrolysing fats with alkali, which produces soap is called Saponification. Production of soap by alkaline hydrolysis of fats is one of the oldest chemical manufacturing process. In early middle ages, crude soap was prepared from fat and wood ash. In modem age, the fat and aqueous alkali are heated and stirred together and the soaps are then precipitated by adding salts. The glycerol is recovered by evaporation of aqueous solution and the soap is pressed into desired shape and size. For special purposes, bactericidal agents, scents and emollients can be added to the soap.

2. **Saponification :** The number of milligrams of KOH required to saponify one gram of fat is called the saponification number of that fat. The number provides informations on the average chain length of the fatty acid. The higher the number, shorter the average chain length of the fatty acids present in that fat.
3. **Hydrogenation :** Unsaturated plant fats (oils) are solidified to produce margarine and vegetable shortenings by hydrogenation of the oil. This is done by passing hydrogen gas in the presence of finely divided nickel as a catalyst. In the process, unsaturated fatty acids in the oil are saturated and the M.P. of the resultant fat increases :



4. **Hydrogenolysis :** Oils and fats are converted into glycerol and a long chain aliphatic alcohol when excess of hydrogen is passed through them under pressure and in presence of copper chromium catalyst. The splitting of fat by hydrogen is called hydrogenolysis.

Q.5. Write about the glycoconjugate.

Ans. **Glycoconjugate**

A carbohydrate chemically linked to another compound, *e.g.,* lipid or protein Glycoconjugates are essential in living things. They are carbohydrates that are covalently linked to another biomolecule via glycosylation and the carbohydrate constituent of the complex is called a glycan. Glycosylation is a process that forms glycoconjugates. In general, this biochemical process occurs in the cytoplasm of a cell. In eukaryotes, it occurs in the lumen of the endoplasmic reticulum (particularly, *N*-linked glycosylation) and in the cisterna of the Golgi apparatus (particularly, O-linked glycosylation). Glycosylation, particularly *O*-GlcNAc modification, occurs in the nucleus.

Glycoconjugates are involved in cell to cell communications, such as cell-cell recognition. They are also involved in cell to matrix interactions and in the process of detoxification. They are also essential in long term immune protection. Thus, glycoconjugate vaccines (*e.g.,* immunization against influenza) are contrived to boost longer immune protection against carbohydrate antigens.

Examples of glycoconjugates are glycoproteins, glycopeptides, peptidoglycans, glycosides, glycolipids, and lipopolysaccharides. For instance, a glycolipid is a carbohydrate (*e.g.,* certain oligosaccharides and polysaccharides) attached to a lipid is called a glycolipid. A glycoprotein is a carbohydrate attached to a protein.

1. glycosylation
2. glycoprotein
3. glycolipid
4. peptidoglycan
5. glycoside
6. lipopolysaccharide.

Q.6. What do you mean by glycoprotein? Write in brief.

Ans. A **glycoprotein** pertains to any protein covalently attached to a carbohydrate unit through the process of glycosylation. Some of the common carbohydrate constituents of glycoproteins are β-D-glucose, β-D-galactose, β-D-mannose, α-L-fucose, *N*-acetylglucosamine, *N*-acetylgalactosamine, *N*-acetylneuraminic acid, and xylose. The carbohydrate constituent is attached to the protein via the —OH group of serine or threonine (*i.e., O*-glycosylated) or via the amide NH_2 of asparagine (*i.e.,* N-glycosylated).

While technically describing conjugates in which the carbohydrate is less than 4 percent by weight, the term is often used generically to include the mucoproteins and proteoglycans. However, differences in the usage of the terms : glycoprotein, proteoglycan, peptidoglycan, and glycopeptide exist, and therefore, prudence in the usage of these terms has to be exercised. For instance, proteoglycans may be regarded as a subset of glycoproteins since both of them have a protein core. However, there are differences in several aspects. In

structure, glycoproteins have carbohydrate chains attached to a polypeptide side chain whereas proteoglycans have glycosaminoglycan chains attached to the polypeptide. Glycoproteins have lower percentage of non-protein content by weight than proteoglycans (which, in turn, have higher, about 50-60%).

Q.7. Write about the chemical properties of amino acids.

Ans. **Chemical Properties of Amino Acids**

1. **Zwitterionic property :** A zwitterion is a molecule with functional groups, of which at least one has a positive and one has a negative electrical charge. The net charge of the entire molecule is zero. Amino acids are the best-known examples of zwitterions. They contain an amine group (basic) and a carboxylic group (acidic). The $—NH_2$ group is the stronger base, and so it picks up H^+ from the —COOH group to leave a zwitterion. The (neutral) zwitterion is the usual form of amino acids that exist in the solution.
2. **Amphoteric property :** Amino acids are amphoteric in nature that is they act as both acids and base due to the two amine and carboxylic groups present.
3. **Ninhydrin test :** When 1 ml of Ninhydrin solution is added to a 1 ml protein solution and heated, the formation of a violet colour indicates the presence of α-amino acids.
4. **Xanthoproteic test :** The xanthoproteic test is performed for the detection of aromatic amino acids (tyrosine, tryptophan, and phenylalanine) in a protein solution. The nitration of benzoid radicals present in the amino acid chain occurs due to a reaction with nitric acid, giving the solution yellow coloration.
5. **Reaction with Sanger's reagent :** Sanger's reagent (1-fluoro-2, 4-dinitrobenzene) reacts with a free amino group in the peptide chain in a mild alkaline medium under cold conditions.
6. **Reaction with nitrous acid :** Nitrous acid reacts with the amino group to liberate nitrogen and form the corresponding hydroxyl.

Q.8. Write a short note on primary and secondary structure of proteins.

Ans. **Frederick Sanger** (1953), first time presented the primary structure of **insulin**. Since then sequencing of amino acids has been completed for myoglobin, haemoglobin, cytochrome-C, lysozyme and chymotrypsinogen etc.

1. **Primary Structure :** The primary structure of a protein refers to the linear sequence of amino acids in its polypeptide chain and location of disulphide bridges if any. It represents the number, nature and sequence of amino acid molecules in the polypeptide chain. Each protein molecule is formed of several thousand amino acid molecules linked by peptide bonds.
2. **Secondary Structure :** The folding or coiling of linear polypeptide chain into a specific coil represents secondary structure. It is determined by hydrogen bonding between the carboxyl oxygen and amide hydrogen atoms of the component amino acids of the peptide chain. These bonds can occur either between different polypeptide chains of protein or within the molecules of one polypeptide chain. By folding amino acid residues which may lie far apart in their primary sequence are brought in close proximity. This produces a regular helical structure.

Q.9. Write about the triacylglycerols.

Ans. **Triacylglycerols**

Triacylglycerols (formerly triglycerides) are the esters of glycerol with fatty acids. The fats and oils that are widely distributed in both plants and animals are chemically triacylglycerols. They are insoluble in water and non-polar in character and commonly known as **neutral fats**.

Fats as stored fuel : Triacylglycerols are the most abundant group of lipids that primarily function as fuel reserves of animals. The fat reserve of normal humans (men 20%, women 25% by weight) is sufficient to meet the body caloric requirements for 2-3 months. The biochemical explanations as to why fat has been chosen as a fuel reserve in animals is given in lipid metabolism.

Fats primarily occur in adipose tissue : Adipo cytes of adipose tissue-predominantly found in the subcutaneous layer and in the abdominal cavity—are specialized for storage of triacylglycerols. The fat is stored in the form of globules dispersed in the entire cytoplasm. And surprisingly, triacylglycerols are not the structural components of biological membranes.

Structures of acylglycerols : Monoacylglycerols, diacylglycerols and triacylglycerols, respectively consisting of one, two and three molecules of fatty acids esterified to a molecule of glycerol. Among these, triacylglycerols are the most important biochemically.

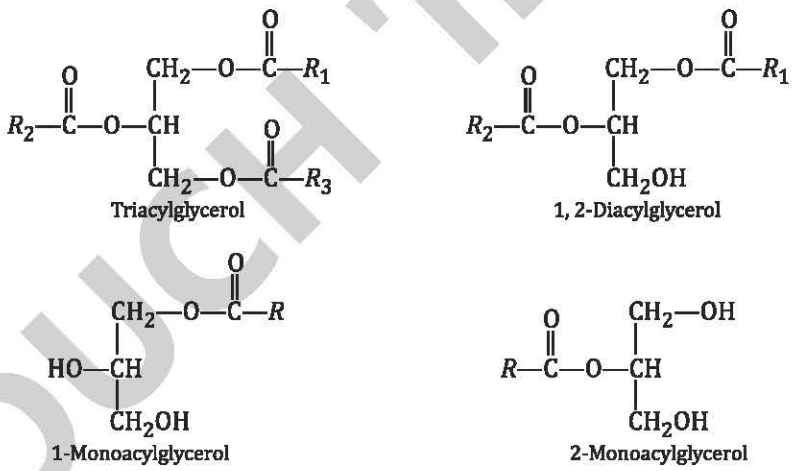


Fig. General structures of acylglycerols
(For palmitoyl $R = C_{15}H_{31}$; for stearoyl $R = C_{17}H_{35}$; For linoceoyl $R = C_{17}H_{31}$)

Simple triacylglycerols contain the same type of fatty acid residue at all the three carbons *e.g.,* tristearoyl glycerol or tristearin.

Mixed triacylglycerols are more common. They contain 2 or 3 different types of fatty acid residues. In general, fatty acid attached to C_1 is saturated, that attached to C_2 is unsaturated while that on C_3 can be either. Triacylglycerols are named according to placement of acyl radical on glycerol *e.g.,* 1, 3 palmitoyl 2-linoleoyl glycerol.

Triacylglycerols of plants have higher content of unsaturated fatty acids compared to that of animals.

Q.10. Write about the phospholipids and their types.

Ans. **Phospholipids**

These are complex or compound lipids containing phosphoric acid, in addition to fatty acids, nitrogenous base and alcohol. There are two classes of phospholipids.

1. **Glycerophospholipids :** Glycerophospholipids are the major lipids that occur in biological membranes. They consist of glycerol 3-phosphate esterified at its C_1 and C_2 with fatty acids. Usually, C_1 contains a saturated fatty acid while C_2 contains an unsaturated fatty acid.

   (i) **Phosphatidic acid :** This is the simplest phospholipid. It does not occur in good concentration in the tissues. Basically, phosphatidic acid is an intermediate in the synthesis of triacylglycerols and phospholipids. The other glycerophospholipids containing different nitrogenous bases or other groups may be regarded as the derivatives of phosphatidic acid.

   (ii) **Lecithin (Phosphatidylcholine) :** These are the most abundant group of phospholipids in the cell membranes. Chemically, lecithin (**Greek** : *lecithos*-egg yolk) is a phosphatidic acid with choline as the base. Phosphatidylcholines represent the storage form of body's choline. Choline, containing labile methyl groups is involved in methylation reactions, besides nerve transmission.

      (a) **Dipalmitoyl lecithin** is an important phosphatidylcholine found in lungs. It is a surface active agent and prevents the adherence of inner surface of the lungs due to surface tension. Respiratory distress syndrome in infants is a disorder characterized by the absence of dipalmitoyl lecithin.

      (b) **Lysolecithin** is formed by removal of the fatty acid either at C_1 or C_2 of lecithin.

   (iii) **Cephalins (Phosphatidylethanolamine) :** Ethanolamine is the nitrogenous base present in cephalins. Thus, lecithin and cephalin differ with regard to the base.

   (iv) **Phosphatidylinositol :** The steroisomer myoinositol is attached to phosphatidic acid to give phosphatidylinositol (Pl). This is an important component of cell membranes. The action of certain hormones (*e.g.,* oxytocin, vasopressin) is mediated through Pl. In response to hormonal action, Pl is cleaved to diacylglycerol and inositol triphosphate. Both these compounds act as second messengers for hormonal action.

   (v) **Phosphatidylserine :** The amino acid serine is present in this group of glycerophospholipids. Phosphatidylthreonine is also found in certain tissues.

   (vi) **Plasmalogens :** When a fatty acid is attached by an **ether** linkage at C_1 of glycerol in the glycerophospholipids, the resultant compound is plasmalogen. Phosphatidal ethanolamine is the most important which is similar in structure to phosphatidyl ethanolamine but for the ether linkage (in place of ester). An unsaturated fatty acid occurs at C_1. Choline, inositol and serine may substitute ethanolamine to give other plasmalogens. Brain and muscle contain a good concentration (about 10% of phospholipids) of plasmalogens.

   (vii) **Cardiolipin :** It is so named as it was first isolated from heart muscle. Structurally, a cardiolipin consists of two molecules of phosphatidic acid held by an additional

glycerol through phosphate groups. It is an important component of inner mitochondrial membrane. Cardiolipin is the only phosphoglyceride that possesses antigenic properties.

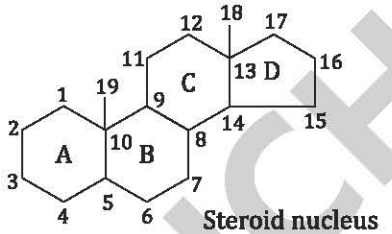
2. **Sphingomyelins :** Sphingosine is an amino alcohol present in sphingomyelins (sphingophospholipids). They do not contain glycerol at all. Sphingosine is attached by an amide linkage to a fatty acid to produce ceramide. The alcohol group of sphingosine is bound to phosphorylcholine in sphingomyelin structure. Sphingomyelins are important constituents of myelin and are found in good quantity in brain and nervous tissues.

Q.11. Write a short note on steroids and cholesterol.

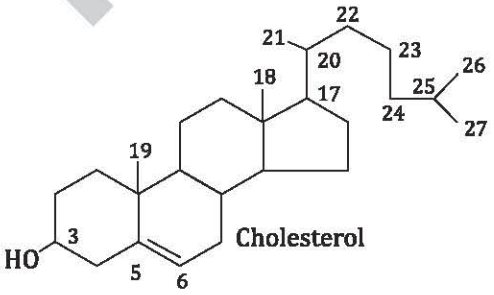
Ans. Steroids are the compounds containing a cyclic steroid nucleus (or ring) namely cyclopentanoperhydrophenanthrene (CPPP). It consists of a phenanthrene nucleus (rings A, B and C) to which a cyclopentane ring (D) is attached.

The steroid nucleus represents saturated carbons, unless specifically shown as double bonds. The methyl side chains (19 and 18) attached to carbons 10 and 13 are shown as single bonds. At carbon 17, steroids usually contain a side chain.

There are several steroids in the biological system. These include cholesterol, bile acids, vitamin D, sex hormones, adrenocortical hormones, sitosterols, cardiac glycosides and alkaloids. If the steroid contains one or more hydroxyl groups it is commonly known as sterol (means solid alcohol).



Steroid nucleus



Cholesterol

Cholesterol is exclusively found in animals and is the most abundant animal sterol. It is widely distributed in all cells and is a major component of cell membranes and lipoproteins. Cholesterol (*Greek* : *chole*-bile) was first isolated from bile. Cholesterol literally means 'solid alcohol from bile'.

SECTION-C LONG ANSWER TYPE QUESTIONS

Q.1. What are carbohydrates? Also describe classification and biological role of carbohydrates.

Ans. **Carbohydrates**

The class of substances known as carbohydrates is comprised of a large number or relatively heterogenous compounds. They are especially constituents of plants (cellulose and starch), but also occur and serve important functions in animals. Carbohydrates serve as the chief source of energy in the food of many animals. The name carbohydrates originated from the fact that the first compounds of this group to be studied were found to have an emperical

formula $C_x(H_2O)_y$, and were thought to be hydrates of carbon. Since that time, however, carbohydrates which do not have H and O present in the proportion to form water (*e.g.,* rhamnose, $C_6H_{12}O_6$) have been discovered, and other carbohydrates containing N and S are also known. Despite the relative unsuitability of the name it is still retained. Although it is difficult to define such a heterogenous group, the carbohydrates may be thought of as polyhydroxyaldehydes or ketones and derivatives of them. Oxidation, reduction or substitution of one or more of the functional groups can result in compounds which are also classed as carbohydrates.

Classification of Carbohydrates : The carbohydrates may be classified according to their complexity. Acid hydrolysis of complex carbohydrates results in the formation of what are known as **monosaccharides.** Monosaccharides may be defined as single straight chain molecules which cannot be hydrolysed into simpler substances. They are further grouped as **trioses, tetroses** and **pentoses** etc., depending upon the number of carbon atoms in the chain. The later are also further classified into aldoses and ketoses, depending upon the presence of aldehyde or ketone group.

The union of two or more monosaccharides results in the formation of **oligosaccharides** and **polysaccharides.** Conversely, hydrolysis of compound carbohydrates (oligo and polysaccharides) will yield the composite number of monosaccharide units. The term oligosaccharide includes a heterogenous group, containing perhaps 10 or 12 monosaccharide units. Molecules larger than these are known as **polysaccharides** carbohydrates occurring naturally can be classified into following four categories depending upon their structural complexity and behaviour towards hydrolysis. These categories are : 1. Monosaccharides, 2. Oligosaccharides, 3. Polysaccharides, 4. Glycosides.

1. **Monosaccharides or Simple Sugars :** Monosaccharides are crystalline, colourless compounds. These molecules are either polyhydroxy aldehydes or polyhydroxy ketones which cannot be hydrolyzed to simpler compounds. These molecules are readily soluble in water and insoluble in nonpolar solvents such as diethyl ether and benzene. These molecules have sweet taste. Monosaccharides are further subdivided based on :
   - the number of carbon atoms present in their structure,
   - the type of carbonyl group, and
   - chirality.

   Most of the natural monosaccharides exhibit a chain length of 3-7 carbons, for that reason the names have been given for these classes :

   (i) **Trioses ($C_3H_6O_3$) :** These carbohydrates are the first and smallest monosaccharide having three carbon chains. Triose with aldehyde group is called as aldotriose (glyceraldehyde) and if it contains ketone group, it is called as ketotriose (dihydroxyacetone).

   (ii) **Tetroses ($C_4H_8O_4$) :** Four carbon chain monosaccharide molecules are called as **aldotetroses** (Erythrose, Threose) or **ketotetroses.** (Erythrulose).

   (iii) **Pentoses ($C_5H_{10}O_5$) :** Monosaccharide molecules with five carbon chains are known as **aldopentoses** (Ribose, Xylose, Arabinose, D-Lyxose) or **ketopentoses** (Ribulose, Xylulose).

(iv) **Hexoses ($C_6H_{12}O_6$) :** Six carbon chain monosaccharide molecules are present as **aldohexoses** (Glucose, Allose, Altrose, Mannose, Gulose, Idose, Galactose, Talose) or **ketohexoses** (Fructose, Sorbose, Tagatose, Psicose).

(v) **Heptoses ($C_7H_{14}O_7$) :** Seven chain monosaccharide molecules are present as aldoheptoses and ketoheptoses *e.g.,* Sedoheptulose.

2. **Oligosaccharides :** Oligosaccharides are short polymers, made up of 3-10 monosaccharide units joined by glycosidic bonds. One of its well known examples is raffinose, also called **melitose.** Raffinose is a trisaccharide largely found in legumes and cruciferous vegetables, including beans, peas, cabbage, brussels sprouts, and broccoli. It consists of galactose connected to sucrose via α (1-6) glycosidic linkage.

   Oligosaccharides can be further classified on the basis of their hydrolysis-product as under :

   (i) **Disaccharides :** When oligosaccharides yield two-molecules of monosaccharides as product of hydrolysis, the latter are called disaccharides. The general molecular formula of a disaccharide is $C_{12}H_{22}O_{11}$. Examples are : Lactose, Malose, Sucrose, Melibiose, Cellobiose, Gentiobiose, Trehalose etc.

   (ii) **Trisaccharides :** When an oligosaccharide yields 4-molecules of monosaccharides on hydrolysis, the latter are called trisaccharides. Examples are Raffinose, Centionose and Melezitose.

   (iii) **Tetrasaccharides :** When an oligosaccharide yields 4-molecules of monosaccharides on hydrolysis, the letter are referred to as tetra-saccharides. Example is stachyose, the most common tetrasaccharide.

   Oligosaccharide's classification further extends like above mentioned to represent pentasaccharides (5-molecules of monosaccharides), hexasaccharides (6-molecules of monosaccharides), heptasaccharides (7-molecules of monosaccharides) and so on.

3. **Polysaccharides :** Polysaccharides are polymers of the simple sugars and their derivatives containing more than 20 or so monosaccharide units, and some have hundreds or thousands of units. Their molecular weights range up to 1 million or more. Polysaccharides can be long straight chains or branched. They have been further divided into two classes :

   (i) **Homopolysaccharides :** These polysaccharides are made up of only one type of monosaccharides. On hydrolysis these produces only one type of monosaccharides *e.g.,* Starch, cellulose, Glycogen and Agar.

   (ii) **Heteropolysaccharides :** These polysaccharides are made up of more than two type of monosaccharides. On hydrolysis these produces more than type of monosaccharides *e.g.,* Chitin, Mucin, Pectin, Chondroitin sulphate.

4. **Glycosides :** Glycosides are compounds that yield one or more sugars upon hydrolysis. The term glycoside is a generic term for natural product that is chemically bond to a sugar. Thus the glycoside composes of two parts : the sugar and the aglycone. The aglycon may be a terpene, a flavonoid, a coumarine or any other natural product.

Glycoside showed extra-chemical diversity. Among the sugars found in natural glycosides, D-glucose is the most abundant one, L-rhammose and L-fructose also occur quite frequently. Of the pentoses : L-arabinose is more common than D-xylose. The sugar part can be disaccharide.

Biological Significance of Carbohydrates

1. **Structural Components of Cells :** In plant cells carbohydrates (cellulose) constitute the structural frame work. In animal cells, these form protective fuzzy coat on the surface of cells.
2. **Storage :** These are stored in body for immediate source of energy. In plants, the stored carbohydrate is starch and in animals glycogen.
3. **Role in Metabolism :** Carbohydrates play a key role in the metabolism of amino acids and fatty acids.
4. **Major Source of Energy :** Carbohydrates are main source of energy for living cell. These are used as respiratory fuels. In presence of oxygen these decompose into CO_2 and water and liberate energy to be utilized by body cells.
5. **Special Functions :** (i) Some glycoproteins act as hormones, (ii) Glycoproteins on cell surface help in cell recognition and help in immune system of the body. (iii) **Heparin** (a mucopolysaccharide) acts as anticoagulant.

Q.2. What do you mean by lipids? Also classify the lipids and mention their biological importance.

Ans. **Lipids**

The lipids form a group of naturally occurring fat-like substances which are all insoluble in water but soluble in the fat solvents such as ether, chloroform and benzene.

The lipids can be divided into simple lipids, including the fats and waxes and the compound lipids, including the phospholipids and glycolipids.

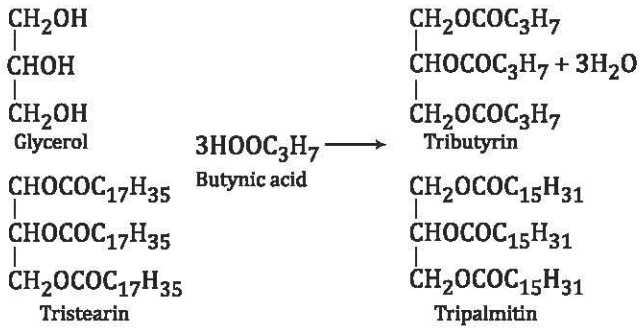
I. Simple Lipids

These are of two types :

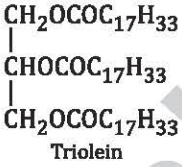
1. **Fats and oils :** They are esters of glycerol and fatty acids ; oils are fats which are liquid at room temperature. The very large number of different fats which are found in nature may be accounted for by the fact that individual species of plants and animals have characteristically different fats and the fat of one tissue may be quite different from that of another tissue in the same individual.

   Finally, because there are a large number of different fatty acids, and since glycerol may be esterified with different fatty acids, the number of different fats increases appreciably. Glycerol is a trihydric alcohol. It can react with three molecules of an acid to form triglyceride. For instance, it can react with butyric acid, C_3H_7COOH to yield glycerol tributyrate or tributyrin, one of the simplest of the fats. Glycerol may also react with one molecule of a fatty acid to form a monoglyceride and with two molecules to form a diglyceride.

   With stearic acid ($C_{17}H_{35}COOH$) glycerol forms glyceryl tristearate or tristearin, and with palmitic acid ($C_{15}H_{31}COOH$) it yields glyceryl tripalmitate or tripalmitin.



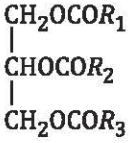
Both tristearin and tripalmitin occur in large quantities in beef and mutton fat. With the unsaturated acid, oleic acid ($C_{17}H_{33}COOH$), glycerol yields glyceryl trioleate or triolein which is the main constituent of olive oil.



Triolein

It can be seen, therefore, that the general formula for a fat is

where *R* varies according to the fatty acid present. It is possible for three different fatty acids to combine with one molecule of glycerol in triglyceride, so that the general formula of a fat is more correctly written thus :



where R_1, R_2 and R_3 may be derived from different fatty acids.

The saponification value of a fat is the number of milligrams of potassium hydroxide required to saponify one gram of fat. Fats may also be hydrolysed by superheated steam, and by enzymes called lipases such as that found in the external secretion of pancreas.

2. **Waxes :** The waxes are esters of fatty acids not with glycerol but with complex monohydric alcohol. Beeswax, for example, is an ester of palmitic acid with myricyl alcohol ($C_{30}H_{61}OH$) and spermaceti from the sperm whale is an ester of palmitic acid with cetyl alcohol ($C_{16}H_{33}OH$). Many animal waxes are esters of the steroid alcohol, cholesterol.

II. Compound or Conjugated Lipids

These are of two types :

1. **Phospholipids :** The phospholipids or phosphatides are widely distributed in animal tissues and play an important part in the structure of the cell, particularly the cell

membrane, and the process of fat metabolism. They are specially abundant in brain and nerve tissues. They can combine with protein to give biologically important compounds known as lipoproteins and a considerable proportion of protein of blood plasma is loosely combined with phospholipids. They differ from fats in having phosphoric acid and an orgainc nitrogenous base.

The following are the important phosphatides found in animal tissues :

(a) Phosphatidylcholine (Lecithin),

(b) Phosphatidylethanolamine (Cephalin),

(c) Phosphatidylserine,

(d) Phosphatidylinositol,

(e) Sphingomyelins,

(f) Plasmalogens.

2. **Glycolipids :** The chief glycolipids are the cerebrosides which occur in particularly large amounts in brain tissue and in the myelin sheath of nerves. They include the substances phrenosin and kerosin, and are peculiar in containing galactose in their structure. On hydrolysis, they yield fatty acids, sphingosine and galactose.

Biological Importance of Lipids

1. **Rich source of energy :** Fats provide food of high calorific value (9.3 kcal/g).
2. **Fat Transport :** Phospholipids play an important role in the absorption and transportation of fatty acids.
3. **Hormone Synthesis :** Adrenocorticoids, sex hormones, vitamin D and cholic acid are synthesized from cholesterol.
4. **As Food Reserve :** Fats are stored in the body as reserve food, because these could be readily stored in the body on account of insoluble characteristic. Triglycerides stored in the adipocytes (fat cells) of adipose tissue are the principal fat reserve.
5. **As Heat Insulators :** Fat deposite in the subcutaneous tissue act as insulators conserving body heat.
6. **Solvent :** Lipids act as a solvent for fat soluble vitamins like Vit. A, D, and E.
7. **Structural Constituents :** Phospholipids, glycolipids and sterols are structural components of all the membrane systems of the cell (*i.e.,* cell membrane, nuclear membrane, membranes of ER).
8. **As Shock Absorber :** The fat deposited around the visceral organs and underneath the skin acts as cushion and absorbs mechanical shock.
9. **As Electric Insulators :** Myelin sheath around modullated nerve fibres form an electric insulation.

Q.3. Describe the structure and classification α-amino acids.

Ans.

Amino Acids

Amino acids are a group of organic compounds containing two functional groups-amino and carboxyl. The amino group (—NH_2) is basic while the carboxyl group (—COOH) is acidic in nature.

General Structure of Amino Acids

The amino acids are termed as α-amino acids, if both the carboxyl and amino groups are attached to the same carbon atom, as depicted below

The α-carbon atom binds to a side chain represented by *R* which is different for each of the 20 amino acids found in proteins. The amino acids mostly exist in the ionized form in the biological system (shown above).

Optical isomers of amino acids : If a carbon atom is attached to four different groups, it is asymmetric and therefore exhibits optical isomerism. The amino acids (except glycine) possess four distinct groups (*R*, H, COO^-, NH_3^+) held by α-carbon. Thus all the amino acids (except glycine where *R* = H) have optical isomers.

The structure of *L*- and *D*-amino acids is written based on the configuration of *L*- and *D*-glyceraldehyde as shown in Fig. The proteins are composed of *L*-α-amino acids.

Classification of Amino Acids

There are different ways of classifying the amino acids based on the structure and chemical nature, nutritional requirement, metabolic fate etc.

A. Amino acid classification based on the Structure

A comprehensive classification of amino acids is based on their structure and chemical nature. Each amino acid is assigned a 3 letter or 1 letter symbol. These symbols are commonly used to represent the amino acids. The 20 amino acids found in proteins are divided into seven distinct groups.

The salient features of different groups are described here :

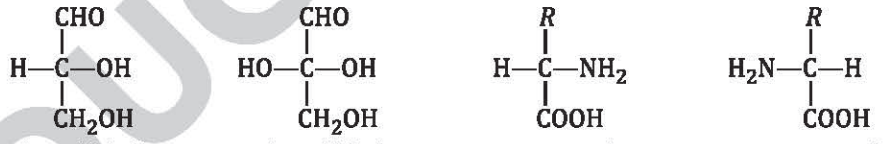


Fig. : *D*- and *L*-forms of amino acid based on the structure of glyceraldehyde.

1. **Amino acids with aliphatic side chains :** These are monoamino monocarboxylic acids. This group consists of the most simple amino acids-glycine, alanine, valine, leucine and isoleucine. The last three amino acids (Leu, lle, Val) contain branched aliphatic side chains, hence they are referred to as branched chain amino acids.
2. **Hydroxyl group containing amino acids :** Serine, threonine and tyrosine are hydroxyl group containing amino acids. Tyrosine-being aromatic in nature-is usually considered under aromatic amino acids.
3. **Sulphur containing amino acids :** Cysteine with sulfhydryl group and methionine with thioether group are the two amino acids incorporated during the course of protein synthesis. Cystine, another important sulfur containing amino acid, is formed

by condensation of two molecules of cysteine. Cystine plays a unique role in protein structure.

4. **Acidic amino acids and their amides :** Aspartic acid and glutamic acids are dicarboxylic monoamino acids while asparagine and glutamine are their respective amide derivatives. All these four amino acids possess distinct codons for their incorporation into proteins.
5. **Basic amino acids :** The three amino acids lysine, arginine (with guanidino group) and histidine (with imidazole ring) are dibasic monocarboxylic acids. They are highly basic in character.
6. **Aromatic amino acids :** Phenylalanine, tyrosine and tryptophan (with indole ring) are aromatic amino acids. Besides these, histidine may also be considered under this category.
7. **Imino acids :** Proline containing pyrrolidine ring is a unique amino acid. It has an imino group (=NH), instead of an amino group ($-NH_2$) found in other amino acids. Therefore, proline is an imino acid. Hydroxy proline (Hyp) is a proline derivative found in proteins.

B. Classification of amino acids based on Polarity

Amino acids are classified into 4 groups based on their polarity. The polarity in turn reflects the functional role of amino acids in protein structure.

1. **Non-polar amino acids :** These amino acids are also referred to as hydrophobic (water hating). They have no charge on the '*R*' group. The amino acids included in this group are—alanine, leucine, isoleucine, valine, methionine, phenylalanine, tryptophan and proline.
2. **Polar amino acids with no charge on '*R*' group :** These amino acids, as such, carry no charge on the '*R*' group. They however possess groups such as hydroxyl, sulfhydryl and amide and participate in hydrogen bonding of protein structure. The simple amino acid glycine (where *R*=H) is also considered in this category. The amino acids in this group are-glycine, serine, threonine, cysteine, glutamine, asparagine and tyrosine.
3. **Polar amino acids with positive '*R*' group :** The three amino acids lysine, arginine and histidine are included in this group.
4. **Polar amino acids with negative '*R*' group :** The dicarboxylic monoamino acids—aspartic acid and glutamic acid are considered in this group.

C. Nutritional classification of Amino Acids

The twenty amino acids are required for the synthesis of variety of proteins, besides other biological functions. However, all these 20 amino acids need not be taken in the diet. Based on the nutritional requirements, amino acids are grouped into two classes : essential and non-essential.

1. **Essential or indispensable amino acids :** The amino acids which cannot be synthesized by the body and, therefore, need to be supplied through the diet are called essential amino acids. They are required for proper growth and maintenance of the individual. The ten amino acids listed below are essential for humans (and also rats) :

Arginine, Valine, Histidine, Isoleucine, Leucine, Lysine, Methionine, Phenylalanine, Threonine, Tryptophan.

[The code A.V. HILL, MP., T.T. (first letter of each amino acid) may be memorized to recall essential amino acids. Other useful codes are H. VITTAL, LMP and MATTVILPhLy.]

Of the ten listed above, two amino acids namely arginine and histidine can be partly synthesized by adult humans, hence these are considered as semi-essential amino acids (remember Ah, to recall). Thus, 8 amino acids are absolutely essential while 2 are semi-essential.

2. **Non-essential or dispensable amino acids :** The body can synthesize about 10 amino acids to meet the biological needs, hence they need not be consumed in the diet. These are—glycine, alanine, serine, cysteine, aspartate, asparagine, glutamate, glutamine, tyrosine and proline.

D. Amino acid classification based on their Metabolic Fate

The carbon skeleton of amino acids can serve as a precursor for the synthesis of glucose (glycogenic) or fat (ketogenic) or both. From metabolic view point, amino acids are divided into three groups :

1. **Glycogenic amino acids :** These amino acids can serve as precursors for the formation of glucose or glycogen. *e.g.,* alanine, aspartate, glycine, methionine etc.
2. **Ketogenic amino acids :** Fat can be synthe sized from these amino acids. Two amino acids leucine and lysine are exclusively ketogenic.
3. **Glycogenic and ketogenic amino acids :** The four amino acids isoleucine, phenyl-alanine, tryptophan tyrosine are precursors for synthesis of glucose as well as fat.

Q.4. What are proteins? Also write their classification.

Ans. **Proteins**

Term protein was given by Berzelius. Proteins are the most complex chemical compounds of high molecular weight. These are compounds of carbon, hydrogen, oxygen, nitrogen, sulphur and phosphorus. The characteristic element is nitrogen. These are most important and most abundant constituents in the body of all living organisms. On the basis of above, Berzelius (1838) suggest the name protein (Gr. proteios = first). Proteins constitute the structural frame work of all the cell components and are the most abundant solids in cell protoplasm.

In neucleus, these occur as uncleoproteins and are intimately associated with cells division and heredity. All the chemical reactions occuring in the body of living organisms are controlled by proteins which are known as enzymes. Certain hormones are also proteins. Proteins are stored as a reserve of amino acids in the seeds of many plants.

Classification of Proteins

Proteins have been variously classified on the basis of structure, solubility and coagutability. According to English School of Physiologists, proteins are separated into three categories :

I. Simple proteins,
II. Conjugated or Compound proteins,
III. Derived proteins.

I. Simple Proteins

Simple proteins on hydrolysis, yield only amino acids. These are of two types :

A. Simple Globular Proteins : These proteins are soluble in one or more solvents. These are of two types :

1. **Soluble in Distilled Water :**
   (i) **Albumins :** (a) These can be precipitated from water by dilute acids and alkalies; or with a neutral salt such as Na_2SO_4 ; or in slightly acidic salts such as $(NH_4)_2SO_4$.
   (b) In the presence of stronger acids or alkalies these are converted into soluble metaproteins.
   (c) On heating, albumins get coagulated.
   (d) Albumins are widely distributed on nature.

   e.g., Egg White or Oval albumin, blood serum albumin, soyabean, albumin, gliadin (wheat protein), legumelin (protein of pulses) and phasiolin (of kidney bean), Casein (milk). These are stored as food reserve.
2. **Pseudoglobulins :** These can be precipitated from water solution with an acid salt $(NH_4)_2SO_4$. These are rare in nature. *e.g.,* **Milk-whey**. These are coagulated an heating.
3. **Protamines :** These are insoluble in water but are soluble in dilute alkalies and 60-80% alcohol. These are found in plants only. *e.g.,* **Gliadin** (Wheat), **Zein** (maize), **hordein** (barley).
4. **Globulins :** These are insoluble in water but readily soluble in dilute neutral salt solution such as NaCl. These coagulate on heating and heatcoagulation is enhanced by the addition of dilute acids. *e.g.,* Egg globulin, vitelline of egg yolk, fibrinogen of blood plasma, myogen and myosinogen of the muscles are animal globulins. Vegetable globulins include—**legumin** (peas); **tuberin** (potatoes) and **edestin** (wheat).

B. Simple Fibrous Proteins : Due to the fibrelike molecular, structure, the fibrous proteins are insoluble in cold water and any other cold reagent. These are also known as scleroproteins. These are found exclusively in animals. *e.g.,*

1. **Keratins :** Found in outer layer of skin and hair, feathers, horns, hood and nails. It is indigestible.
2. **Collagen :** Collagen proteins are found in white fibrous connective tissue which constitute tendons, aponeurons, duramater and fascia. These form ground substance of bone and cartilage. These are digested very slowly.
3. **Elastin :** It is found in yellow elastic tissue like ligaments and blood vessels. It is also present in the ground substance of elastic cartilage. It is insoluble and hard to digest.
4. **Fibroin :** This proteins is present in silk.

II. Conjugated Proteins

Conjugated proteins are composed of a simple protein united with some non-protein substance. This non-protein group is known as "prosthetic group". For example, in haemoglobin, protein globin is combined with an iron containing porphyrin compound heme.

On the basis of nature of prosthetic group the conjugated proteins have been divided into following classes :

1. **Chromoproteins :** The simple protein is combined with a pigment. *e.g.,* Haemoglobin, Cytochrome, Flavoproteins.
2. **Glycoproteins :** In this the simple protein is combined with Carbohydrates (74%) *e.g.,* Mucin of saliva, heparin of bile juice, immunoglobulins of plasma. Mucopolysaccharides of cartilage and tendon.
3. **Nucleoproteins :** In these, protein molecules are combined with nucleic acids. These proteins are protamines or histones. *e.g.,* Chromatin material of the nuclei of cells.
4. **Lipoproteins :** Lipoproteins are formed by the combination of simple proteins with lipids. These are located in the brain, plasma, egg and milk.
5. **Phosphoproteins :** In phosphoproteins, proteins are combined with phosphoric acid or ortho or pyrophosphate. These are soluble in dilute alkalies and are precipitated by the addition of acids. *e.g.,* Ovovitelline of egg and Caseinogen and Casein of milk.
6. **Mucoproteins :** These are simpler glycoproteins but in them carbohydrate, hexosamine is more than 4% *e.g.,* Haptoglobins of blood serum and Ovomucoid of egg white.
7. **Flavoproteins :** These are enzymes. Their, protein moiety (apoenzyme) is permanently attached to flavin compound (FMN or FAD). Flavin represent the prosthetic group.

   Flavoproteins are enzymes of Kreb's cycle and participate in the electron transport system (ETS) of respiratory chain.
8. **Metalloproteins :** These are proteins bound to some metallic ion like non copper or zinc.

III. Derived Proteins

The derived proteins are actually derived from some previously existing protein either by its hydrolysis or by coagulation. These are :

1. **Metaproteins :** These are derived by the hydrolysis of complex proteins; *e.g.,* by action of digestive enzymes, acids or alkalies. These may be acid metaproteins, alkali metaproteins, proteoses or albuminoses, peptones and peptids.
2. **Conjugated Proteins :** The coagulated or denatured proteins are formed when ordinary proteins are heated.

❑❑❑

UNIT-II

Enzyme Action and Regulation

SECTION-A VERY SHORT ANSWER TYPE QUESTIONS

Q.1. What are enzymes?

Ans. Enzymes are defined as 'simple or compound proteins acting as specific catalyst.' They may also be defined as organic substances capable of catalying chemical reaction in the living systems.

Q.2. Who prepared the first pure enzyme?

Ans. **J.B. sumner** was the first to crystallize an enzyme, an achievement that revolved the protein nature of enzymes.

Q.3. What is enzyme action called?

Ans. The part of the enzyme where the substrate binds is called the active site (since that's where the catalytic 'action' happens). A substrate enters the active site of the enzyme. This forms the enzyme-substrate complex.

Q.4. What is activation energy?

Ans. The amount of energy which is required for crossing of energy-barrier of a molecule is known as activation energy.

Q.5. What is an enzyme made of?

Ans. Enzymes are proteins comprised of amino acids linked together is one or more polypeptide chains. This sequence of amino acids in a polypeptide chain is called the primary structure. This, in turn, determines the three dimensional structure of the enzyme, including the shape of active site.

Q.6. How enzyme action is affected by an increase in temperature?

Ans. As with many chemical reactions, the rate of an enzyme catalysed reaction increases as the temperature increases. However, at high temperature the rate decreases again because the enzyme becomes denatured and can no longer function. As the temperature increases so does the rate of enzyme activity.

Q.7. What is K_m value?

Ans. K_m value is equal to the substrate concentration at which half of the enzyme active sites are saturated with the substrate. It tells about the affinity of enzymes for their substrate. Km is the concentration of substrate at which half of the V_{max} is attained.

Q.8. Who proposed the hypothesis for enzyme action?

Ans. Lock and key hypothesis was proposed by **Emil Fisher** in 1894. This hypothesis helps us to understand the mechanism of action of enzymes.

Q.9. Why do enzymes have a maximum rate of reaction?

Ans. An enzyme exhibits maximum activity over the narrow pH range in which a molecule exists in its properly charged form. The median value of this pH range is called the optimum pH of the enzyme.

Q.10. How are allosteric enzyme regulated?

Ans. Allosteric regulation of enzymes is crucial for the control of cellular metabolism. Allosteric regulation occurs when an activator or inhibitor molecule binds at a specific regulatory site on the enzyme and induces conformational or electrostatic changes that either enhance or reduce enzyme activity.

Q.11. What is prosthetic group?

Ans. The term prosthetic group is used when the non-protein moiety tightly (covalently) binds with the apoenzyme. The coenzyme can be separated by dialysis from the enzyme while the prosthetic group cannot be.

$$\underset{\text{(Active enzyme)}}{\text{Holoenzyme}} \longrightarrow \underset{\text{(Protein part)}}{\text{Apoenzyme}} + \underset{\text{(Non-protein part)}}{\text{Coenzyme}}$$

Q.12. What is active site?

Ans. Enzymes are big in size compared to substrates which are relatively smaller. Evidently, a small portion of the huge enzyme molecule is directly involved in the substrate binding and catalysis.

The active site (or active centre) of an enzyme is defined as the small region at which the substrate(s) binds and participates in the catalysis.

SECTION-B SHORT ANSWER TYPE QUESTIONS

Q.1. What are isoenzymes?

Ans. Isoenzymes : The *multiple forms of an enzyme* catalysing the same reaction are *isoenzymes* or *isozymes*. They, however, differ in their physical and chemical properties which include the structure, electrophoretic and immunological properties, K_m and V_{max} values, pH optimum, relative susceptibility to inhibitors and degree of denaturation.

Explanation for the existence of isoenzymes : Many possible reasons are offered to explain the presence of isoenzymes in the living systems :

1. Isoenzymes synthesized from different genes *e.g.,* malate dehydrogenase of cytosol is different from that found in mitochondria.
2. Oligomeric enzymes consisting of more than one type of subunits *e.g.,* lactate dehydrogenase and creatine phosphokinase.
3. An enzyme may be active as monomer or oligomer *e.g.,* glutamate dehydrogenase.
4. In glycoprotein enzymes, differences in carbohydrate content may be responsible for isoenzymes *e.g.,* alkaline phosphatase.

Q.2. Differentiate between cofactor and coenzyme.

Ans. Cofactors : Coenzymes are thermostable, dialyzable (dissolvable) organic compounds accounting for about only 1% of the entire enzyme molecule (holoenzyme). Some of the common example of coenzymes are NAD, NADP, FAD, FMN, CoA etc. Sometimes, the prosthetic group are metallic (Cl^-, K^+, Mg^{++}, Ca^{++}, Fe^{++}, Cu^{++} etc.) in nature instead of being

organic. This metallic prosthetic group is referred to as 'cofactor' or 'activator' to make a distinction from organic prosthetic group which is called coenzyme.

Coenzymes : Certain enzymes, particularly the complex-protein enzymes, are made up of two parts : (i) the protein part called 'apoenzyme' and (ii) the non-protein part called 'prosthetic' group (either coenzyme or cofactor). The complete enzyme is called 'holoenzyme'.

complex-protein enzyme $\rightleftharpoons$ protein part + prosthetic group

or holoenzyme $\rightleftharpoons$ apoenzyme + coenzyme or cofactor

Q.3. Write about the enzyme specificity.

Ans. Enzyme Specificity

Enzymes are highly specific in their action when compared with the chemical catalysts. The occurrence of thousands of enzymes in the biological system might be due to the specific nature of enzymes. Three types of enzyme specificity are well-recognised.

1. Stereospecificity,
2. Reaction specificity,
3. Substrate specificity.

Specificity is a characteristic property of the active site.

1. **Stereospecificity or optical specificity :** Stereoisomers are the compounds which have the same molecular formula, but differ in their structural configuration. The enzymes act only on one isomer and, therefore, exhibit stereoisomerism.

   e.g., L-amino acid oxidase and D-amino acid oxidase act on L- and D-amino acids respectively.

   Hexokinase acts on D-hexoses;

   Glucokinase on D-glucose;

   Amylase acts on α-glycosidic linkages;

   Cellulase cleaves β-glycosidic bonds.

   Stereospecificity is explained by considering three distinct regions of substrate molecule specifically binding with three complementary regions on the surface of the enzyme (Fig.). The class of enzymes belonging to isomerases do not exhibit stereospecificity, since they are specialized in the interconversion of isomers.

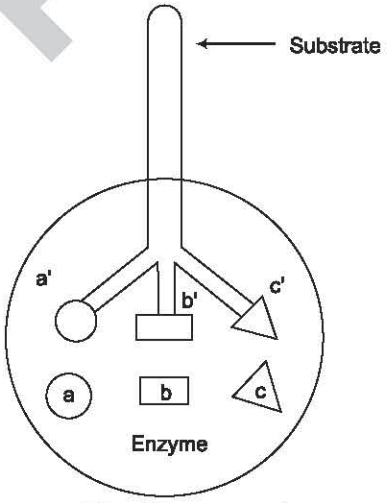
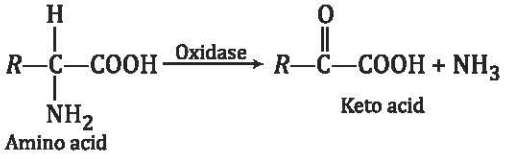
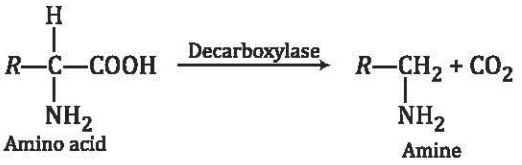


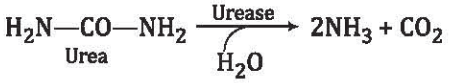
Fig. : Diagrammatic representation of stereospecificity (a', b', c')—three point attachment of substrate to the enzyme (a, b, c)

2. **Reaction specificity :** The same substrate can undergo different types of reactions, each catalysed by a separate enzyme and this is referred to as reaction specificity. An amino acid can undergo transamination, oxidative deamination, decarboxylation, racemization etc. The enzymes however, are different for each of these reactions.
3. **Substrate specificity :** The substrate specificity varies from enzyme to enzyme. It may be either absolute, relative or broad.





(i) **Absolute substrate specificity :** Certain enzymes act only on one substrate *e.g.,* glucokinase acts on glucose to give glucose 6-phosphate, urease cleaves urea to ammonia and carbon dioxide.



(ii) **Relative substrate specificity :** Some enzymes act on structurally related substances. This, in turn, may be dependent on the specific group or a bond present. The action of trypsin and chymotrypsin is a good example for group specificity (Refer Fig.). Trypsin hydrolyses peptide linkage involving arginine or lysine. Chymotrypsin cleaves peptide bonds attached to aromatic amino acids (phenylalanine, tyrosine and tryptophan). Examples of bond specificity glycosidases acting on glycosidic bonds of carbohydrates, lipases cleaving ester bonds of lipids etc.

(iii) **Broad specificity :** Some enzymes act on closely related substrates which is commonly known as broad substrate specificity, *e.g.,* hexokinase acts on glucose, fructose, mannose and glucosamine and not on galactose. It is possible that some structural similarity among the first four compounds makes them a common substrate for the enzyme hexokinase.

Q.4. What are the enzymes? Describe factors affecting enzyme activity.

Ans.

Enzymes

Enzymes are 'biological catalyst's produced by the living cells and are able to accelerate the rate of chemical reactions occurring in living cells. Enzymes are made of protein.

Factors Affecting Enzyme Activity

Some important factors which affects the activity of enzyme are given below :

1. **Temperature :** The enzyme activity is optimum at normal body temperature. At 0°C the activity is minimum. An increase in temperature upto a certain limit increases the activity of enzyme, maximum being at about 45°C after which the activity of enzyme is retarded. Beyond 60-70°C the enzyme become denatured and the activity is permanently stopped.

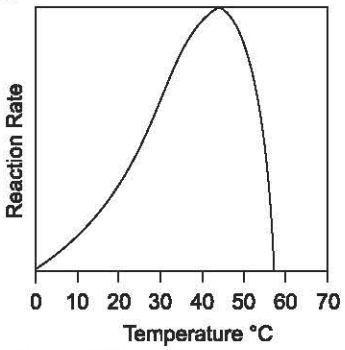


Fig. 1 : Effect of temperature on enzymic reaction

2. **pH :** Hydrogen ion concentration (pH) affects the enzyme upto a certain limit. Some enzymes *e.g.,* Trypsin are active in alkaline medium more than 7 (pH), Diastase in neutral pH (pH = 7) while pepsin shows their optimum activity in acidic medium (pH = less than 7).
3. **Water :** Water is essential for enzyme activity. In absence of water the activity of enzyme is suppressed so much that in dry seeds the enzymes are almost inactive.

Water provides medium for enzyme reaction to take place and in many cases it is one of the reactants.

4. **Substrate Concentration :** An increase in the activity of enzyme is reported by the increase in concentration of substrate till all the active site of enzyme molecules are saturated with substrate. After that the reaction of enzyme becomes constant (Fig. 2).

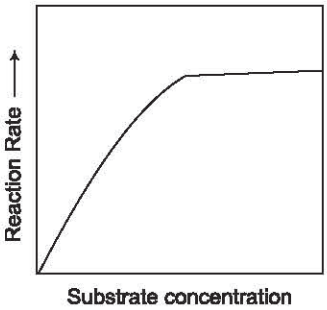


Fig. 2 : Effect of substrate concentration on enzyme

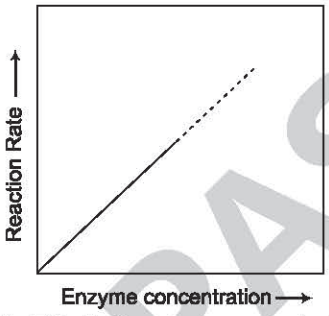


Fig. 3 : Effect of enzyme concentration on the rate of reaction

5. **Enzyme Concentration :** Reaction rate of enzyme increases with the increase in enzyme concentration (Fig. 3).
6. **Inhibitors :** Inhibitor inhibits the enzyme activity completely or partially depending upon the nature of enzyme.

Q.5. Write a short note on allosteric enzymes and their action.

Ans.

Allosteric Enzymes

This type of enzymes have an additional binding site for effector molecules other than the active site. The binding brings about conformational changes, thereby changing its catalytic properties. The effector molecule can be an inhibitor or activator.

All the biological systems are well regulated. There are various regulatory measures in our body, that control all the processes and respond to the various inside and outside environmental changes. Whether it is gene expression, cell division, hormone secretion, metabolism or enzyme activity, everything is regulated to ensure proper development and survival. Allostery is the process of enzyme regulation, where binding at one site influences the binding at subsequent sites.

Allosteric Regulation Mechanism

There are two types of allosteric regulation on the basis of substrate and effector molecules :

1. **Homotropic Regulation :** Here, the substrate molecule acts as an effector also. It is mostly enzyme activation and also called cooperativity, *e.g.,* binding of oxygen to haemoglobin.
2. **Heterotropic Regulation :** When the substrate and effector are different. The effector may activate or inhibit the enzyme, *e.g.,* binding of CO_2 to haemoglobin.

On the basis of action performed by the regulator, allosteric regulation is of two types : inhibition and activation.

1. **Allosteric Inhibition :** When an inhibitor binds to the enzyme, all the active sites of the protein complex of the enzyme undergo conformational changes so that the activity of the enzyme decreases.
2. **Allosteric Activation :** When an activator binds, it increases the function of active sites and results in increased binding of substrate molecules.

There are two models proposed for the mechanism of regulation of allosteric enzymes :

1. **Simple Sequential Model :** It was given by **Koshland.** In this model, the binding of substrate induces a change in the conformation of the enzyme from T (tensed) to R (relaxed). The substrate binds according to the induced fit theory. A conformational change in one unit stimulates similar changes in other subunits. This explains the cooperative binding. The same way inhibitors and activators bind, the T form is favoured, when the inhibitor binds and R form is favoured, when the activator binds. The binding at one subunit affects the conformation of other subunits.

   The sequential model explains the negative cooperativity in enzymes, *e.g.,* tyrosyl *t*RNA synthetase, where the binding of substrate inhibits the binding of another substrate.

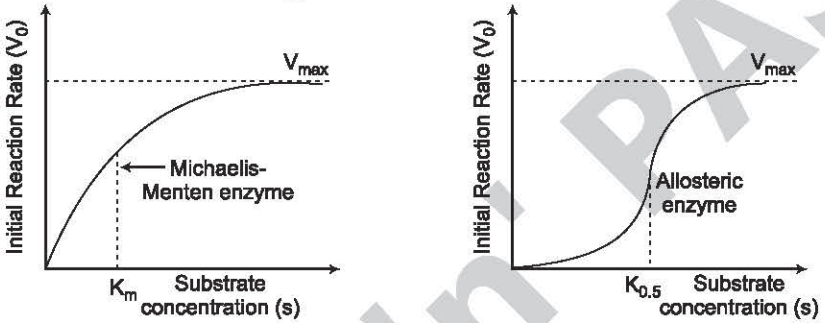


Fig.

2. **Concerted or Symmetry Model :** According to this model, there is a simultaneous change in all the subunits of an enzyme. All the subunits are either present in R form (active form) or T form (inactive form), having less affinity to a substrate. An inhibitor shifts the equilibrium of T $\rightleftharpoons$ R, towards T, and activator shifts the equilibrium towards R form and favours the binding. It explains the cooperative regulation of activators as well as inhibitors.

Q.6. Write a short note on enzyme kinetics and K_m value.

Ans.

Enzyme Kinetics and K_m Value

The enzyme (E) and substrate (S) combine with each other to form an unstable enzyme-substrate complex (ES) for the formation of product (P).

$$E + S \underset{k_2}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_3} E + P$$

Here k_1, k_2 and k_3 represent the velocity constants for the respective reactions, as indicated by arrows.

K_m, the Michaelis-Menten constant (or Brig's and Haldane's constant), is given by the formula

$$K_m = \frac{k_2 + k_3}{k_1}$$

The following equation is obtained after suitable algebraic manipulation.

$$v = \frac{V_{max}[S]}{K_m + [S]} \quad \text{...(1)}$$

where v = Measured velocity, v_{max} = Maximum velocity, S = Substrate concentration

K_m = Michaelis-Menten constant.

Let us assume that the measured velocity (V) is equal to $\frac{1}{2}V_{max}$. Then the equation (1) may be substituted as follows :

$$\frac{1}{2}V_{max} = \frac{V_{max}[S]}{K_m + [S]}$$

$$K_m + [S] = \frac{2V_{max}[S]}{V_{max}}$$

$$K_m + [S] = 2[S]$$

$$K_m = [S]$$

K stands for a constant and m stands for Michaelis (in K_m).

K_m or the **Michaelis-Menten constant** is defined as the **substrate concentration** (expressed in moles/litre) to **produce half-maximum velocity** in an enzyme catalysed reaction. It indicates that half of the enzyme molecules (*i.e.*, 50%) are bound with the substrate molecules when the substrate concentration equals the K_m value.

K_m value is a constant and a characteristic feature of a given enzyme. It is a representative for measuring the strength of ES complex. A ***low K_m value indicates a strong affinity between enzyme and substrate***, whereas a high K_m value reflects a weak affinity between then. For majority of enzymes, the K_m values are in the range of 10^{-5} to 10^{-2} moles.

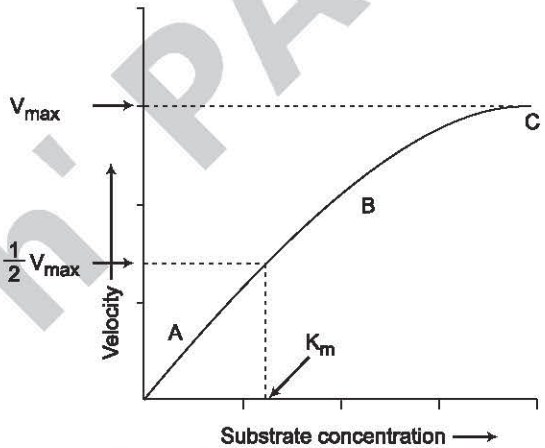


Fig. 1 : Effect of substrate concentration on enzyme velocity (A-linear; B-curve; C-almost unchanged)

Lineweaver-Burk double reciprocal plot : For the determination of K_m value, the substrate saturation curve is not very accurate since V_{max} is approached asymptotically. By taking the reciprocals of the equation (1), a straight line graphic representation is obtained.

$$\frac{1}{v} = \frac{K_m + [S]}{V_{max}[S]}$$

$$\frac{1}{v} = \frac{K_m}{V_{max}} \times \frac{1}{[S]} + \frac{[S]}{V_{max}[S]}$$

$$\frac{1}{v} = \frac{K_m}{V_{max}} \times \frac{1}{[S]} + \frac{1}{V_{max}}$$

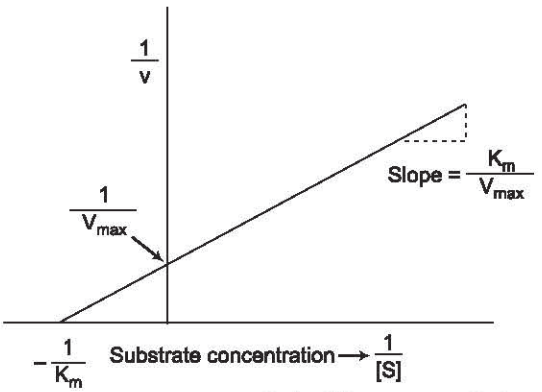


Fig. 2 : Lineweaver-Burk double reciprocal plot

The above equation is similar to $y = ax + b$. Therefore, a plot of the reciprocal of the velocity $\left(\frac{1}{v}\right)$ vs. the reciprocal of the substrate concentration $\left(\frac{1}{[S]}\right)$ gives a straight line. Here the slope is K_m / V_{max} and whose y intercept is $1/V_{max}$.

The Lineweaver-Burk plot is shown in Fig. It is much easier to calculate the K_m from the intercept on x-axis which is $-(1/K_m)$. Further, the double reciprocal plot is useful in understanding the effect of various inhibitions.

SECTION-C LONG ANSWER TYPE QUESTIONS

Q.1. Describe the nomenclature and classification of enzyme.

Ans. Nomenclature and Classification of Enzyme

In the early days, the enzymes were given names by their discoverers in an arbitrary manner. For example, the names pepsin, trypsin and chymotrypsin convey no information about the function of the enzyme or the nature of the substrate on which they act. Sometimes, the suffix-ase was added to the substrate for naming the enzymes *e.g.,* lipase acts on lipids; nuclease on nucleic acids; lactase on lactose. These are known as trivial names of the enzymes which, however, fail to give complete information of enzyme reaction (type of reaction, cofactor requirement etc.)

Enzymes are sometimes considered under two broad categories : (i) **Intracellular enzymes :** They are functional within cells where they are synthesized. (ii) **Extracellular enzymes :** These enzymes are active outside the cell; all the digestive enzymes belong to this group.

The International Union of Biochemistry (IUB) appointed an Enzyme Commission in 1961. This committee made a thorough study of the existing enzymes and devised some basic principles for the classification and nomenclature of enzymes. Since 1964, the ***IUB system of enzyme classification*** has been in force. Enzymes are divided into ***six major classes*** in that order). Each class on its own represents the general type of reaction brought about by the enzymes of that class.

1. **Oxidoreductases :** Enzymes involved in oxidation-reduction reactions.

   Oxidoreductases : Alcohol dehydrogenase (alcohol : NAD^+ oxidoreductase cytochrome oxidase, L- and D-amino acid oxidases.

   $$\text{Oxidation} \longrightarrow \text{Reduction}$$

   $$AH_2 + B \longrightarrow A + BH_2$$

2. **Transferases :** Enzymes that catalyse the transfer of functional groups.

   Transferases : Hexokinase (ATP : D-hexose 6-phosphotransferase, transaminases, transmethylases, phosphorylase.

   Group transfer $\quad A - X + B \longrightarrow A + B - X$

3. **Hydrolases :** Enzymes that bring about hydrolysis of various compounds.

   Hydrolases : Lipase (triacylglycerol acyl hydrolase, choline esterase, acid and alkaline phosphatases, pepsin, urease.

   Hydrolysis $\quad A - B + H_2O \longrightarrow AH + BOH$

4. **Lyases :** Enzymes specialised in the addition or removal of water, ammonia, CO_2 etc.

   Lyases : Aldolase (ketose 1-phosphate aldehyde lyase, fumarase, histidase.

   $$\text{Addition} \longrightarrow \text{Elimination}$$

   $$A - B + X - Y \longrightarrow AX - BY$$

5. **Isomerases :** Enzymes involved in all the isomerization reactions.

Isomerases : Triose phosphate isomerase (D-glyceraldehyde 3-phosphate ketoisomerase, retinol isomerase, phosphohexose isomerase.

Interconversion of isomers $A \longrightarrow A'$

6. **Ligases :** Enzymes catalysing the synthetic reactions (*Greek* : ligate—to bind) where two molecules are joined together and ATP is used.

   Ligases : Glutamine synthetase (L-glutamate ammonia ligase, acetyl CoA carboxylase, succinate thiokinase.

   Condensation (usually dependent on ATP).

$$A + B \xrightarrow[ATP \quad ADP + Pi]{} A - B$$

[The word ***OTHLIL*** (first letter in each class) may be memorised to remember the six classes of enzymes in the correct order).

Each class in turn is subdivided into many subclasses which are further divided. A four digit Enzyme Commission (E.C.) number is assigned to each enzyme representing the class (first digit), subclass (second digit), sub-sub class (third digit) and the individual enzyme (fourth digit). Each enzyme is given a specific name indicating the substrate, coenzyme (if any) and the type of the reaction catalysed by the enzyme. Although the IUB names for the enzymes are specific and unambiguous, they have not been accepted for general use as they are complex and cumbersome to remember. Therefore, the trivial names, along with the E.C. numbers as and when needed, are commonly used and widely accepted.

Q.2. What do you mean by enzyme inhibition? Also explain their types.

Ans.

Enzyme Inhibition

Enzyme inhibitor is defined as a substance which binds with the enzyme and brings about a decrease in catalytic activity of that enzyme. The inhibitor may be organic or inorganic in nature. There are three broad categories of enzyme inhibition.

A. Reversible Inhibition

The inhibitor binds non-covalently with enzyme and the enzyme inhibition can be reversed if the inhibitor is removed. The reversible inhibition is further sub-divided into :

1. **Competitive inhibition :** The inhibitor (I) which closely resembles the real substrate (S) is regarded as a ***substrate analogue***. The inhibitor competes with substrate and binds at the active site of the enzyme but does not undergo any catalysis. As long as the competitive inhibitor holds the active site, the enzyme is not available for the substrate to bind. During the reaction, ES and El complexes are formed as shown below :

$$\begin{array}{ccccc} E + S & \rightleftharpoons & ES & \longrightarrow & E + P \\ + & & & & \\ I & & & & \\ \Updownarrow & & & & \\ E.I. & & & & \end{array}$$

The relative concentration of the substrate and inhibitor and their respective affinity with the enzyme determines the degree of competitive inhibition. The inhibition could be overcome by a high substrate concentration. In competitive inhibition, the K_m ***value increases*** whereas V_{max} remains unchanged.

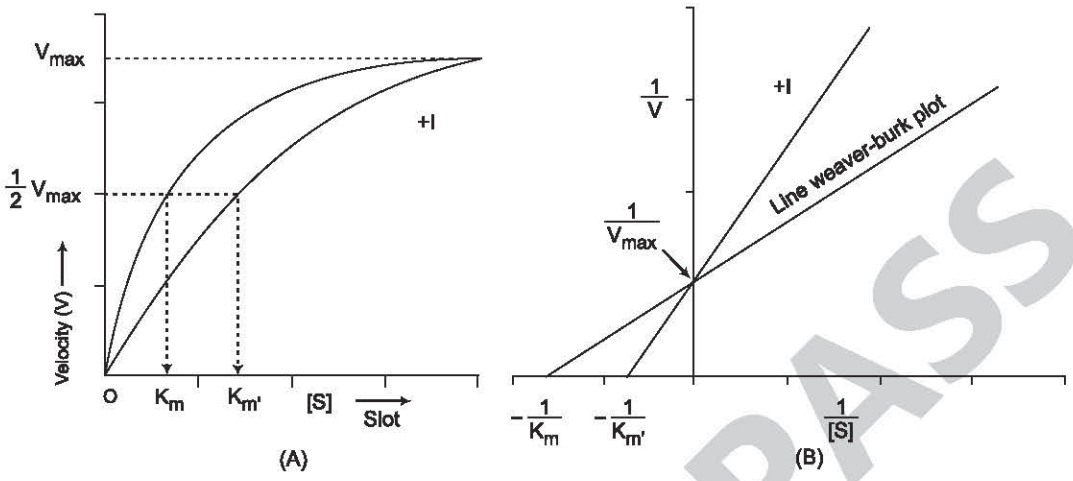
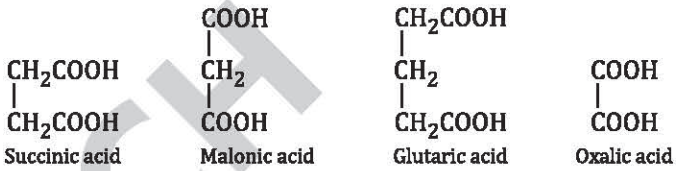


Fig. 1 : Effect of competitive inhibitor (i) on enzyme velocity : (A) Velocity (V) versus substrate (S) plot. (B) Lineweaver-Burk plot (Green shaded lines with inhibitor, competitive inhibitor increases K_m, unalters V_{max}).

The enzyme succinate dehydrogenase (SDH) is a classical example of competitive inhibition with succinic acid as its substrate. The compounds, namely, malonic acid, glutaric acid and oxalic acid, have structural similarity with succinic acid and compete with the substrate for binding at the active site of SDH.



Among the above compounds, malonic acid is the most potent competitive inhibitor of SDH. Some more examples of the enzymes with substrates and competitive inhibitors are given in Table.

Table : Selected examples of enzymes with their respective substrates and competitive inhibitors

Enzyme	Substrate	Inhibitor	Significance of inhibitor
Xanthine oxidase	Hypoxanthine	Allopurinol	Used in the control of gout to reduce excess production of uric acid from hypoxanthine.
Monoamine oxidase	Catecholamines (epinephrine, norepinephrine)	Ephidrene, amphetamine	Useful for elevating catecholamine levels.
Dihydrofolate reductase	Dihydrofolic acid	Aminopterin, amethopterin, methotrexate	Employed in the treatment of leukemia and other cancers.
Acetylcholine esterase	Acetylcholine	Succinyl choline	Used in surgery for muscle relaxation, in anaesthetised patients.

	Para aminobenzoic acid (PABA)	Sulphanilamide	Prevents bacterial synthesis of folic acid.
	Vitamin K	Dicumarol	Acts as an anticoagulant.
	Pyridoxine (vitamin B_6)	Isonicotinic acid hydrazide (INH)	INH is an antituberculosis drug, its prolonged use leads to B_6 deficiency.

2. **Non-competitive inhibition :** The inhibitor binds at a site other than the active site on the enzyme surface. This binding impairs the enzyme function. The inhibitor has no structural resemblance with the substrate. However, there usually exists a strong affinity for the inhibitor to bind at the second site. In fact, the inhibitor does not interfere with the enzyme-substrate binding. But the catalysis is prevented, possibly due to a distortion in the enzyme conformation.

   The inhibitor generally binds with the enzyme as well as the ES complex. The overall relation in non-competitive inhibition is represented below :

$$\begin{array}{ccccc} E + S & \rightleftharpoons & ES & \longrightarrow & E + P \\ + & & + & & \\ I & & I & & \\ \Downarrow\uparrow & & \Downarrow\uparrow & & \\ E.I. + S & & E.I.S & & \end{array}$$

   For non-competitive inhibition, the K_m value is unchanged while V_{max} is lowered.

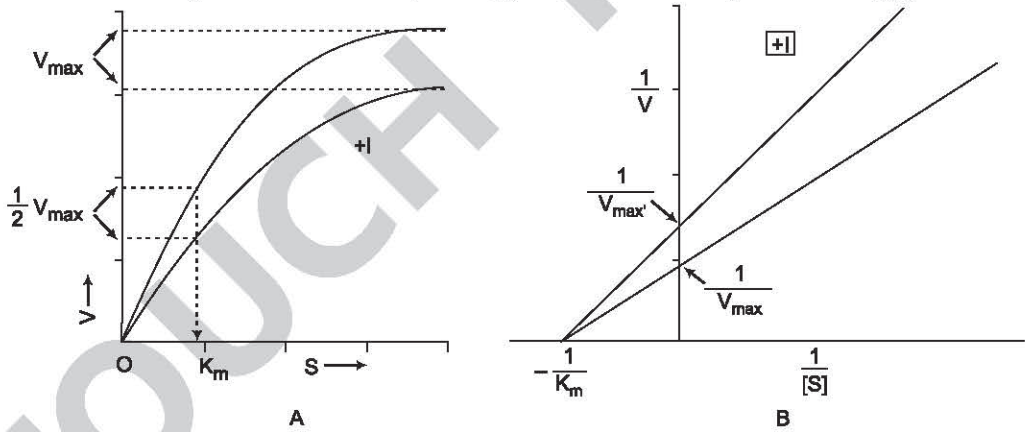


Fig. 2 : Effect of non-competitive inhibitor (I) on enzyme velocity (A) Velocity (v) versus substrate (S). (B) Lineweaver-Burk plot (Green shaded lines with inhibitor, non-competitive inhibitor does not change K_m but decreases V_{max})

   Heavy metal ions (Ag^+, Pb^{2+}, Hg^{2+} etc.) can non-competitively inhibit the enzymes by binding with cysteinyl sulfhydryl groups. The general reaction for Hg^{2+} is shown :

$$E - SH + Hg^{2+} \rightleftharpoons E - S \ldots . Hg^{2+} + H^+$$

   Heavy metals also lead to the formation of covalent bonds with carboxyl groups and histidine, often resulting in irreversible inhibition.

3. **Un-competitive inhibition :** This is the third class of reversible inhibition which, however, is not very common. In this case, the inhibitor does not bind with enzyme but only binds with enzyme substrate complex.

$$E + S \rightleftharpoons ES \longrightarrow E + P$$
$$+$$
$$I$$
$$\Updownarrow$$
$$E.S.I.$$

Un-competitive inhibitor decreases both K_m and V_{max} values of the enzyme.

B. Irreversible inhibition

The inhibitors bind covalently with the enzymes and inactivate them, which is irreversible. These inhibitors are usually toxic substances which may be present naturally or man-made.

Iodoacetate is an irreversible inhibitor of the enzymes like papain and glyceraldehyde 3-phosphate dehydrogenase. Iodoacetate combines with sulfhydryl (—SH) groups at the active site of these enzymes and makes them inactive. *Diisopropyl fluorophosphate* (DFP) is a ***nerve gas*** developed by the Germans during Second World War. DFP irreversibly binds with enzymes containing serine at the active site, *e.g.,* serine proteases, acetylcholine esterase.

Many organophosphorus insecticides like melathion are toxic to animals (including man) as they block the activity of acetylcholine esterase (essential for nerve conduction), resulting in paralysis of vital body functions. Pencillin antibiotics also act as irreversible inhibitors of serine containing enzymes in bacterial cell wall synthesis.

C. Allosteric Inhibition

A non-competitive inhibitor which attaches to the enzyme at allosteric site *i.e.,* any place on enzyme except active site, is called allosteric inhibitor. An allosteric inhibitor by binding to allosteric site **alters** the protein conformation in active site of enzyme which consequently changes the shape of active site. Thus enzyme no longer remains able to bind to its specific substrate. Hence enzyme is unable to perform it's catalytic activity *i.e.,* enzyme is now inactive. This process is called allosteric inhibition.

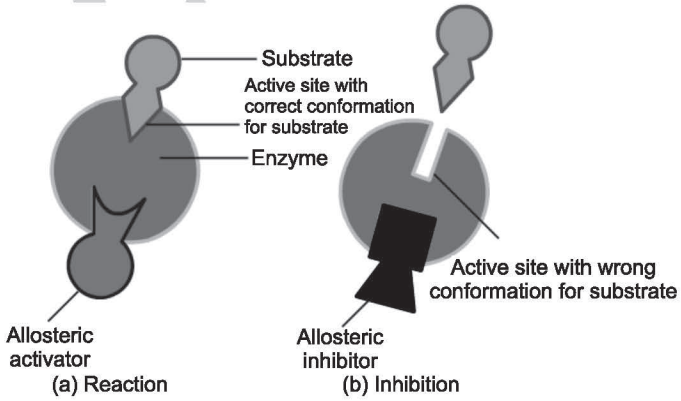


Fig. 3 : Allosteric inhibition

For example : ATP act as allosteric inhibitor of enzyme pyruvate kinase during glycolysis. Pyruvate kinase speeds up the last step of glycolysis by transferring the phosphate from phosphoenol pyruvate(PEP) to ADP to form ATP. The formed ATP itself distorts the shape of the active site by binding to the allosteric site of pyruvate kinase. Hence it actually act as allosteric inhibitor in this case.

Q.3. Describe enzyme and their properties. Also explain the mechanism of enzyme.

Ans. **Enzymes**

These are 'biological catalysts' produced by the living cells and are able to accelerate the rate of chemical reactions occurring in living cells. We all know that life involves in a perfect coordination of a vast majority of chemical reactions many of which are extremely complicated. All these reactions when performed *in vitro* conditions at low temperatures and atmospheric pressure take place very slowly. But, these reactions proceed at extremely high rates in the living cells at the same low temperature and atmospheric pressure. How does it happen so? Who are responsible to do so? In fact, as said in the beginning, these are the enzymes (or the biological catalysts) synthesized inside the cells that make it possible.

The term 'enzyme' was coined by **F. W. Kuhne** (1878) to designate tile biological catalysts that were earlier called **'fertnents'** by **Berzelius** (1827).

Enzymes therefore are defined as "simple or compound proteins acting as specific catalysts". They may also be defined as "organic substances capable of catalysing chemical reaction in the living systems."

All enzymes are proteins without any known exceptions they are soluble and colloidal proteins and accelerate the biological reactions without themself being used up. They are effective in very small quantity and are extremely unstable because they are easily inactivated or denatured.

Properties of Enzymes

1. **Colloidal Nature :** Enzyme molecules are mostly of giant size. Due to this they possess extremely low diffusion rates and form colloidal system; in water. Enzymes are nondialyzable due to being colloidal in nature although some contain dialyzable or dissociable components in the form of coenzymes.
2. **Catalytic Nature :** Enzymes are catalytic in nature and highly speed, the rate of chemical reactions occurring in organisms tissues. Normally, the, enzymes do not participate in chemical reactions or if they do so, they are recovered as such without undergoing any qualitative or quantitative change at the of these reactions. This is why, the enzymes are capable of catalyzing the transformation of a large quantity of substrates in very small quantities. For convenience catalase enzyme can transform 5,000,000 molecules of H_2O_2 into H_2O and O_2 per minute when the condition are favourable.
3. **Specificity Action :** Enzymes are very specific in their action. Their specificity of action lies in the fact that they may act upon one specific type of substrate or upon a group of structurally related substrates. Urease is an enzymes that acts only on urea to produce ammonia and carbon dioxide whereas lactic dehydrogenase acts upon Lactic acid produce ammonia pyruvic and lactic acids and also a number of other structurally related compounds.
4. **Heat Sensitivity (Thermobility) :** Enzymes are very sensitive to heat. The rate of an enzyme action speeds up 2 to 3 times when there is 10°C rise in temperature. But, above 60°C the enzymes coagulate and thus become inactivated. Decreasing temperatures to near or below 0°C also inactivates the enzymes but this inactivating is reversible and the enzymes reactivates when temperature increases to optimum.

5. **pH Sensitivity :** The functioning of an enzyme is very much controlled by the pH value or the H^+ ion concentration of the medium, Each enzyme functions to its the best at specific pH value and its activity is increased or decreased if any considerable change is brought in till pH value of the medium. However, the approximate optimum value of pH lies near neutrality for most of the enzymes.
6. **Reversibility of Enzyme Action :** Many enzymes catalyse reversible reactions. For example, lipase which catalyzes the synthesis of fat from glycerol and fatty acids also catalyzes the reversal of the reaction *i.e.,* conversion of fat into glycerol and fatty acids. Similarly, enzyme emulsion catalyzes the synthesis as well as hydrolysis of glycosides.

Mechanism of Enzymes

To explain the mechanism of enzyme-action following theory is proposed :

1. **Enzyme Substrate Complex Formation Theory :** Michaelis and Menton (1913) evolved a theory to explain the mode of enzyme action in biological reactions while working on the hydrolysis of sugar by enzyme invertase. They explained that the enzyme first binds reversibly with the substrate through its active site resulting in the formation of an enzyme substrate complex. Substrate is bound with enzyme in such a way in the enzyme substrate complex that a rapid reaction takes place between them. Stimultaneously the end product is released and the enzymes now becomes free.

   This reversible reaction can be represented as follows :

   Enzyme + Substrate $\rightleftharpoons$ Enzymes – Substrate Complex $\rightleftharpoons$ End product + Enzyme
2. **Lock and Key Model :** This model was proposed by a German chemist **Emil Fischer** in 1890. According to this model the enzyme substrate complex formation is analogous to the fitting of Lock and Key. Just as only particular shaped Keys fit into particular shaped Locks, similarly only certain types of molecules will, establish a close (it with given type of enzyme. According to this concept a structurally well defined catalytic site will accept only those substrate molecules which has a matching shape and will repell others that differs structurally. In other words, the catalytic site of the enzymes by itself is complementary in shape to that of the substrate.

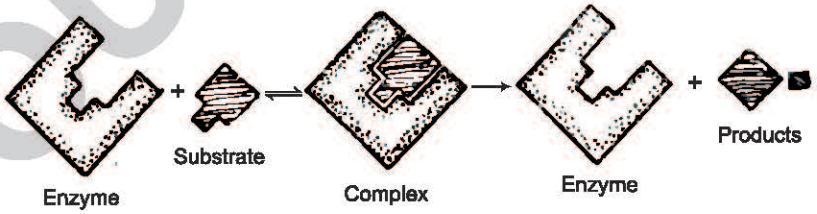


Fig. 1 : Diagrammatic representation of the mechanism of enzyme action through Lock and Key Model

3. **Induced Fit Model :** This model was proposed by **D. Koshland** in 1966. An essential feature of the "induced fit" model is the flexibility of file region of catalytic site. In the Fischer model the catalytic site is presumed to be pre-shaped to fit the substrate. In the induced fit model, the substrate induces a conformational change in the enzyme. According to this postulate, the catalytic sites of some enzymes are not rigid. In these enzymes, the shape of the catalytic site is modified by the binding of substrate. The catalytic site has a shape complementary to that of the substrate only after the

substrate is bound. This process of dynamic recognition is called **induced fit.** It brings amino residues or other groups on the enzyme in the correct spatial orientation for substrate binding.

Q.4. Describe the regulation of enzyme activity in the living system.

Ans. Regulation of Enzyme activity in the Living System

The various factors that influence enzyme activity in the laboratory (*in vitro*) have been discussed. Some of these factors like temperature and pH are quite constant in the living cell. In biological system, regulation of enzyme activities occurs at different stages in one or more of the following ways to achieve cellular economy :

1. **Allosteric regulation or Allosteric Inhibition :** Some of the enzymes possess additional sites, known as allosteric sites (*Greek : allo*—other), besides the active site. Such enzymes are known as allosteric enzymes. The allosteric sites are unique places on the enzyme molecule.

   Allosteric effectors : Certain substances referred to as allosteric modulators (effectors or modifiers) bind at the allosteric site and regulate the enzyme activity. The enzyme activity is increased when a positive (+) allosteric effector binds at the allosteric site known as activator site. On the other hand, a negative (–) allosteric effector binds at the allosteric site called inhibitor site and inhibits the enzyme activity.

   Classes of allosteric enzymes : Enzymes that are regulated by allosteric mechanism are referred to as allosteric enzymes. They are divided into two classes based on the influence of allosteric effector on K_m and V_{max}.

   (i) **K-class of allosteric enzymes,** the effector changes the K_m and not the V_{max}. Double reciprocal plots, similar to competitive inhibition are obtained *e.g.,* phosphofructokinase.

   (ii) **V-class of allosteric enzymes,** the effector alters the V_{max} and not the K_m. Double reciprocal plots resemble that of non-competitive inhibition *e.g.,* acetyl CoA carboxylase. The terms competitive and non-competitive are not used for allosteric regulation of enzymes, since the mechanism of action is totally different.

   Conformational changes in allosteric enzymes : Most of the allosteric enzymes are oligomeric in nature. The subunits may be identical or different. The non-covalent reversible binding of the effector molecule at the allosteric site brings about a conformational change in the active site of the enzyme, leading to the inhibition or activation of the catalytic activity. In the concerted model, allosteric enzymes exist in two conformational states—the T (tense or taut) and the R (relaxed). The T and R states are in equilibrium.

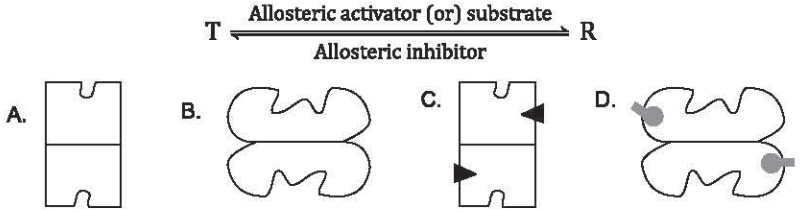


Fig. 1 : Diagrammatic representation of an allosteric enzyme : A. T-form; B. R-form; C. Effect of allosteric inhibitor; D. Effect of allosteric activator

Allosteric inhibitors favour T state whereas activators and substrates favour R state. The substrate can bind only with the R form of the enzyme. The concentration of enzyme molecule in the R state increases as more substrate is added, therefore the binding of the substrate to the allosteric enzyme is said to be cooperative. Allosteric enzymes give a sigmoidal curve (instead of hyperbola) when the velocity (v) versus substrate (S) concentration are plotted.

The term homotropic effect is used if the substrate influences the substrate binding through allosteric mechanism, their effect is always positive. Heterotropic effect is used when an allosteric modulator effects the binding of substrate to the enzyme. Heterotropic interactions are either positive or negative. Selected examples of allosteric enzymes responsible for rapid control of biochemical pathways are given in table.

Feedback regulation : The process of inhibiting the first step by the final product, in a series of enzyme catalysed reactions of a metabolic pathway is referred to as feedback regulation. Look at the series of reactions given below :

$$A \xrightarrow{e_1} B \xrightarrow{e_2} C \xrightarrow{e_3} D \xrightarrow{e_4} E$$

A is the initial substrate, B, C, and D are the intermediates and E is the end product, in a pathway catalysed by four different enzymes (e_1, e_2, e_3, e_4). The very first step ($A \rightarrow B$ by the enzyme e_1) is the most effective for regulating the pathway, by the final end product E. This type of control is often called negative feedback regulation since increased levels of end product will result in its (e_1) decreased synthesis. This is a real cellular economy to save the cell from the wasteful expenditure of synthesizing a compound which is already available within the cell.

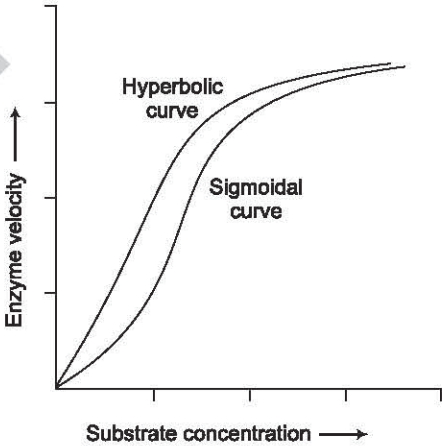


Fig. 2 : Effect of substrate concentration on allosteric enzyme (black line-sigmoidal curve) in comparison with normal enzyme (green line-hyperbolic curve).

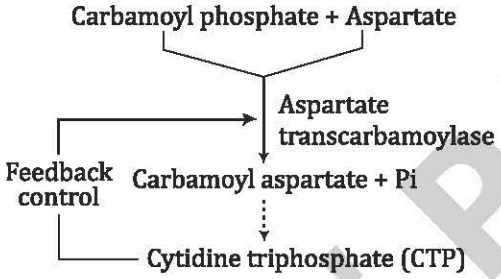
Feedback inhibition or end product inhibition is a specialised type of allosteric inhibition necessary to control metabolic pathways for efficient cellular function.

Aspartate transcarbamoylase (ATCase) is a good example of an allosteric enzyme inhibited by a feedback mechanism. ATCase catalyses the very first reaction in pyrimidine biosynthesis.

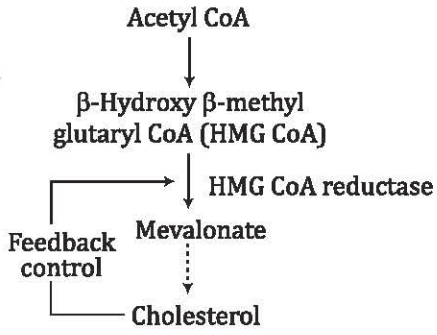
Table : Some enzymes with allosteric effectors

Enzyme	Metabolic pathway	Allosteric	
		Inhibitor	Activator
Hexokinase	Glycolysis	Glucose 6-phosphate	—
Phosphofructokinase	Glycolysis	ATP	AMP, ADP

Isocitrate dehydrogenase	Krebs cycle	ATP	ADP, NAD^+
Pyruvate carboxylase	Gluconeogenesis	—	Acetyl CoA
Fructose 1, 6-bisphosphatase	Gluconeogenesis	AMP	—
Carbamoyl phosphate synthetase I	Urea cycle	—	N-Acetylglutamate
Tryptophan oxygenase	Tryptophan metabolism	—	L-Tryptophan
Acetyl CoA carboxylase	Fatty acid synthesis	Palmitate	Isocitrate



Carbamoyl phosphate undergoes a sequence of reactions for synthesis of the end product, CTP. When CTP accumulates, it allosterically inhibits the enzyme aspartate transcarbamoylase by a feedback mechanism. HMG CoA reductase is a regulatory enzyme in cholesterol biosynthesis which is inhibited by the end product cholesterol, through feedback control.



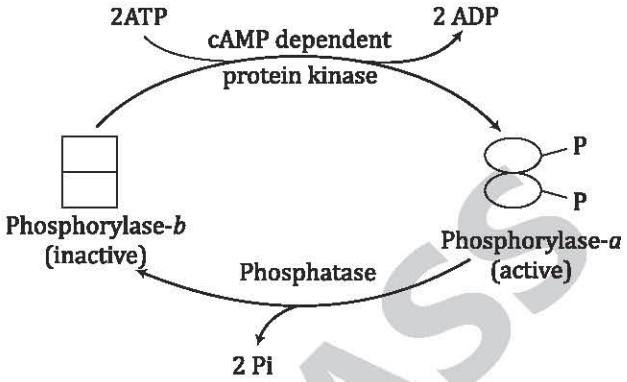
The end products, controlling metabolic pathways by inhibiting the reactions in the very early stages, have great advantage to the cellular function since a particular compound is produced only when it is needed and not otherwise.

2. **Activation of latent enzymes :** Latent enzymes, as such, are inactive. Some enzymes are synthesized as ***proenzymes*** or ***zymogens*** which undergo irreversible covalent activation by the breakdown of one or more peptide bonds. For instance, proenzymes—namely chymotrypsinogen, pepsinogen and plasminogen, are respectively—converted to the active enzymes chymotrypsin, pepsin and plasmin.

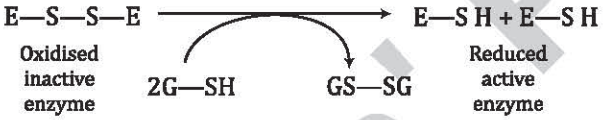
   Certain enzymes exist in the active and inactive forms which are interconvertible, depending on the needs of the body. The interconversion is brought about by the reversible covalent modifications, namely phosphorylation and dephosphorylation, and oxidation and reduction of disulphide bonds. The control is actually exerted by the hormones (epinephrine, thyroxine, insulin etc.) through the mediation of cyclic AMP. An example of the existence of phospho- and dephospho-enzymes is discussed here under :

   Glycogen phosphorylase is a muscle enzyme that breaks down glycogen to provide energy. This enzyme is a homodimer (two identical subunits) and exists in two interconvertible forms. Phosphorylase *b* (dephospho enzyme) is inactive which is

converted by phosphorylation of serine residues to active form phosphorylase *a*. The inactive enzyme phosphorylase *b* is produced on dephosphorylation as illustrated as follows :



There are some enzymes which are active in dephosphorylated state and become inactive when phosphorylated *e.g.,* glycogen synthase, acetyl CoA carboxylase. A few enzymes are active only with sulfhydryl (—SH) groups, *e.g.,* succinate dehydrogenase, urease. Substances like glutathione bring about the stability of these enzymes.



3. **Compartmentation :** There are certain substances in the body (*e.g.,* fatty acids, glycogen) which are synthesized and also degraded. There is no point for simultaneous occurrence of both the pathways. Generally, the synthetic (anabolic) and breakdown (catabolic) pathways are operative in different cellular organelles to achieve maximum economy. For instance, enzymes for fatty acid synthesis are found in the cytosol whereas enzymes for fatty acid oxidation are present in the mitochondria. The control for the synthesis and breakdown of fatty acids is brought about by regulating the transport of common intermediates across the mitochondrial membrane. Depending on the needs of the body—through the mediation of hormonal and other controls-fatty acids are either synthesized or oxidized.

   Mitochondrion is regarded as the power house of the cell where most of the energy producing pathways are located. The intracellular location of certain enzymes and metabolic pathways is given in Table.

Table : Distribution of certain enzymes and metabolic pathways in cellular organelles

Organelle	Enzyme/Metabolic pathway
Cytoplasm	Aminotransferases; peptidases; glycolysis; hexose monophosphate shunt; fatty acid synthesis; purine and pyrimidine catabolism.
Mitochondria	Fatty acid oxidation; amino acid oxidation; Krebs cycle; urea synthesis; electron transport chain and oxidative phosphorylation.
Nucleus	Biosynthesis of DNA and RNA.
Endoplasmic reticulum (microsomes)	Protein biosynthesis; triacylglycerol and phospholipid; synthesis; steroid synthesis and reduction; cytochrome P_{450} ; esterase.
Lysosomes	Lysozyme; phosphatases; phospholipases; hydrolases; proteases; lipases; nucleases.

Golgi apparatus	Glucose 6-phosphatase; 5'-nucleotidase; glucosyl-and galactosyl-transferases.
Peroxisomes	Catalase; urate oxidase; D-amino acid oxidase; long chain fatty acid oxidation.

4. **Control of enzyme synthesis :** Most of the enzymes, particularly the rate limiting ones, are present in very low concentration. Nevertheless, the amount of the enzyme directly controls the velocity of the reaction, catalysed by that enzyme. Many rate limiting enzymes have short half-lives. This helps in the efficient regulation of the enzyme levels.

   There are two types of enzymes :

   (i) **Constitutive enzymes** (house-keeping enzymes) : The levels of which are not controlled and remain fairly constant.

   (ii) **Adaptive enzymes :** Their concentrations increase or decrease as per body needs and are well-regulated. The synthesis of enzymes (proteins) is regulated by the genes.

   Induction and repression : The term induction is used to represent increased synthesis of enzyme while repression indicates its decreased synthesis. Induction or repression which ultimately determines the enzyme concentration at the gene level through the mediation of hormones or other substances.

   Examples of enzyme induction : The hormone insulin induces the synthesis of glycogen synthetase, glucokinase, phosphofructokinase and pyruvate kinase. All these enzymes are involved in the utilization of glucose. Insulin represses the synthesis of many key enzymes involved in glucose synthesis (gluconeogenesis). The net result is that insulin increases the utilization and decreases the synthesis of glucose by regulating the corresponding enzyme levels. The hormone cortisol induces the synthesis of many enzymes *e.g.,* pyruvate carboxylase, tryptophan oxygenase and tyrosine aminotransferase.

   Examples of repression : In many instances, substrate can repress the synthesis of enzyme. Pyruvate carboxylase is a key enzyme in the synthesis of glucose from non-carbohydrate sources like pyruvate and amino acids. If there is sufficient glucose available, there is no necessity for its synthesis. This is achieved through repression of pyruvate carboxylase by glucose.

5. **Enzyme degradation :** Enzymes are not immortal, since it will create a series of problems. There is a lot of variability in the half-lives of individual enzymes. For some, it is in days while for others in hours or in minutes, *e.g.,* LDH_4-5 to 6 days; LDH_1 -8 to 12 hours; amylase –3 to 5 hours. In general, the key and regulatory enzymes are most rapidly degraded. If not needed, they immediately disappear and, as and when required, they are quickly synthesized. Though not always true, an enzyme with long half-life is usually sluggish in its catalytic activity.

6. **Isoenzymes :** Multiple forms of the same enzyme will also help in the regulation of enzyme activity, Many of the isoenzymes are tissue-specific. Although isoenzymes of a given enzyme catalyse the same reaction, they differ in K_m, V_{max} or both. *e.g.,* isoenzymes of LDH and CPK.

❑❑❑

UNIT-III

Metabolism of Carbohydrates and Lipids

SECTION-A VERY SHORT ANSWER TYPE QUESTIONS

Q.1. What is pathway for glucose synthesis by non-carbohydrates precursors?

Ans. Synthesis of glucose from non-carbohydrate source is carried out by gluconeogenesis. It is the universal pathway, found in all plants, animals and microorganisms.

Q.2. What is the site for gluconeogenesis?

Ans. Gluconeogenesis in animals takes place in the liver as well as some extent in the kidney cortex. The kidney is capable of making glucose during the condition of starvation and can make up to 50% of glucose.

Q.3. Which enzyme is responsible for the conversion of pyruvate to phosphoenolpyruvate (PEP)?

Ans. The conversion of pyruvate to PEP take place in two stages, the first reaction is catalyzed by pyruvate carboxylase which converts pyruvate to oxaloacetate and in second reaction oxaloacetate is converted by pyruvate carboxykinase to PEP.

Q.4. What is the site for gluconeogenesis?

Ans. Gluconeogenesis in animals take place in the liver as well as some as some extent in the kidney cortex. The kidney is capable of making glucose during the condition of starvation and can make up to 50% of glucose.

Q.5. What is the precursor of glycogen?

Ans. Glucose-1-phosphate and uridine triphosphate work together to activate UDP-glucose which acts as a precursor of glycogen.

Q.6. Which substrate is not the precursor of gluconeogenesis?

Ans. Only leucine or lysine is the substrate which is not used for gluconeogenesis as these amino acids produce only acetyl-CoA upon degradation. Animals cannot carry out gluconeogenesis by two acetyl carbon of acetyl-CoA.

Q.7. Which hormone maintains blood glucose level by activation of gluconeogenesis?

Ans. Glucagon acts opposite to insulin and is secreted by the α-cells of the pancreatic islets. It maintains blood glucose level by the activation of glycogenolysis and gluconeogenesis.

Q.8. Which hormone is secreted in an emergency or in stress condition?

Ans. Epinephrine is also known as emergency hormone and it is secreted in the condition of stress and emergencies like injury, pain, fear, accident and grief. It increase the level of sugar in the blood by stimulating glycogenolysis.

Q.9. What are major sites for glycogen storage?

Ans. Glycogen is stored in muscle and liver only. The amount of glycogen is high in the liver but a larger amount of glycogen stored in the greater bunch of skeletal muscles. The liver uses

its glycogen for the synthesis of glucose for all of the body while muscles use its glycogen for its own energy.

Q.10. What is lipid metabolism?

Ans. Lipid metabolism is the process that most of the fat ingested by the body is emulsified into small particles by bile and then the lipase secreted by the pancreas and small intestine hydrolyses the fatty acids in the fat into free fatty acids and monoglycerides.

Q.11. What is the first step in lipid metabolism?

Ans. Lipids are generally stored as triglycerides and the first step in lipid metabolism is the conversion to glycerol and fatty acids. Glycerol (dihydroxyacetone phosphate) can enter the glycolysis pathway and proceed to the krebs cycle and oxidative phosphorylation.

Q.12. How is lipid metabolism regulated?

Ans. Regulation of lipid metabolism by leptin, insulin and adiponectin. Insulin and leptin are secreted in direct proportion and adiponectin in negative proportion to the size of the adipose mass. These three hormones are key molecules in the regulation of lipid metabolism.

Q.13. Where are lipids stored?

Ans. Triglycerides and lipids both high-energy molecules are stored in adipose tissue until they are need.

Q.14. What is lipogenesis and lipolysis?

Ans. Lipolysis is the hydrolysis of fats and other lipid molecules into fatty acids whereas lipogenesis is the synthesis of fatty acids and triglyceride from acetyl coenzyme A and other substrates.

Q.15. Where is myristic acid found?

Ans. Myristic acid is found naturally in palm oil, coconut oil and butter fat. Tetradecanoic acid is a straight chain 14 carbon, long chain saturated fatty acid mostly found in milkfat.

Q.16. What is triglyceride synthesis?

Ans. Triglycerides are synthesised by esterification of fatty acids to glycerol. Fatty acid esterification takes place in the endoplasmic reticulum of cells by metabolic pathways in which acyl groups in fatty acyl-CoAs are transferred to the hydroxyl groups of glycerol-3-phosphate and diacylglycerol.

Q.17. What is ketogenesis?

Ans. Ketogenesis is a biochemical phenomenon, which generates ketone bodies after disitegrating fatty acids and ketogenic amino acids.

Q.18. Where does ketogenesis occur?

Ans. The process of ketogenesis mainly takes place in the mitochondria of cells of the liver. Here, fatty acids are supplied to mitochondria through carnitine palmitoyl transferase and disintegrated into acetyl CoA via β-oxidation.

Q.19. What is the difference between ketosis and ketogenesis?

Ans. Ketosis is the state wherein our body tends to produce ketones at detectable levels, whereas ketogenesis is a chemical phenomenon, which generates those ketones. Therefore, ketosis is caused as a result of ketogenesis while ketogenesis is initiated from a lack of glucose.

SECTION-B SHORT ANSWER TYPE QUESTIONS

Q.1. Write a short note on hormonal control of carbohydrate metabolism.

Ans. Hormonal Control of Carbohydrate Metabolism

The supply of glucose to the blood by the liver and its utilization in the tissues must be regulated for the 'smooth' functioning of the metabolic processes in the body. Hormones secreted by the endocrines play an important role in the metabolism.

They can be classified into two varieties : (i) those which regulate the normal function and are essential for carbohydrate metabolism, and (ii) those which influence and are not essential for carbohydrate metabolism.

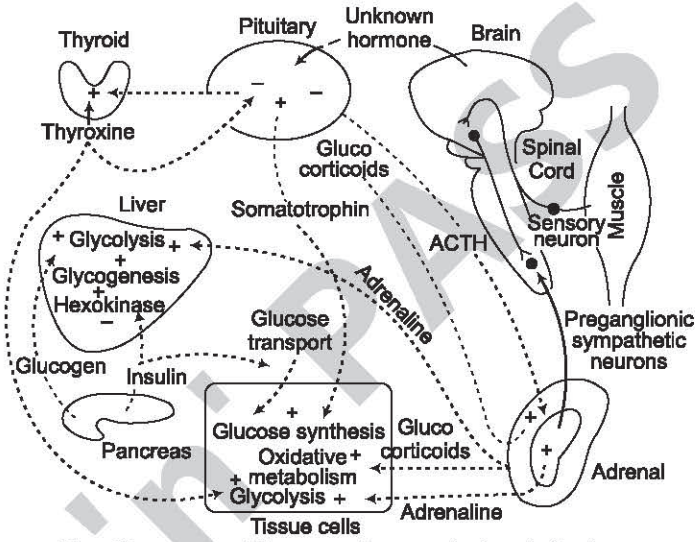


Fig. : Nervous and hormonal control of carbohydrate metabolism.

1. **Insulin** : Insulin administration decreases the release of glucose to the systemic blood by the liver, and increases the rate of utilization of glucose by tissue cells. The blood glucose level falls because of the decreased glycogenolysis or increased hepatic glycogenesis. The synthesis of glucose from proteins is also decreased. In the liver which is freely permeable to glucose, insulin exerts a regulatory influence upon the activity of glucokinase.
2. **Adrenal cortical hormones :** Adrenal oxysteroid hormones increase the blood sugar level, liver glycogen and total body carbohydrate. These hormones influence by increasing the output of glucose by the liver, and decrease the utilization of glucose by the tissues. The synthesis of carbohydrates from protein is also increased by the stimulation of activity of certain transaminases.
3. **Adenohypophyseal factors** : The adrenocorticotrophic hormones (ACTH) and thyroid stimulating hormones increase the secretions of adrenal cortex and thyroid glands by stimulating them, which on their turn effect the carbohydrate metabolism. Anterior pituitary extracts increase the blood sugar and decrease the respiratory quotient. These 'diabetic' symptoms are due to somatotropin which depresses the utilization of glucose.
4. **Epinephrine :** The action of epinephrine is to increase the blood sugar and lactic acid, which is due to an increase in the rate of glycogenolysis in the liver and muscles. Epinephrine stimulates phosphorylase activity and diminishes the uptake of glucose by tissue cells.

5. **Thyroxine :** The thyroid hormone increases the breakdown of glycogen and thereby the blood sugar. Thyroxine also increases the absorption of hexoses from the intestine.
6. **Glucagon :** The physiological importance of this substances is not known. It is produced by the α-cells of islets of Langerhans and causes an increase in blood sugar by accelerating hepatic glycogen breakdown.

Q.2. Write a short note on oxidation of odd numbered fatty acids.

Ans. **Oxidation of odd-numbered fatty acids**

Oxidation of odd-numbered fatty acids also leads to the formation of acetyl-CoA and acetoacetic acid. All the enzymes which act in the fatty acid cycle also act upon odd-numbered fatty acids of approximately the same chain length. Removal of C_2 units from an odd-numbered fatty acid ultimately leads to the formation of propionyl-CoA (CH_3CH_2CO-CoA). Propionyl-CoA is converted into propionic acid.

Kidney and heart preparations oxidize odd-numbered fatty acid to propionic acid, while liver can oxidize C_3 acids. It was previously pointed out that liver oxidizes even-numbered fatty acids quantitatively to acetoacetic acid. Liver can also oxidize odd-numbered fatty acids (C_5 to C_{17}) to this keto acid, but the quantity produced is slightly in excess than one equivalent, thus indicating a difference in the oxidative mechanism by the liver mitochondria. Propionic acid in animal tissues is oxidized into succinic acid and this mechanism involves the addition of CO_2 to the 3-carbon compound. Succinic acid is oxidized into CO_2 and H_2O through the citric acid cycle.

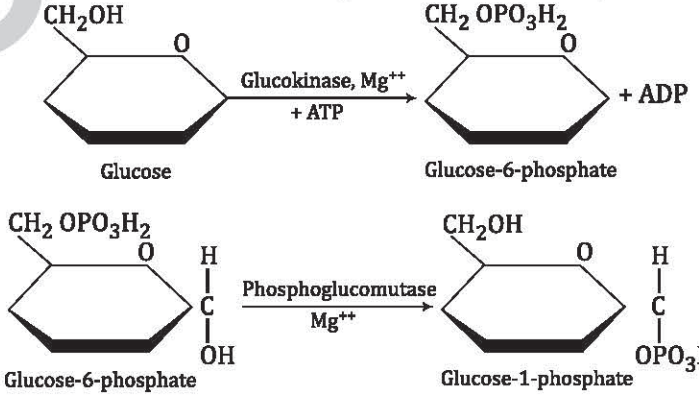
Fixation of carbon dioxide in the purified swine heart preparation occurs when propionic acid is converted into propionyl-CoA by an enzyme aceto COA-kinase. ATP is essential in the reaction. Methyl malonyl-CoA formed by the fixation process is converted into succinic acid through an intermediate product, succinyl-CoA.

In the mitochondria of the liver succinyl-CoA may be formed by another pathway. CO_2 is attached to the terminal carbon atom of a C_3 compound. Formation of propionyl CoA is interesting because it is also formed in the oxidative degradation of amino acids, such as isoleucine and valine.

Q.3. What do you mean by glycogenesis process?

Ans. **Glycogenesis**

The formation of glycogen usually takes place in liver and muscle. About 200 gm. of glycogen in equal amounts is present in these two organs of a human body.



The initial step in the synthesis of glycogen is the addition of a phosphate group to glucose, called as "phosphorylation" a term first introduced by **Neuberg** in 1910. For this process, an enzyme hexokinase, ATP and magnesium ions are essential. In the presence of all these, glucose is converted to glucose-6-phosphate.

Phosphoglucomutase transfers the phosphate group to carbon-1 position, in the presence of magnesium ions. Glucose-1, 6-diphosphate acts as an intermediate.

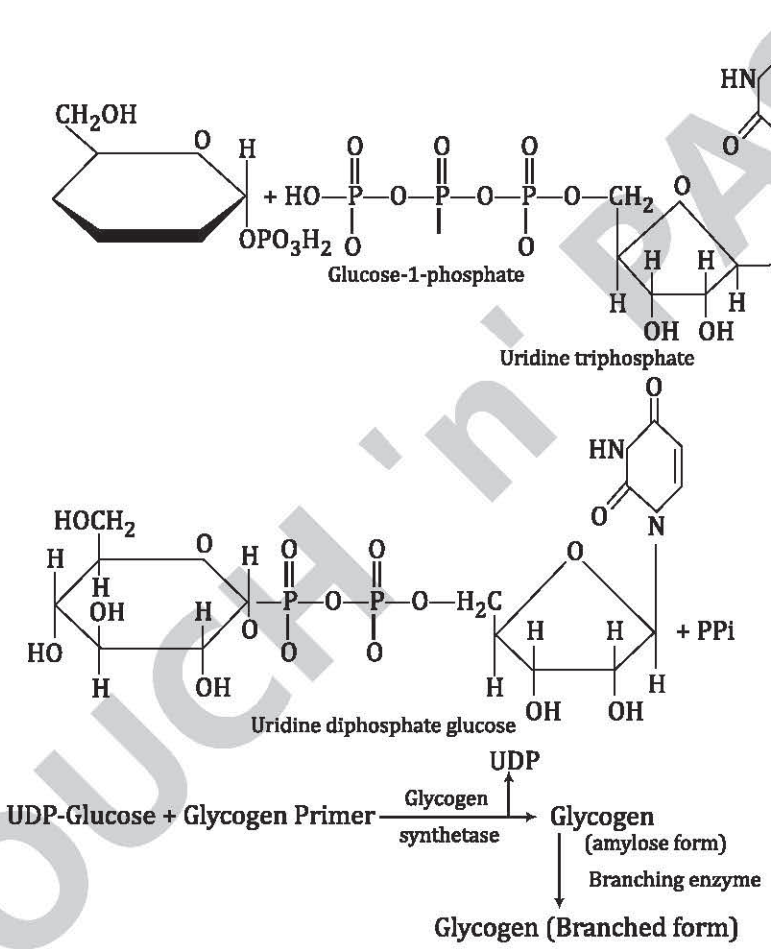


Fig. : Uridine pathyway of glycogenesis.

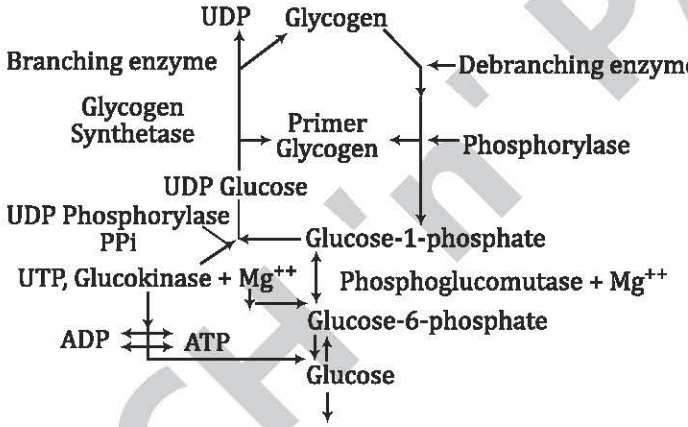
Under the influence of a pyrophosphorylase, glucose-1-phosphate reacts with **uridine triphosphate** (UTP) to form **uridine diphosphateglucose** (UDPG) an intermediate, also important in the formation of galactose, glucuronic acid and mucopolysaccharides. The enzyme **uridine diphosphoglucose-glycogen glucosyl-transferase** ("Glycogen synthetase") transfers the glucose moieties of UDPG to the free carbon-4 positions in the already existing polysaccharide chains. A "primer" of branched polysaccharide with α 1-4 linkages is essential for the reaction leading to the synthesis of glycogen. UDP reacts with ATP producing again UTP, so that the cycle can be repeated.

Q.4. Write a short note on glycogenolysis.

Ans. **Glycogenolysis**

When the blood sugar level falls below normal, or for other purposes, the liver glycogen is broken down into glucose. This is the reverse process of glycogenesis and is known as "glycogenolysis". During this process, the successive outer 1, 4-linked glucose units are phosphorylated by the action of the enzyme phosphorylase and split off as glucose-1-phosphate. The 1, 6-branching points are hydrolyzed by an enzyme, the debranching enzyme (amylo-1, 6-glucosidase). The action of these two enzymes is repeated until more 1, 6-branching points are exposed. Glucose-1-phosphate can be again converted to glucose-6-phosphate by the action of the enzymes phosphoglucomutase and to glucose by glucose-6-phosphatase.

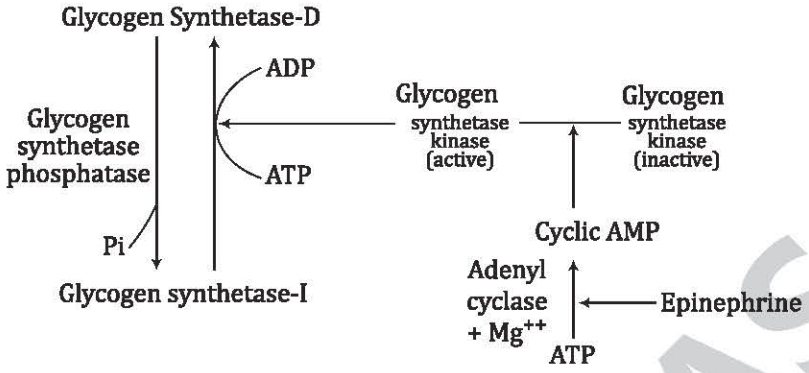
The overall process of glycogenolysis may be represented as follows :



Control of glycogenesis : Extremely important and effective regulatory mechanisms control the synthesis and degradation of glycogen, out of which glycogen synthetase is the most important key control point in at least muscles. This enzyme exists in both phosphorylated and dephosphorylated forms. ATP and glycogen synthetase kinase can convert the dephosphorylated form of glycogen synthetase into a less active phosphorylated form. Glucose -6-phosphate can increase the activity of this enzyme to a considerable extent, while free UDP accumulated due to limited supply of glucose and ATP inhibits the activity of the phosphorylated form. Depending upon the effect of glucose-6-phosphate, the two forms of glucose synthetase can be called as dependent (D) and independent (I) forms.

Glycogen synthetase kinase also exists in active and inactive forms. Cyclic-AMP formed from ATP in the presence of adenyl cyclase and magnesium ions converts the inactive form into an active form. Epinephrine and glucose stimulate the formation of cyclic-AMP. In the muscles a protein factor in the presence of calcium ions can also increase the activity of glycogen synthetase kinase. Insulin has also got a stimulating effect on the activation of glycogen synthetase in the muscle, the exact mechanism of which is still unknown.

The overall controlling mechanism can be given as follows :



Q.5. Write about the glycogenesis pathway.

Ans. Glycogenesis : The synthesis of glycogen from glucose is glycogenesis. Glycogenesis takes place in the cytosol and requires ATP and UTP, besides glucose.

1. **Synthesis of UDP-glucose :** The enzymes hexokinase (in muscle) and glucokinase (in liver) convert glucose to glucose 6-phosphate. Phosphoglucomutase catalyses the conversion of glucose 6-phosphate to glucose 1-phosphate. Uridine diphosphate glucose (UDPG) is synthesized from glucose 1-phosphate and UTP by UDP-glucose pyrophosphorylase. Pyrophosphate (PPi) produced in this reaction is hydrolysed to inorganic phosphate (Pi) by pyrophosphatase. This will ensure the optimal synthesis of UDPG.
2. **Requirement of primer to initiate glycogenesis :** A small fragment of pre-existing glycogen must act as a 'primer' to initiate glycogen synthesis. It is recently found that in the absence of glycogen primer, a specific protein-namely 'glycogenin' can accept glucose from UDPG. The hydroxyl group of the amino acid tyrosine of glycogenin is the site at which the initial glucose unit is attached. The enzyme glycogen initiator synthase transfers the first molecule of glucose to glycogenin. Then glycogenin itself takes up a few glucose residues to form a fragment of primer which serves as an acceptor for the rest of the glucose molecules.
3. **Glycogen synthesis by glycogen synthase :** Glycogen synthase is responsible for the formation of 1, 4-glycosidic linkages. This enzyme transfers the glucose from UDP-glucose to the non-reducing end of glycogen to form α-1, 4 linkages. The UDP released can be converted back to UTP by nucleoside diphosphate kinase.
4. **Formation of branches in glycogen :** Glycogen synthase can catalyse the synthesis of a linear unbranched molecule with 1, 4 α-glycosidic linkages, Glycogen, however, is a branched treelike structure. The formation of branches is brought about by the action of a branching enzyme, namely glucosyl α-4-6 transferase. (amylo α 1, 4 → 1, 6 transglucosidase). This enzyme transfers a small fragment of five to eight glucose residues from the non-reducing end of glycogen chain (by breaking α-1, 4 linkages) to another glucose residue where it is linked by α-1, 6 bond. This leads to the formation of a new non-reducing end, besides the existing one. Glycogen is further elongated and branched, respectively, by the enzymes glycogen synthase and glucosyl 4-6 transferase.

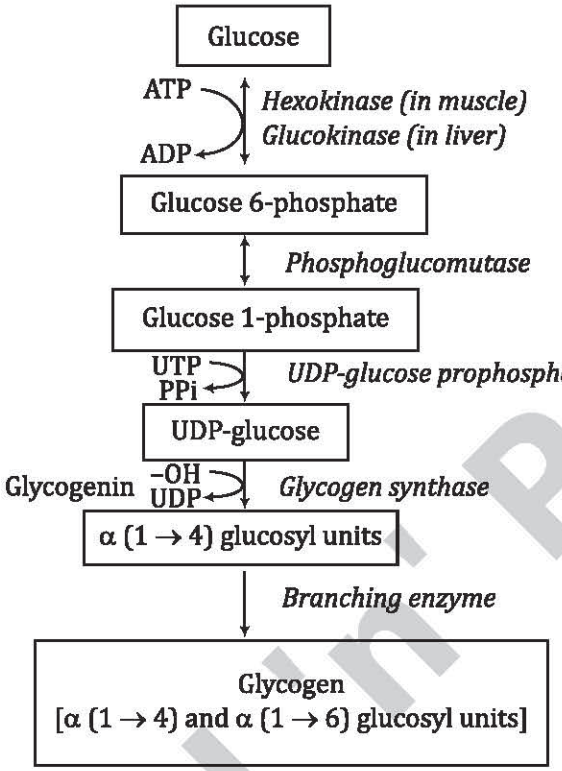


Fig. Glycogenesis pathway

The overall reaction of the glycogen synthesis for the addition of each glucose residue is

$$(\text{Glucose})_n + \text{Glucose} + 2\text{ATP} \longrightarrow (\text{Glucose})_{n+1} + 2\text{ADP} + \text{Pi}$$

Of the two ATP utilized, one is required for the phosphorylation of glucose while the other is needed for conversion of UDP to UTP.

Q.6. Write about the significnace of ketogenesis.

Ans.

Significances of Ketogenesis

1. Ketogenesis is used to get energy by the brain, heart and skeletal muscles under fasting condition.
2. The ketogenic diet (low-carb, fat-rich diet) is used these days to lose weight. The idea is to utilise excess fat stored in the body to get energy, but excess ketone bodies production can lead to various complications and ketoacidosis.
3. In ketoacidosis condition, the kidneys excrete extra ketone bodies with the water resulting in fluid loss.
4. Diabetic patients are greatly affected by ketoacidosis because insulin hormone is the main regulator of the process.
5. Symptoms of ketoacidosis include frequent urination, breath smelling like fruits or acetone, nausea, shortness of breath, fatigue, excessive thirst, etc.
6. Level of ketone bodies present in the body can be tested by blood serum or urine sample analysis.

SECTION-C LONG ANSWER TYPE QUESTIONS

Q.1. Describe the glycolysis pathway with the suitable structure.

Ans. **Glycolysis : Oxidation of Glucose**

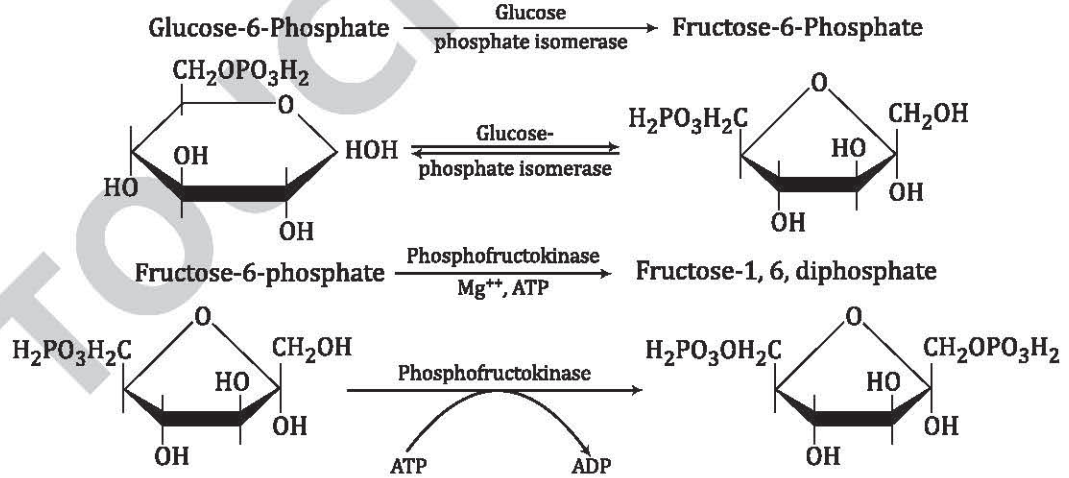
Apart form its conversion to glycogen in the muscle and liver, glucose is utilized to form chemical energy as ATP. Carbon dioxide and water are the by products. In fact, this is the principal fate of glucose under normal conditions. The broad reaction may be represented as :

$$C_6H_{12}O_6 + 6O_2 \longrightarrow 6CO_2 + 6H_2O + ATP \text{ (Energy)}$$

About 80% to 90% of the glucose metabolized is converted to pyruvic and lactic acids mainly in liver and muscles. The process is mostly anaerobic and termed as "glycolysis" along the Embden-Mayerhof pathway. The pyruvic acid and lactic acid formed are oxidized aerobically in cell mitochondria to carbon dioxide and water by way of acetyl CoA and the citric acid cycle, with associated oxidative phosphorylation and ATP formation. The major portion of the ATP is produced in the aerobic oxidation of pyruvic acid.

During glycolysis, it has been shown how glucose-6-phosphate is formed in the muscles from glucose. The next step involves the interconversion of glucose-6-phosphate to fructose-6-phosphate.

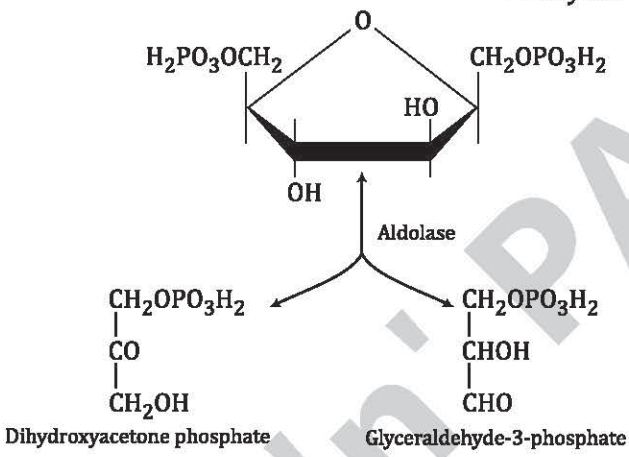
1. **Interconversion of glucose-6-phosphate and fructose-6-phosphate :** Glucose-6-phosphate and fructose-6-phosphate are freely interconvertible. The reaction is catalyzed by the enzyme phosphoglucose isomerase. At equilibrium, however, glucose-6-phosphate predominates, having a concentration of twice that of fructose-6 phosphate.



2. **Conversion of fructose-6-phosphate to fructose-1, 6-diphosphate :** Fructose-6-phosphate is next phosphorylated to form fructose-1, 6-diphosphate by the enzyme phosphofructokinase in the presence of Mg^{++} and ATP. The diphosphate is called Harden-Young ester. The reaction is irreversible as the energy exchange is about 4500 calories.

3. **Formation of triose phosphates :** The next step is the splitting of fructose-1, 6-diphosphate by the enzyme aldolase to form D-glyceraldehyde-3-phosphate and dihydroxyacetone phosphate. This is a reversible reaction.

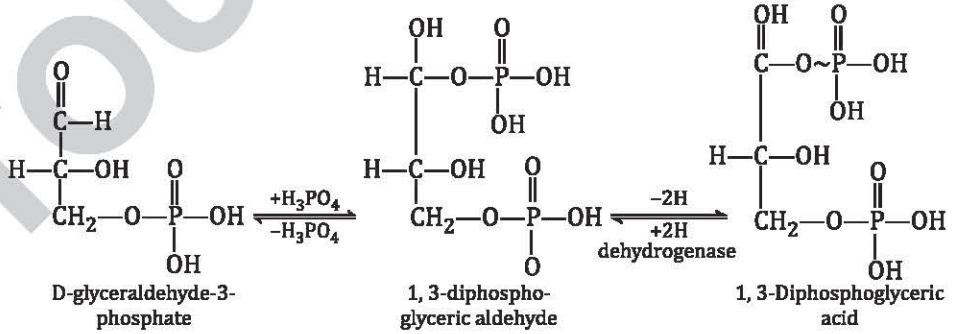
Fructose-1, 6-diphosphate $\xrightarrow{\text{Aldolase}}$ Glyceraldehyde-3-phosphate + Dihydroxyacetone phosphate



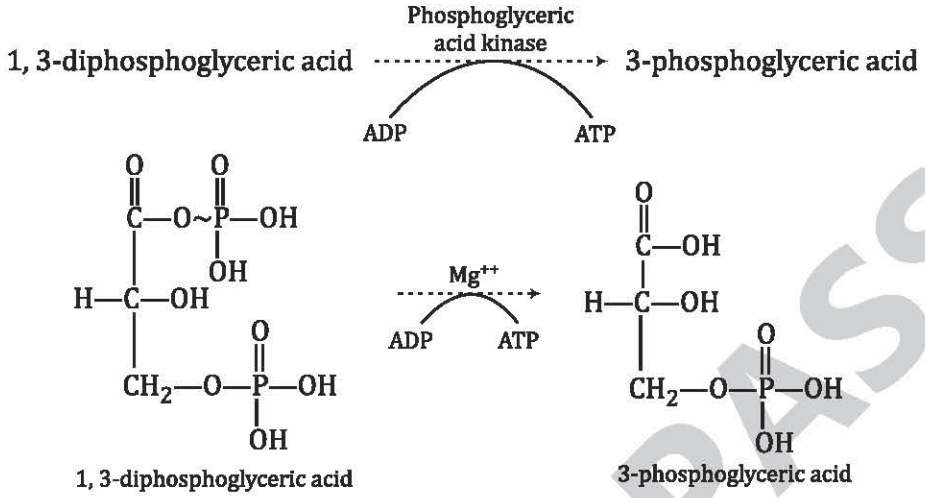
The two triose monophosphates are freely interconverted by triose phosphate isomerase.

4. **Oxidation of glyceraldehyde-3-phosphate :** The next step in glycolysis is the phosphorylation and oxidation of the two molecules of D-glyceraldehyde-3-phosphate to two molecules of 1, 3-diphosphoglyceric acid, catalyzed by the enzyme phosphoglyceraldehyde dehydrogenase, DPN^+ and inorganic phosphate are required. 1, 3-diphosphoglyceric aldehyde is the possible intermediate compound.

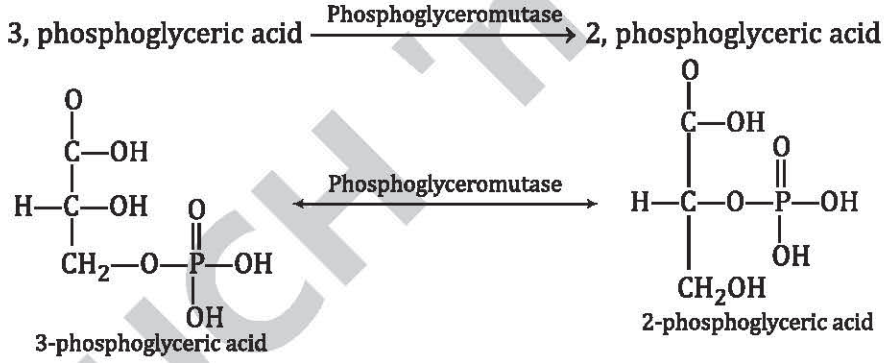
Glyceraldehyde-3-phosphate + H_3PO_4 + DPN $\rightleftharpoons$ 1, 3-diphosphoglyceric acid + DPNH + H^+



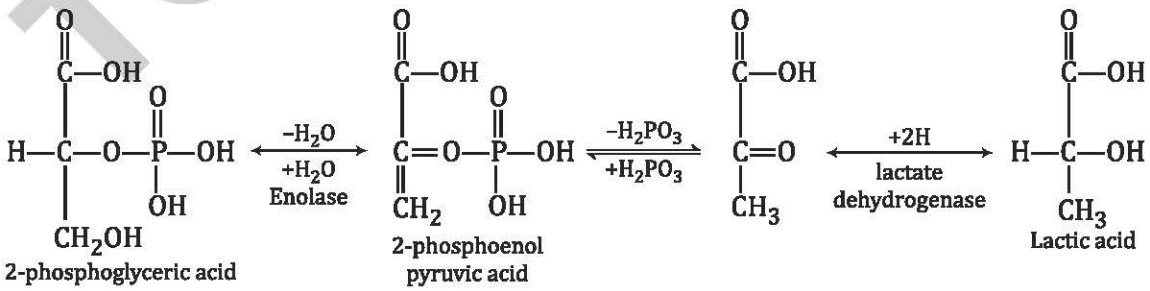
Transphosphorylation of 1, 3-diphosphoglyceric acid : 1, 3-diphosphoglyceric acid contains a high energy bond; and in the presence of an acceptor, ADP, magnesium ions, and the enzyme phosphoglyceric acid kinase, 3-phosphoglyceric acid and ATP (energy) are formed.



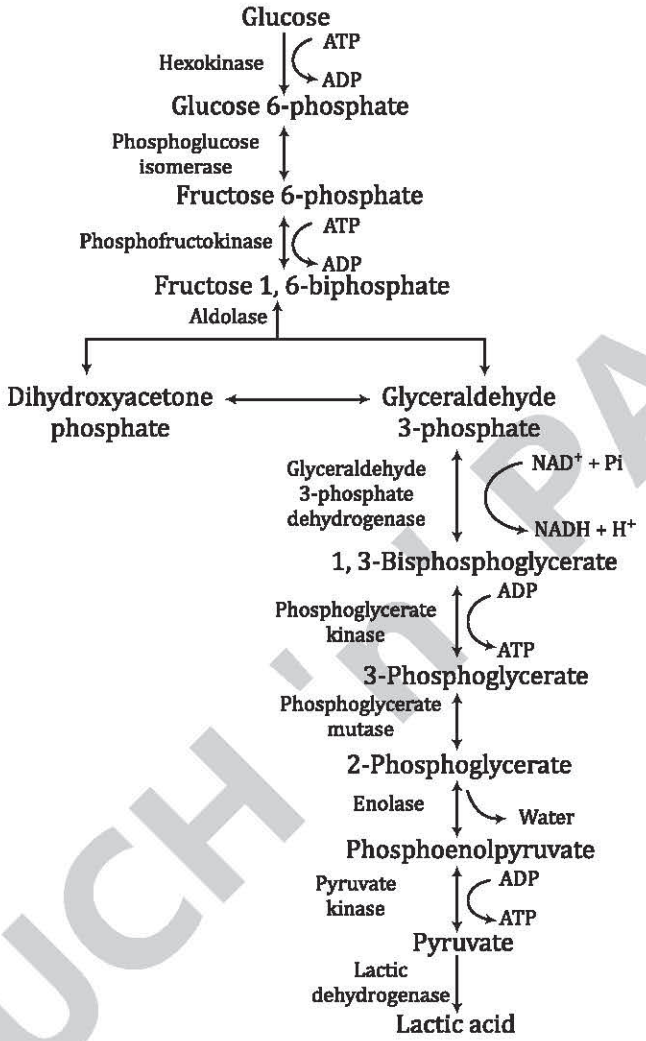
5. **Recovery of phosphate and formation of pyruvic acid :** The next stage involves the recovery of phosphate groups from 3-phosphoglyceric acid, which is converted initially to 2-phosphoglyceric acid by the action of phosphoglyceromutase.



2-phosphoglyceric acid is converted to phosphoenol-pyruvic acid by dehydration in the presence of an enzyme enolase. This molecule contains a higher-energy phosphate bond. 2-phosphopyruvic acid then loses its phosphoric acid releasing energy and forming pyruvic acid, which is finally reduced by lactate dehydrogenase to form lactic acid.



The complete process of glycolysis may be summarised as follows :



Q.2. Describe the history and pathway of Krebs cycle.

Ans.

Krebs Cycle or Citric acid Cycle

Brief history : The citric acid cycle was proposed by Hans Adolf Krebs in 1937, based on the studies of oxygen consumption in pigeon breast muscle. The cycle is named in his honour and he was awarded the Nobel Prize for Physiology and Medicine in 1953.

The citric acid cycle (Krebs cycle or tricarboxylic acid—TCA cycle) is the most important metabolic pathway for the energy supply to the body. About 65-70% of the ATP is synthesized in Krebs cycle. Citric acid cycle essentially involves the oxidation of acetyl CoA to CO_2 and H_2O. This cycle utilizes about two-thirds of total oxygen consumed by the body. The name TCA cycle is used, since, at the outset of the cycle, tricarboxylic acids (citrate, cisaconitate and isocitrate) participate.

TCA cycle—the central metabolic pathway : The citric acid cycle is the final common oxidative pathway for carbohydrates, fats and amino acids. This cycle not only supplies

energy but also provides many intermediates required for the synthesis of amino acids, glucose, heme etc. Krebs cycle is the most important central pathway connecting almost all the individual metabolic pathways (either directly or indirectly).

Location of TCA cycle : The enzymes of TCA cycle are located in mitochondrial matrix, in close proximity to the electron transport chain. This enables the synthesis of ATP by oxidative phosphorylation without any hindrance.

Krebs cycle basically involves the combination of a two carbon acetyl CoA with a four carbon oxaloacetate to produce a six carbon tricarboxylic acid, citrate. In the reactions that follow, the two carbons are oxidized to CO_2 and oxaloacetate is regenerated and recycled. Oxaloacetate is considered to play a catalytic role in citric acid cycle.

TCA cycle—an open cycle : Krebs cycle is a cyclic process. However, it should not be viewed as a closed circle, since many compounds enter the cycle and leave. TCA cycle is comparable to a heavy traffic circle in a national highway with many connecting roads. Each intermediate of the cycle connecting another pathway is a road!

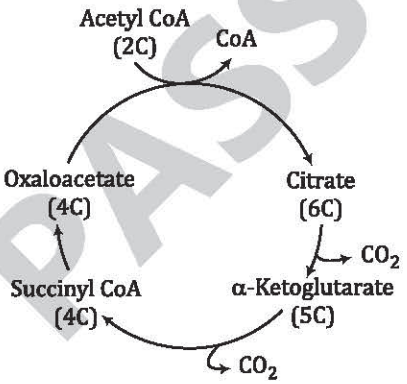


Fig. 1 : An overview of Krebs cycle.

Reactions of citric acid cycle : Oxidative decarboxylation of pyruvate to acetyl CoA by pyruvate dehydrogenase complex is discussed above. This step is a connecting link between glycolysis and TCA cycle. A few authors, however, describe the conversion of pyruvate to acetyl CoA along with citric acid cycle. The events of TCA cycle are described in Fig. 2.

Step 1. Formation of citrate : Krebs cycle proper starts with the condensation of acetyl CoA and oxaloacetate, catalysed by the enzyme citrate synthase. This is an aldol condensation reaction leading to the formation of an intermediate citryl CoA, which, on hydrolysis, yields citrate. Citrate is freely permeable across the mitochondrial membrane. It serves as a good source of cytosolic acetyl CoA which is used for the synthesis of fatty acids. Citrate inhibits phosphofructokinase and activates acetyl CoA carboxylase. The latter is the key enzyme in fatty acid synthesis.

Step 2 and 3. Citrate is isomerized to isocitrate by the enzyme aconitase. This is achieved in a two stage reaction of dehydration followed by hydration through the formation of an intermediate—*cis*-aconitate.

Step 4 and 5. Formation of α-ketoglutarate : The enzyme isocitrate dehydrogenase (ICD) catalyses the conversion (oxidative decarboxylation of isocitrate to oxalosuccinate and then to α-ketoglutarate. The formation of NADH and the liberation of CO_2 occurs at this stage. Three types of ICD are known. One : NAD^+ specific, located only in mitochondria. Two : $NADP^+$ specific present in mitochondria, and cytosol (third). The mitochondrial NAD^+ dependent ICD is responsible for the conversion of isocitrate to α-ketoglutarate.

Step 6. Conversion of α-ketoglutarate to succinyl CoA occurs through oxidative decarboxylation, catalysed by α-ketoglutarate dehydrogenase complex. This enzyme is dependent on five cofactors—TPP, lipoamide, NAD^+, FAD and CoA. The mechanism of the reaction is analogous to the conversion of pyruvate to acetyl CoA (Fig. 2). At this stage of the TCA cycle, second NADH is produced and the second CO_2 is liberated.

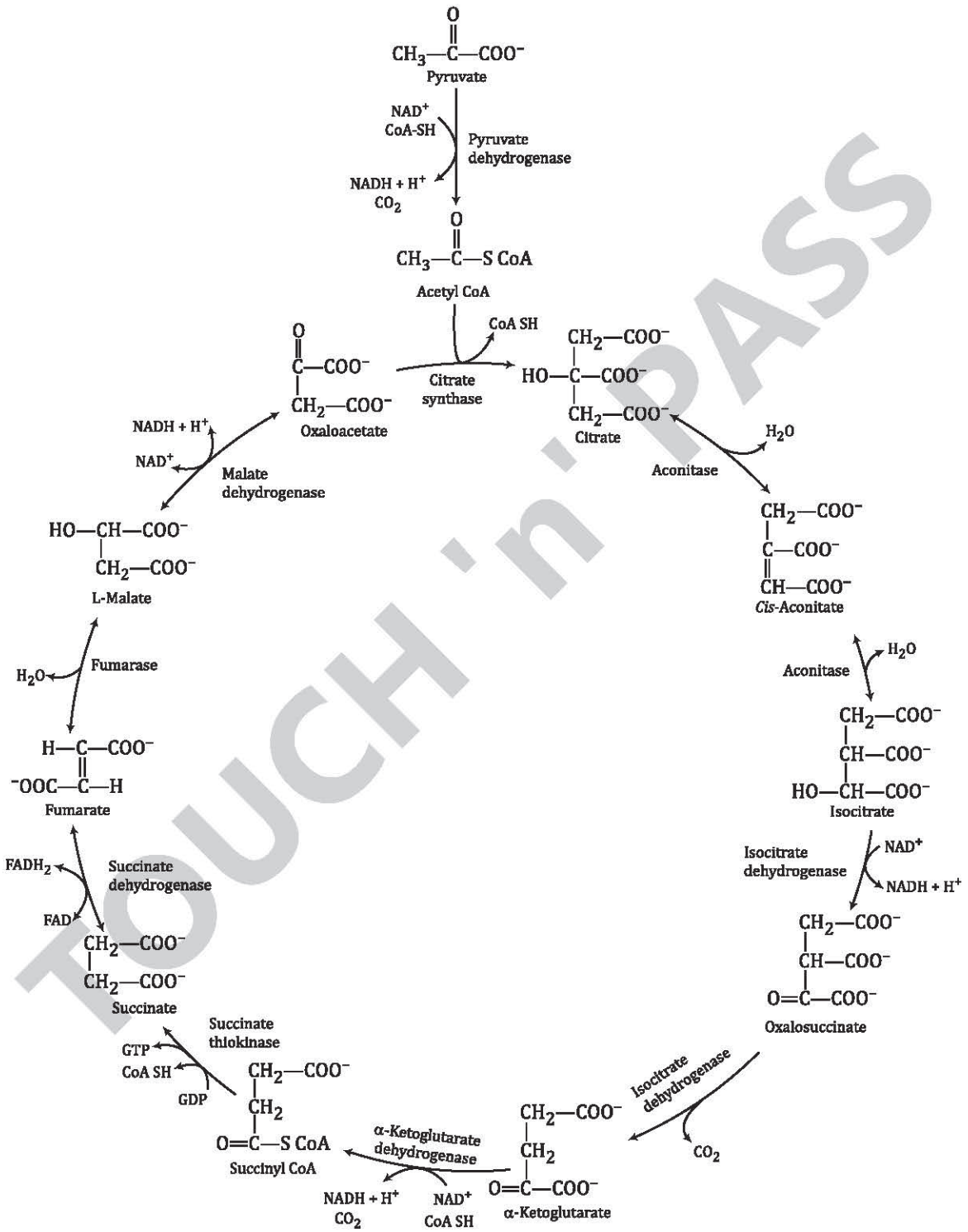


Fig. 2 : The citric acid (Krebs) cycle.

Step 7. Formation of succinate : Succinyl CoA is converted to succinate by succinate thiokinase. This reaction is coupled with the phosphorylation of GDP to GTP. This is a substrate level phosphorylation. GTP is converted to ATP by the enzyme phosphokinase.

$$GTP + ADP \longleftrightarrow ATP + GDP$$

Step 8. Conversion of succinate to fumarate : Succinate is oxidized by succinate dehydrogenase to fumarate. This reaction results in the production of $FADH_2$ and not NADH. This is due to the fact that the reducing power of succinate is not adequate to reduce NAD^+, hence FAD is utilized.

Step 9. Formation of malate : The enzyme fumarase catalyses the conversion of fumarate to malate with the addition of H_2O.

Step 10. Conversion of malate to oxaloacetate : Malate is then oxidized to oxaloacetate by malate dehydrogenase. The third and final synthesis of NADH occurs at this stage. The oxaloacetate is regenerated which can combine with another molecule of acetyl CoA and continue the cycle.

Summary of TCA cycle : The events of Krebs cycle may be summarized as

$$\text{Acetyl CoA} + 3\ NAD^+ + FAD + GDP + Pi + 2H_2O \longrightarrow 2CO_2 + 3NADH + 3H^+ + FADH_2 + GTP + CoA$$

Regeneration of oxaloacetate in TCA cycle : The TCA cycle basically involves the oxidation of acetyl CoA to CO_2 with simultaneous regeneration of oxaloacetate. As such, there is no net consumption of oxaloacetate or any other intermediate in the cycle.

Requirement of O_2 by TCA cycle : There is no direct participation of oxygen in Krebs cycle. However, the cycle operates only under aerobic conditions. This is due to the fact that NAD^+ and FAD (from NADH and $FADH_2$, respectively) required for the operation of the cycle can be regenerated in the respiratory chain only in the presence of O_2. Therefore, citric acid cycle is strictly aerobic in contrast to glycolysis which operates in both aerobic and anaerobic conditions.

Energetics of citric acid cycle : During the process of oxidation of acetyl CoA via citric acid cycle, 4 reducing equivalents (3 as NADH and one as $FADH_2$) are produced. Oxidation of 1 NADH by electron transport chain coupled with oxidative phosphorylation results in the synthesis of 3 ATP, whereas $FADH_2$ leads to the formation of 2 ATP. Besides, there is one substrate level phosphorylation. A total of 12 ATP are produced from one acetyl CoA, as shown :

Energy reaction	ATP synthesized
$3\ NADH \longrightarrow 3NAD^+$	9
$FADH_2 \longrightarrow FAD$	2
Substrate phosphorylation (GTP)	1
Total ATP for one acetyl CoA	**12**

Q.3. What is pentose-phosphate pathway? Also explain the their steps with the suitable structure.

Ans. Alternate Pathways-Pentose Phosphate Pathway

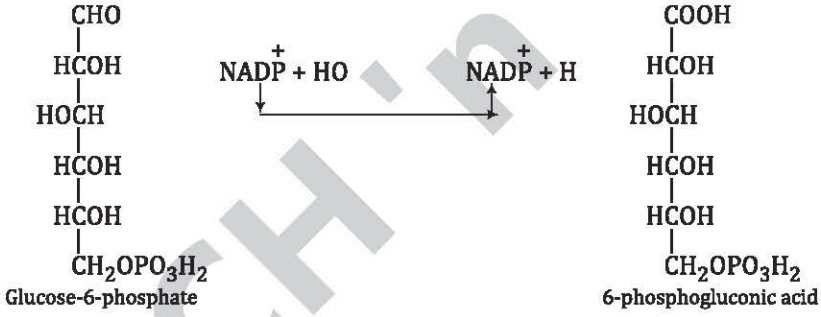
The glycolysis by Embden-Mayerohof pathway for a number of years was considered to be the main pathway for the conversion of glucose to lactic and pyruvic acids. Though 90% of glucose

is metabolized by this route, yet alternate pathways exist. Even when glycolysis and citric acid cycle are blocked, mammalian tissues can metabolize glucose at a reduced rate. Further in tissues compounds like, ribose, deoxyribose, glucosamine, uronic acids, sialic acid, neuraminic acid and sedoheptulose occur and these compounds can not be formed by the already discussed pathways.

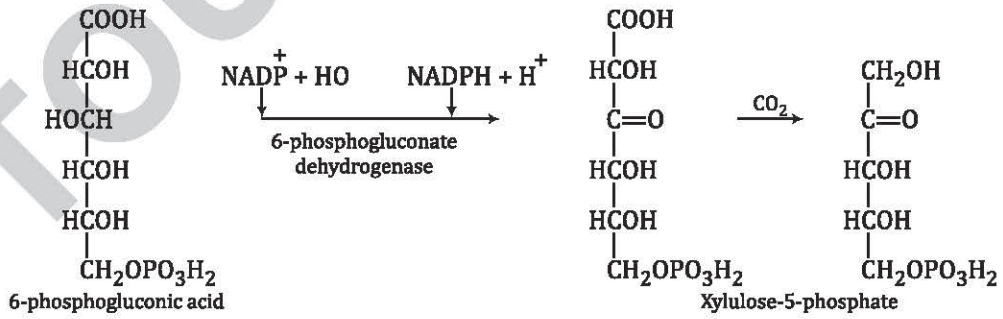
Warburg in 1931 discovered the enzyme glucose-6 phosphate dehydrogenase and later 6-phosphogluconate dehydrogenase in yeast. This discovery led to indentification of one alternate pathway of glucose metabolism, namely, the pentose phosphate pathway, some times also called Warburg-Dickens pathway or the phosphogluconate shunt or the hexose monophosphate sunt. This pathway is the major pathway for the biosynthesis of pentoses, sedoheptulose, the hexosamine, uronic acids, neuraminic acid and some other carbohydrate derivatives. It also serves for the oxidation of glucose to carbon dioxide and formation of $NADPH_2$ and ATP.

The outline of pentose phosphate pathway has been described in the cycle given here, which can be divided into two phases :

1. **Conversion of hexose to pentose : First step** is the oxidation of glucose-6-phosphate to 6-phosphogluconic acid by glucose-6-phosphate dehydrogenase and NADP.



Second step : 6-phosphogluconic acid is further oxidized to an unstable intermediate which loses CO_2 to give the pentose, xylulose-5-phosphate. NADP and 6-phosphogluconate dehydrogenase are required.



Xylulose-5-phosphate is converted into a variety of other compounds.

2. **Conversion of pentose to hexose :** Three main types of reactions are involved :
   (i) **Transketolation :** Two sugar phosphate molecules react and a—CO—CH_2OH group is transferred from one to another. Two pentose molecules, in this way, can

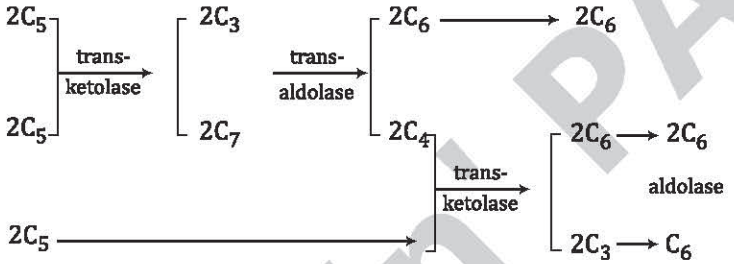
react together to give a triose phosphate and a heptose phosphate. Thus $C_5 + C_5 \rightleftharpoons C_3 + C_7$.

(ii) **Transaldolation :** In a similar way a—CHOH—CO—CH_2OH group can be transferred in a reaction between a triose phosphate and a heptose phosphate molecules, yielding a hexose phosphate and a tetrose phosphate :

$$C_3 + C_7 \rightleftharpoons C_6 + C_4.$$

(iii) Two triose phosphate molecules can combine to form a hexose diphosphate molecule, as in the glycolytic pathway.

These three types of reactions can be utilized to convert pentose quantitatively to hexose. Six pentose phosphate molecules are taken into consideration as shown below in pairs :

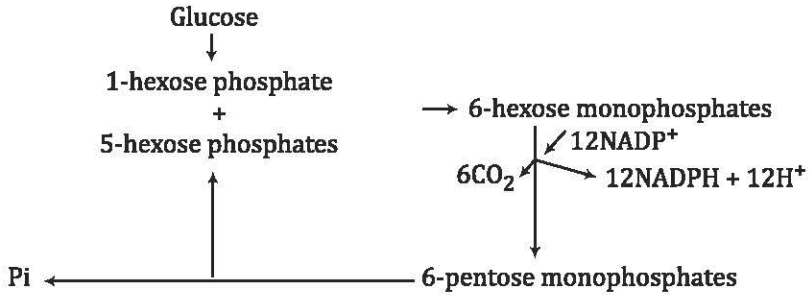


Two of the pentosephosphate molecules yield two hexose phosphate and two tetrose phosphate molecules via transketolation and transaldolation.

The tetrose phosphate molecules so formed undergo transketolation with the remaining pair of pentose phosphates to give two more hexose phosphates and two triose phosphates. The enzyme aldolase converts the two triose phosphates to give fructose-1, 6-diphosphate, which is hydrolysed by fructose-1, 6-diphosphatase to yield another hexose monophosphate. Thus the overall reaction involves the conversion of six pentose phosphate molecules to yield 5 molecules of hexose phosphates.

$$6C_5 \rightleftharpoons 5C_6$$

In the pentose phosphate pathway the two types of reactions described above are combined. Six hexose phosphates are oxidized to give six pentose monophosphates and six molecules of CO_2. Six pentose monophosphates are then reconverted into five hexose monophosphates. Five hexose monophosphate molecules can combine with one more hexose monophosphates and repeat the cycle :



The overall effect of the reaction is the complete oxidation of one glucose molecule. The energy is derived entirely from the transport of 24 hydrogen atoms from NADPH to molecular oxygen. Theoretically, $12 \times 3 = 36$ molecules are produced. Conversion of glucose to glucose-b-phosphate consumes one molecule of ATP. If this is deducted 35 molecules are the net gain which is less than the yield in glycolysis and citric acid cycle. However, it is doubtful if this cycle functions as the source of energy. This cycle may be important for the conversion of NADP into NADPH as biosynthesis reactions like fatty acids synthesis require large number of NADPH molecules. This cycle may be important in liver and adrenal cortex. Muscles use only the glycolysis.

An important feature of this pathway is that ATP is required for its operation once glucose-6-phosphate has been formed. Thus, the pathway may continue to operate under relatively anaerobic conditions.

Q.4. Write about the β-oxidation and ω-oxidation.

Ans. **Metabolism of Glycerol**

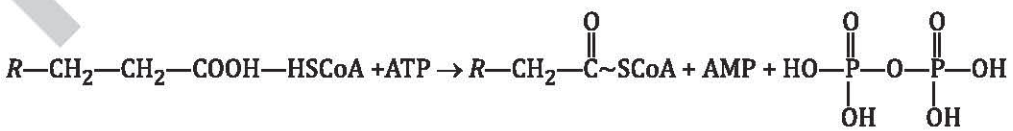
The major pathway for the fatty acids is by the "β-oxidation". In this process, the fatty acids are oxidized at the carbon atom β to the carboxyl group, and is converted into a fatty acid chain, having two carbon atoms less and acetyl coenzyme A. This process of removal of two carbon atoms from the chain is continued until the entire fat molecule is converted to CoA.

β-Oxidation : The β-oxidation theory is supported by the experiments of Knoop who fed animals with fatty acids of varied lengths but containing a phenyl-group in the ω-carbon atom. He found in the urine either benzoic acid or phenyl acetic acid, in the form of the conjugated derivatives, hippuric acid and phenaceturic acid, respectively. Benzoic acid was present when the fatty acid contained odd number of carbon atoms, while phenaceturic acid was obtained when even number of carbon atoms were present. Knoop concluded that the carbon atoms could not be removed one after the other during the oxidation of fatty acid, but came off in pairs, from the β-carbon atom.

Green, Lynen and Kennedy theory : The researches of the followers led by Green, Lynen and Kennedy supply the more recent information with regard to the mechanism of fatty acid oxidation.

In the mitochondria, five reactions are involved in the formation of acetyl coenzyme A.

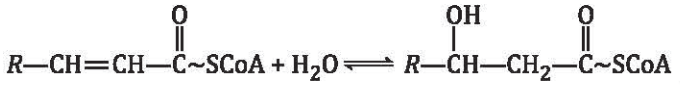
1. From the free fatty acid, the initial reaction is the formation of acyl coenyme A derivative. This is known as the "activation".



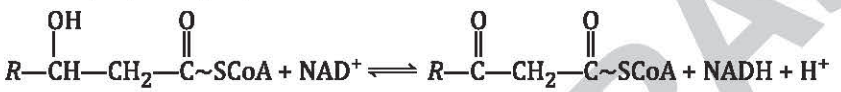
   In the reaction at least three thiokinases are involved. One of them acts on acetic and propionic acids, the second acts on acids having four to twelve carbon atoms and the third acts on acids having more than twelve carbon atoms.

2. **Desaturation :** Acyl dehydrogenases dehydrogenate the activated fatty acid at α and β positions. These enzymes contain a flavoprotein, flavoadenine nucleotide.

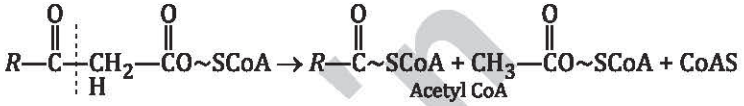
3. **Hydration :** A molecule of water is added across the double bond in the next reaction. β-hydroxyacyl CoA derivative, in the presence of enol hydrase, is formed.



4. **Oxidation :** In the presence of β-hydroxyacyl dehydrogenases and NAD^+, the hydroxyl group of the β-hydroxyacyl CoA derivative is oxidized to a keto group.



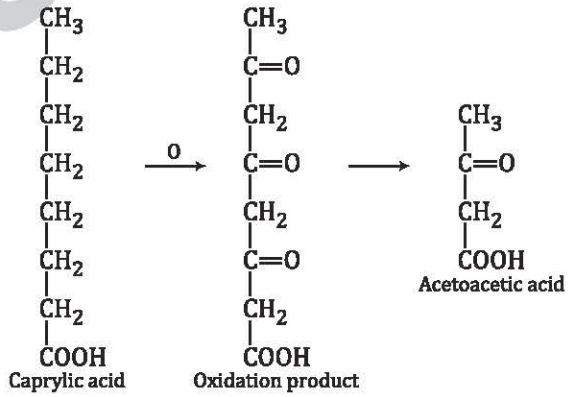
5. **Thiolytic cleavage :** The next step is cleavage of the β-keto derivative by a molecule of coenzyme A. As it involves hydrolysis with the sulphydryl group of CoA, it is called thiolysis. The enzymes involved are thiolases.



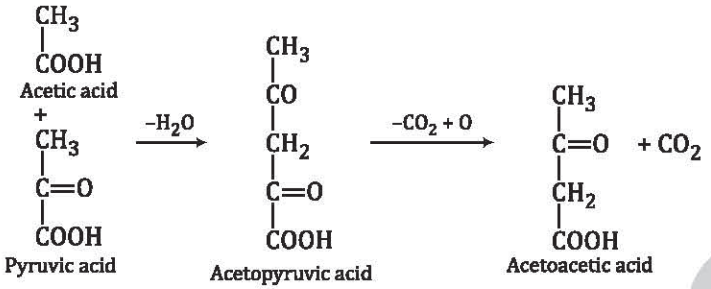
The products are a mole of acetyl CoA and an activated fatty acid, which is two carbons shorter than the fatty acid. By repeating the process the entire fatty acid is converted to acetyl CoA.

Multiple alternate oxidation : According to Jowelt and Quastef, who have suggested an alternative for the β-oxidation theory, starting with the β-carbon atom of a fatty acid, alternate carbon atoms are oxidized to ketones before the molecule breaks down. According to the β-oxidation theory, whatever size the fatty acid may be, each molecule should give rise to one molecule of acetoacetic acid. However, fatty acids containing more than eight carbon atoms give more acetic acid than those with fewer carbon atoms.

If fatty acids are oxidized according to the multiple alternate oxidation theory, the above fact can be explained.



Kreb's-Johnston theory : According to this theory, acetoacetic acid is obtained when acetic acid, resulting from beta oxidation, condenses with pyruvic acid to form acetopyruvic acid, which on decarboxylation and oxidation gives acetoacetic acid.



Omega oxidation : Some fatty acids can undergo oxidation at the carbon atom farthest removed from the carboxyl group ('omega' carbon), producing a dicarboxylic acid, which is subjected to β-oxidation and cleavage to form successively smaller dicarboxylic acids. The oxidation proceeds step by step, forming first w-hydroxy acid, followed by successive dehydrogenations to an w-aldehydic acid and finally dicarboxylic acid. Omega oxidation is a minor pathway of fatty acid metabolism.

Q.5. What are the ketone bodies? Also explain the ketogenesis process.

Ans.

Ketone Bodies

The compounds namely acetone, acetoacetate and β-hydroxybutyrate (or 3-hydroxybutyrate) are known as ketone bodies. Only the first two are true ketones while β-hydroxybutyrate does not possess a keto (C = O) group. Ketone bodies are water-soluble and energy yielding. Acetone, however, is an exception since it cannot be metabolised.

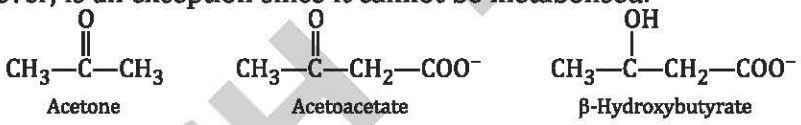


Fig. 1 : Structures of ketone bodies.

Ketogenesis

The synthesis of ketone bodies occurs in the liver. The enzymes for ketone body synthesis are located in the mitochondria matrix. Acetyl CoA, formed by oxidation of fatty acids, pyruvate or some amino acids, is the precursor for ketone bodies. Ketogenesis occurs through the following reactions.

1. Two moles of acetyl CoA condense to form acetoacetyl CoA. This reaction is catalysed by thiolase, an enzyme involved in the final step of β-oxidation. Hence, acetoacetate synthesis is appropriately regarded as the reversal of thiolase reaction of fatty acid oxidation.
2. Acetoacetyl CoA combines with another molecule of acetyl CoA to produce β-hydroxy β-methyl glutaryl CoA (HMG CoA). HMG CoA synthase, catalysing this reaction, regulates the synthesis of ketone bodies.
3. HMG CoA lyase cleaves HMG CoA to produce acetoacetate and acetyl CoA.
4. Acetoacetate can undergo spontaneous decarboxylation to form acetone.
5. Acetoacetate can be reduced by a dehydrogenease to β-hydroxybutyrate.

The carbon skeleton of some amino acids (ketogenic) is degraded to acetoacetate or acyl CoA and, therefore, to ketone bodies, *e.g.,* leucine, lysine, phenylalanine etc.

Utilization of ketone bodies

The ketone bodies, being water-soluble, are easily transported from the liver to various tissues. The two ketone bodies-acetoacetate and β-hydroxybutyrate serve as an important source of energy for the peripheral tissues such as skeletal muscle, cardiac muscle, renal cortex etc. The tissues which lack mitochondria (*e.g.,* erythrocytes) however, cannot utilize ketone bodies. The production of ketone bodies and their utilization becomes more significant when glucose is in short supply to the tissues, as observed in starvation and diabetes mellitus. During prolonged starvation, ketone bodies are the major fuel source for the brain and other parts of central nervous system. It should be noted that the ability of the brain to utilize fatty

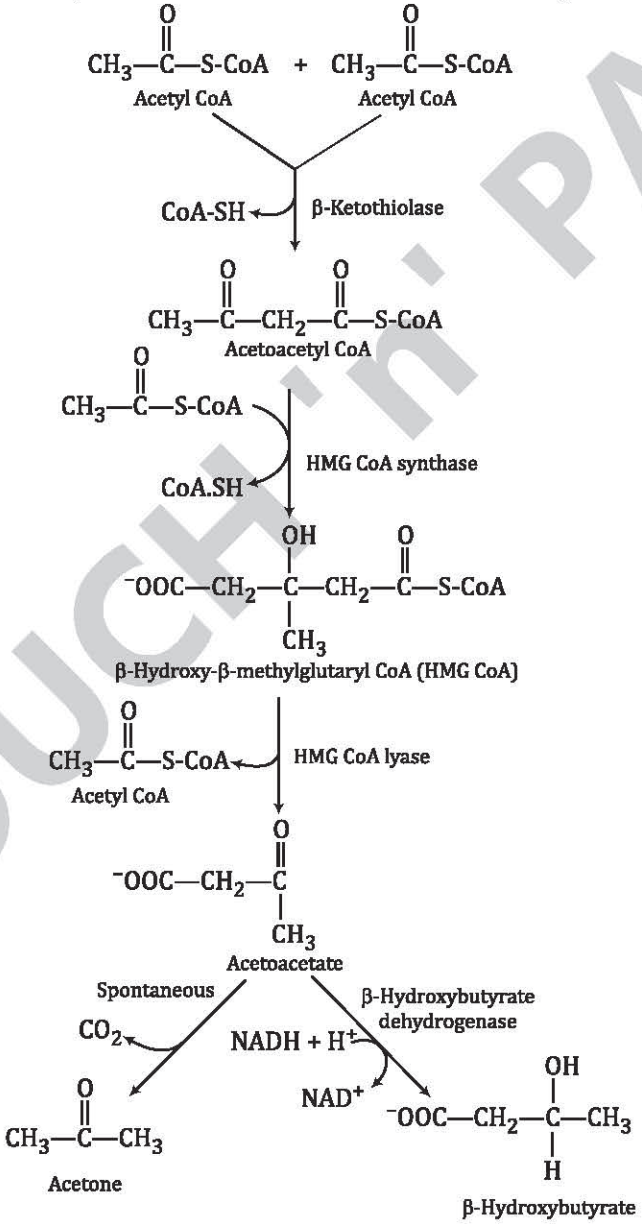


Fig. 2 : Synthesis of ketone bodies (ketogenesis).

acids for energy is very limited. The ketone bodies can meet 50-70% of the brain's energy needs. This is an adaptation for the survival of the organism during the periods of food deprivation.

Reactions of ketone bodies : β-Hydroxybutyrate is first converted to acetoacetate (reversal of synthesis and metabolized. Acetoacetate is activated to acetoacetyl CoA by a mitochondrial enzyme thiophorase (succinyl CoA acetoacetate CoA transferase). The coenzyme A is donated b, succinyl CoA, an intermediate in citric acid cycle. Thiophorase is absent in liver, hence ketone bodies are not utilized by the liver. Thiolase cleaves acetoacetyl CoA to two moles of acetyl CoA.

Q.6. What do you mean by biosynthesis of fatty acids? Also explain the biosynthesis of palmitic acid with the diagrams.

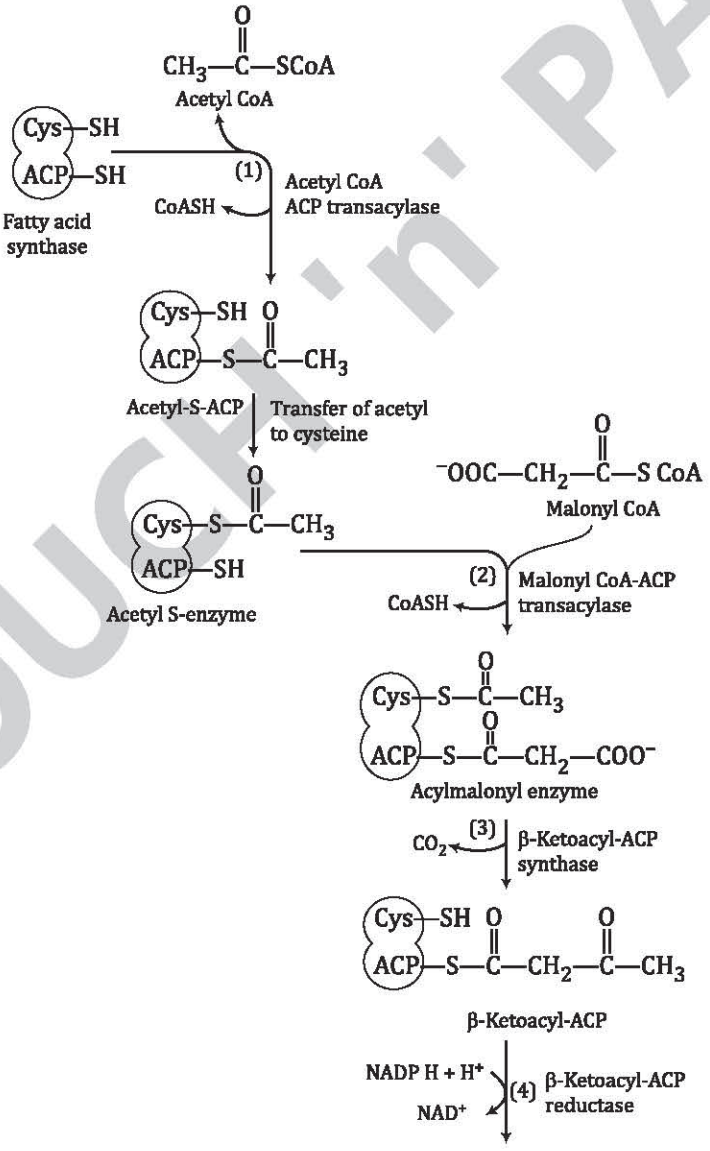
Ans. **Biosynthesis of Fatty Acids**

The dietary carbohydrates and amino acids, when consumed in excess, can be converted to fatty acids and stored as triacylglycerols. ***De novo*** (new) synthesis of fatty acids occurs predominantly in liver kidney, adipose tissue and lactating mammary glands. The enzyme machinery for fatty acid production is located in the cytosomal fraction of the cell. Acetyl CoA is the source of carbon atoms while NADPH provides the reducing equivalents and ATP supplies energy for fatty acid formation. The fatty acid synthesis may be learnt in 3 stages :

1. **Production of acetyl CoA and NADPH :** Acetyl CoA and NADPH are the prerequisites for fatty acid synthesis. Acetyl CoA is produced in the mitochondria by the oxidation of pyruvate and fatty acids, degradation of carbon skeleton of amino acids, and from ketone bodies. Mitochondria, however, are not permeable to acetyl CoA. An alternate or a bypass arrangement is made for the transfer of acetyl CoA to cytosol. Acetyl CoA condenses with oxaloacetate in mitochondria to form citrate. Citrate is freely transported to cytosol where it is cleaved by citrate lyase to liberate acetyl CoA and oxaloacetate. Oxaloacetate in the cytosol is converted to malate. Malic enzyme converts malate to pyruvate. NADPH and CO_2 are generated in this reaction. Both of them are utilized for fatty acid synthesis.
2. **Formation of malony CoA :** Acetyl CoA is carboxylated to malonyl CoA by the enzyme acetyl CoA carboxylase. This is an ATP-dependent reaction and requires biotin for CO_2 fixation. The mechanism of action of acetyl CoA carboxylase is similar to that of pyruvate carboxylase. Acetyl CoA carboxylase is a regulatory enzyme in fatty acid synthesis (details given later).
3. **Reactions of fatty acid synthase complex :** The remaining reactions of fatty acid synthesis are catalysed by a multifunctional enzyme known as fatty acid synthase (FAS) complex. In eukaryotic cells, including man, the fatty acid synthase exists as a dimer with two identical units. Each monomer possesses the activities of seven different enzymes and an acyl carrier protein (ACP) bound to 4'-phosphopantetheine. Fatty acid synthase functions as a single unit catalysing all the seven reactions. Dissociation of the synthase complex results in loss of the enzyme activities. In the lower organisms (prokaryotes), the fatty acid synthesis is carried out by a multienzyme complex in association with a separate acyl carrier protein. This is in contrast to eukaryotes where ACP is a part of fatty acid synthase.

The sequence of reactions for the extra mitochondrial synthesis of fatty acids (palmitate) is depicted in Fig.

1. The two carbon fragment of acetyl CoA is transferred to ACP of fatty acid synthase, catalysed by the enzyme, acetyl CoA-ACP transacylase. The acetyl unit is then transferred from ACP to cysteine residue of the enzyme. Thus ACP site falls vacant.
2. The enzyme malonyl CoA-ACP transacylase transfers malonate from malonyl CoA to bind to ACP.
3. The acetyl unit attached to cysteine is transferred to malonyl group (bound to ACP). The malonyl moiety loses CO_2 which was added by acetyl CoA carboxylase. Thus, CO_2 is never incorporated into fatty acid carbon chain. The decarboxylation is accompanied by loss of free energy which allows the reaction to proceed forward. This reaction is catalyzed by β-ketoacyl ACP synthase.



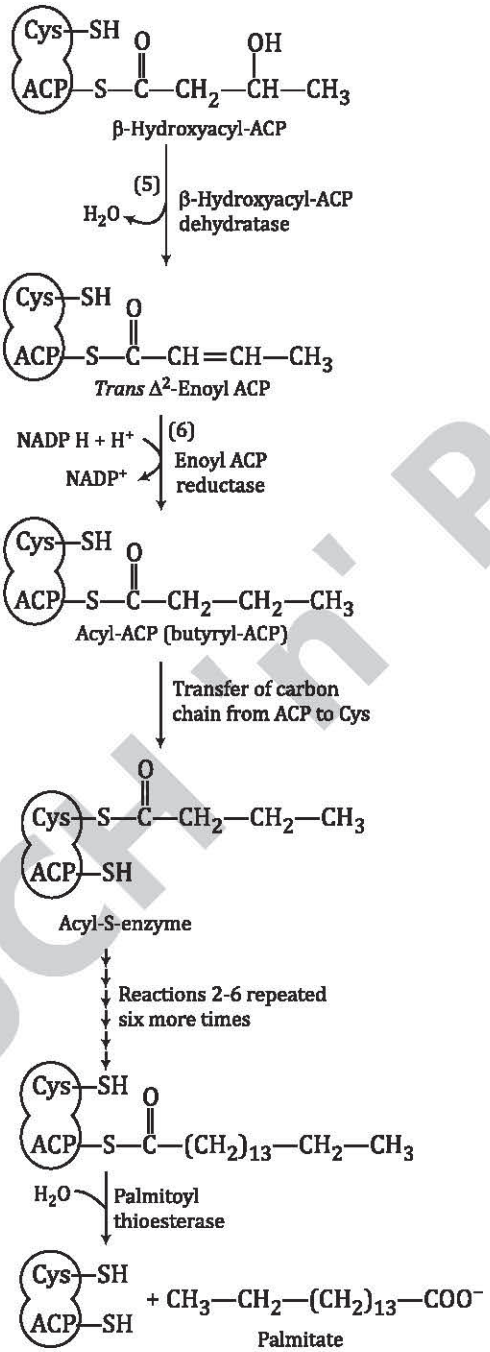


Fig. : Biosynthesis of long chain fatty acid-palmitate. (*Cys*-Cysteine; ACP-Acyl carrier protein; The pathway repeats 7 times to produce palmitate; the first two carbons at the methyl end are directly from acetyl CoA, the rest of the carbons come from malonyl CoA).

4. β-Ketoacyl ACP reductase reduces ketoacyl group to hydroxyacyl group. The reducing equivalents are supplied by NADPH.

5. β-Hydroxyacyl ACP undergoes dehydration. A molecule of water is eliminated and a double bond is introduced between α and β carbons.
6. A second NADPH-dependent reduction, catalysed by enoyl-ACP reductase occurs to produce acyl-ACP. The four-carbon unit attached to ACP is butyryl group.

   The carbon chain attached to ACP is transferred to cysteine residue and the reactions 2-6 are repeated 6 more times. Each time, the fatty acid chain is lengthened by a two-carbon unit (obtained from malonyl CoA). At the end of 7 cycles, the fatty acid synthesis is complete and a 16-carbon fully saturated fatty acid—namely palmitate—bound to ACP is produced.
7. The enzyme palmitoyl thioesterase separates palmitate from fatty acid synthase. This completes the synthesis of palmitate.

Summary of palmitate synthesis : Of the 16 carbons present in palmitate, only two come from acetyl CoA directly. The remaining 14 are from malonyl CoA which, in turn, is produced by acetyl CoA. The overall reaction of palmitate synthesis is summarized.

$$8 \text{ Acetyl CoA} + 7 \text{ ATP} + 14 \text{ NADPH} + 14 \text{ H}^+ \longrightarrow \text{Palmitate} + 8 \text{ CoA} + 7 \text{ ADP} + 7 \text{ Pi} + 6\text{H}_2\text{O}$$

❑❑❑

UNIT-IV

Metabolism of Proteins and Nucleotides

SECTION-A VERY SHORT ANSWER TYPE QUESTIONS

Q.1. What do you mean by non-essential amino acid?

Ans. Non-essential amino acids are those which are produced by the body and need not be supplied in the diet while essential amino acids are not produced in the body so these must be the part of the diet.

Q.2. Name various amino acids essential for infants.

Ans. Only arginine and histidine are considered essential for infants as arginine is required for proper growth and development while histidine provides inflammatory response and the production of hydrochloric acid in the stomach. These are not produced in the body and must be supplemented in the diet.

Q.3. In which form the nitrogen is incorporated into an amino acid?

Ans. Source of nitrogen in all amino acid is ammonium ion. It is the key component of amino acids. The ammonium ion is first in amino acids and then in other biomolecules.

Q.4. Name metabolic pathway intermediate of which have not been used in the synthesis of amino acids?

Ans. All amino acids are derived from the intermediates of metabolic pathways like glycolysis, citric acid cycle and the pentose phosphate pathway (PPP). 20 amino acids have been divided into 6 families on the basis of the primary carbon source of each amino acid.

Q.5. Which does not take part in transmination during amino acid catabolism?

Ans. Except serine rest three amino acids, *i.e.,* proline, threonine and lysine take part in transamination during amino acid catabolism. Amino group donor is specific and called aminotransferase while acceptor is almost always α-ketoglutarate.

Q.6. Name the type of cell in which synthesis of urea cycle takes place?

Ans. Hepatocytes are liver cells in which urea synthesis take place in five enzymatic reactions, first two reactions occur in mitochondria while the rest three reactions take place in the cytosol.

Q.7. Name a hereditary disease which is caused due to an error in amino acid metabolism?

Ans. Phenylketonuria is a hereditary disorder caused by defective amino acid metabolism in which phenylalanine is not converted to tyrosine and deposited in the body. It is caused due to deficiency of enzyme phenylalanine hydroxylase.

Q.8. What is name of the precursor of RNA?

Ans. Uridylate of UMP is a pyrimidine nucleotide formed by the decarboxylation of arotidylate (OMP) during pyrimidine synthesis. UMP further gets converted to a ribonucleotide and act as a precursor of RNA.

Q.9. Name the enzyme, the activity of which is inhibited by the chemothera- peutic agent during deoxyribonucleotide synthesis?

Ans. Methotrexate and aminopterin are two anticancer drugs which inhibits the activity of dihydrofolate reductase. This will stop the formation of deoxyribonucleotide or DNA and the growth of the cell.

Q.10. Which acid is not the precursor of a purine ring?

Ans. Purine ring is derived from various precursors like glutamine (Nz and Na), glycine (C_4, C_5 and N_4) aspartate (N_1), CO_2 (C_6), folate (C_2) and (C_8). Except for lysine all are the precursor of puring ring.

Q.11. What is the final product of purine degradation in mammals?

Ans. Purine nucleotides are sequentially degraded from inosine to hypoxanthine and guanine and finally to the uric acid which is excreted with the urine in the human being while in some other animals it is further degraded to urea and ammonia.

Q.12. What disorder is caused due to the high serum level of urate?

Ans. Gout is caused due to the high amount of uric acid, which is the product of purine degradation. It involves precipitation of sodium urate crystals in the joints and causes inflammation.

Q.13. Name the vitamin which is not a fat soluble vitamin?

Ans. In general, there are only four fat-soluble vitamins (vitamin A, D, E, K). Vitamin C is an ascorbic acid which is water soluble and precursors of all the coenzymes.

Q.14. Name the vitamin, deficiency of which may cause beri-beri?

Ans. Deficiency of thiamine (vitamin B_1) can lead to beri-beri. It is mostly found in the area where polished rice in a major component of the diet.

Q.15. Which acid is a component of the co-enzyme-A?

Ans. Panthothenic acid is used in the synthesis of coenzyme-A, which is also an acyl group carrier. It performs two main functions, activation of an acyl group for transfer and activation of hydrogen of the acyl group.

Q.16. Which vitamin is also known as cobalamin?

Ans. Vitamin-B_{12} is also known as cobalamin, it is a part of vitamin-B complex along with vitamin-B_{11} (Folic acid), Vit-B_6 (Pyridoxine) and Vit-B_2 (riboflavin).

Q.17. Which vitamin functions as hormone as well as visual pigment?

Ans. Vitamin-A is also known as retinol, it is isoprenoid alcohol and essential for vision, growth, reproduction and maintenance of epithelial tissues.

Q.18. Which of the vitamin takes part in blood clotting?

Ans. Vitamin-K plays role in post-translational modification of various blood clotting factors. It is a fat-soluble vitamin which requires complete synthesis of blood coagulation protein.

Q.19. Which vitamin serves as a hormone precursor?

Ans. Vitamin-D acts as a hormone precursor. UV component of sunlight falls on 7-dehydrocholesterol and get converted to cholecalciferol (vitamin-D_3) in the skin. Vitamin-D_3 absorbed into the blood and transported to liver and kidney where with the help of enzyme it formed calcitriol (a steroid hormone).

SECTION-B SHORT ANSWER TYPE QUESTIONS

Q.1. What are metabolism of nucleotides? Also explain biosynthesis of purine nucleotides.

Ans. Metabolism of Nucleotides

Nucleotide metabolism involves several interconnected pathways. Nucleotides can be synthesized de novo, or from components "salvaged" from the degradation products of nucleic acids. When in excess, nucleotides are degraded to products that can either be consumed by other pathways or excreted. Defects in the pathways for de novo synthesis, salvage, and degradation of nucleotides result in clinical disorders, and many drugs target these pathways.

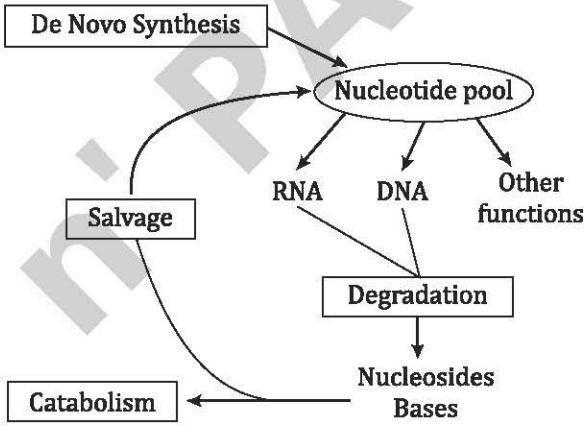


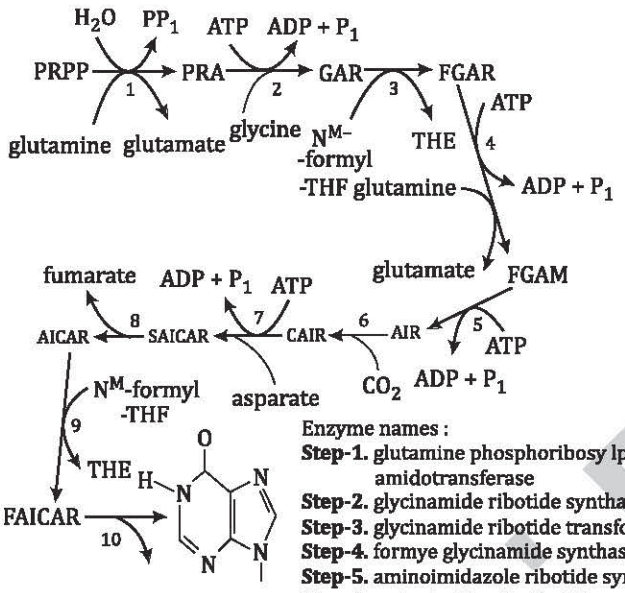
Fig. 1 : Metabolism of nucleotides

Nucleotide anabolism can be broadly characterized as **purine** and **pyrimidine biosynthesis**.

Biosynthesis of Purine Nucleotides

Purine nucleotides are synthesized in cytoplasm of most of the tissues. The major site for purine synthesis is liver. Since purine ring are synthesized from different small components, they are makorly denoted by de novo synthesis. Different sources such as respiratory CO_2, amino group from aspartate, formyl group, amide group from glutamine and glycine etc., are required for formation of purine ring. As a primary requirement of purine synthesis, purine ring are first built upon a ribose-5-phosphate molecule. De novo synthesis of purine is a multi enzyme reaction composed of 10 steps as follow as :

In salvage pathway purines were recycled from degraded nucleotide. Both nucleosides and deoxynucleosides can be salvaged. Phospho ribosyl phyrophosphate (PRPP) is the starting material for salvage pathway. In salvage pathway purines are salvaged by adenine phosphor ribosyl transferase (APRTase) and hypoxanthine guanine phosphoribosyl transferase (HGPRTase). Salvage pathway are encountered in tissues such as RBC and brain, where there is absence of de novo pathway.



Enzyme names :

Step-1. glutamine phosphoribosy lpyrophosphate amidotransferase
Step-2. glycinamide ribotide synthase
Step-3. glycinamide ribotide transformylase
Step-4. formye glycinamide synthase
Step-5. aminoimidazole ribotide synthase
Step-6. aminoimidazole ribotide carboxy lase
Step-7. succiny laminoimidazole carboxamideribotide synthase
Step-8. adenylosuccinate lyase
Step-9. aminoimidazole carboxamide ribotide transformy lase
Step-10. IMP cyclohy drolase

Fig. 2 : Biosynthesis of purine nucleotides

Q.2. Write about the calciferol.

Ans.

Calciferol or Vitamin D

The term vitamin D is used to describe a number of compounds with antirachitic properties which are chemically related to the sterols. In 1921, Mellanby recognized the need for a factor from food (cod liver oil) which could prevent rickets.

In the absence of this vitamin or in its the presence in insufficient amounts, rickets in varying degrees develops. In the childhood, the disease is associated with bow-legs, knock-knees, enlarged joints, etc. The growing parts of the bone, particularly the ends of the long bones of arms and legs are affected. The name calciferol includes a number of chemically related compounds, all of which possess the property of preventing or curing rickets. The two most important are ergocalciferol and cholecalciferol. Calciferol is not readily destroyed by heat.

It is believed that the primary function of vitamin D is to regulate the absorption and utilization of Ca and P. As an evidence of this, a relatively large quantity of Ca and P is lost in the faeces of rickets patients.

That the increased absorption alone is not sufficient to account for the function of the vitamin is brought out by the work of Greenburg. Using radiophosphorus (P_{32}) he studied the influence of vitamin D on the phosphorus metabolism of ricketic rats. The increase in the absorption of phosphate was from 10 to 15 per cent.

Intants and young children require some 400 to 700 I.U. (international unit) of calciferol per day. Only very small amounts are needed by adults, probably less than 100 I.U. daily. It is important to note that toxic effects may be produced by higher doses. The toxic effects,

probably secondary to hypercalcaemia, include general symptoms with renal stones, calcification of arteries and even renal failure.

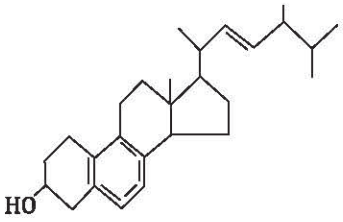


Fig. Calciferol or Vitamin D

Q.3. Write a short note on polypeptide linkage.

Ans. **Polypeptide Chain**

Amino acids in proteins (or polypeptides) are joined together by peptide bonds. The sequence of *R*-groups along the chain is called the **primary structure**. Secondary structure refers to the local folding of the polypeptide chain. Tertiary structure is the arrangement of secondary structure elements in 3-dimensions and quaternary structure describes the arrangement of a protein's subunits.

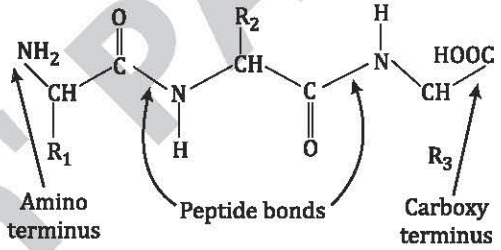


Fig. 1 : Polypeptide chain

Linus Pauling and **Robert Corey** analysed the geometry and dimensions of the peptide bonds in the crystal structures of molecules containing one or a few peptide bonds. Their results are summarised in this diagram where the consensus bond lengths are shown in Angstrom units. Bond angles in degrees are also shown for the peptide N and C atoms.

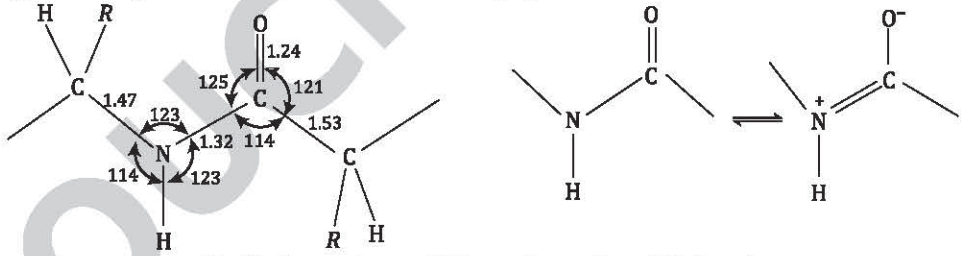


Fig. 2 : Geometry and Dimensions of peptide bonds

Note that the C—N bond length of the peptide is 10% shorter than that found in usual C—N amine bonds. This is because the peptide bond has some double bond character (40%) due to resonance which occurs with amides. The two canonical structures are : As a consequence of this resonance all peptide bonds in protein structures are found to be almost planar, *i.e.,* atoms Calpha (i), C(i), O(i), N(i +1) H(i +1) and Calpha (i +1) are approximately co-planar. This rigidity of the peptide bond reduces the degrees of freedom of the polypeptide during folding.

The peptide bond nearly always has the *trans* configuration since it is more favourable than *cis,* which is sometimes found to occur with proline residues.

As can be seen above, steric hindrance between the functional groups attached to the C-alpha atoms will be greater in the *cis* configuration. However for proline residues, the cyclic nature of the side chain means that both *cis* and *trans* configurations have more equivalent energies.

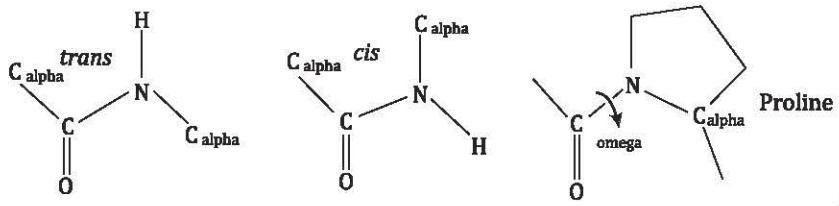


Fig. 3 : *cis* and *trans* configuration

Thus proline is found in the *cis* configuration more frequently than other amino acids. The omega torsion angle of proline will be close to zero degrees for the cis configuration, or most often, 180° for the *trans* configuration.

Q.4. Write a short note on tocopherol vitamin.

Ans. **Tocopherol or Vitamin E**

It has been shown by **Evans, Bishop** and **Sure** that a synthetic diet free of cereal grains causes normal growth in rats but fails to bring about normal reproduction and the latter was only possible by incorporating in this diet small quantities of natural food-cereal grains, green leaves and legumes etc. The necessary factor is known as **vitamin E.** It is also known as "antisterility" vitamin. In the absence of vitamin E the germinal epithelium of the testis of rats is destroyed. In the female rat, ovulation and fertilization take place, but there is death and resorption of the foetus. This situation can be relieved by incorporating vitamin E in the diet.

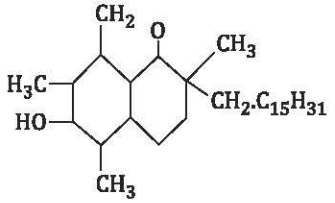


Fig. Tocopnerol or Vitamin E

Vitamin E is soluble in fat solvents and insoluble in water. It is resistant to heat (up to 200°C) but is fairly easily oxidized and destroyed by ultraviolet rays. Tocopherol is found in α, β and γ forms, of which α-form is biologically the most potent and is now readily available as a synthetic product. It can easily be absorbed from the intestinal tract and stored, to some extent, in body fats and muscles etc.

As described above, it is a factor responsible for successful reproduction in rats. If a pregnant rat is deprived of tocopherol, the foetus dies after the first week of gestation and is resorbed, apparently because of mal-development of the foetal mesoderm. Foetal resorption can be prevented by giving vitamin E during the first week of pregnancy. In male rats, vitamin E deficiency leads to progressive atrophy of the the testes with degeneration of the spermforming cells. Permanent sterility results which cannot be relieved by vitamin E.

A large number of animals, including monkeys, require tocopherol for the structural and functional integrity of skeletal, cardiac and smooth muscle. The animal becomes weak and then paralyzed, finally dyes of respiratory paralysis. These changes can be reversed by vitamin E. This nutritional muscular dystrophy clearly implies that tocopherol has an essential, though as yet unknown, role in muscle metabolism.

There is no good evidence that a deficiency syndrome occurs in man and none that human muscular dystrophy has a nutritional value.

Vitamin E is found in small amounts in most vegetables and meat. The richest sources are the vegetable oils, of which wheat germ oil is the most potent, but fish liver oils are almost devoid of it.

Q.5. What do you mean by pyrimidine synthesis?

Ans. **Pyrimidine Synthesis**

Purines are synthesized by building the ring system on the ribose. In contrast, the pyrimidine ring is constructed first, followed by attachment of the pyrimidine base to ribose using a phosphoribosyltransferase similar to those used for purine salvage reactions. In both purine and pyrimidine synthesis, phospho ribosyl phyrophosphate (PRPP) is used as the ribose donor, but the stage of the pathway is different.

The first step of the pyrimidine synthesis pathway is the condensation of bicarbonate with nitrogen derived from glutamine to form carbamoyl phosphate. The enzyme involved is carbamoyl phosphate synthetase II and is different from the enzyme catalyzing the equivalent step in the urea cycle. Carbamoyl phosphate synthetase II has three major differences :

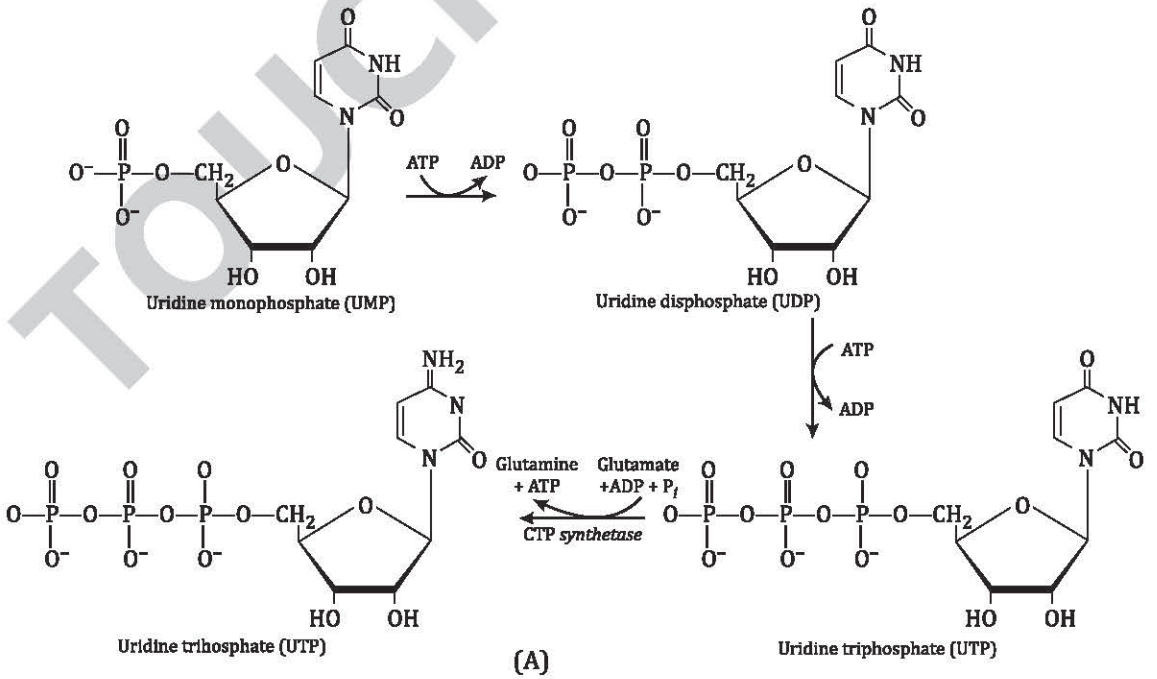
1. It uses nitrogen from glutamine rather than from ammonium.
2. It is a cytosolic rather than a mitochondrial enzyme.
3. Its regulation is completely different.

In animals two separate pools of carbamoyl phosphate were noticed, they are :

1. Mitochondrial pool, used for the urea cycle.
2. Cytosolic pool, used for pyrimidine synthesis.

While in bacteria a single pool of carbamoyl phosphate was used for both purposes, and therefore their pathways are regulated slightly differently. The pyrimidine ring skeleton comes from two molecules, the carbamoyl phosphate from the first step, and the aspartate added in the second step.

The ribose ring is not added until the synthesis of the pyrimidine orotic acid is complete. This orotic acid is then attached to PRPP with release of pyrophosphate. UMP is the first "completed" product. Uridine monophosphate (UMP) can then be phosphorylated to produce



(A)

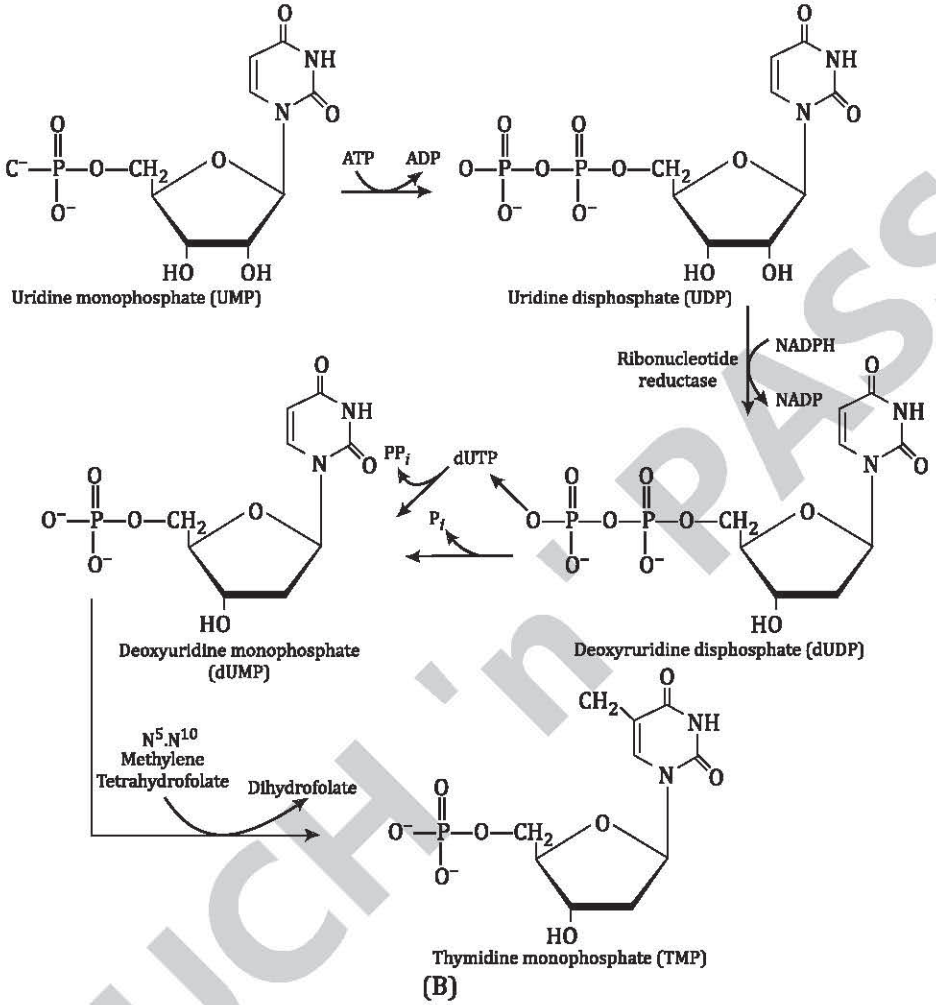


Fig A, B. Pyrimidine synthesis

uridine disphosphate (UDP). UDP acts as a branch point; it can be converted to uridine triphosphate (UTP) and used as a nucleotide, or it can serve as a substrate for the synthesis of the two other major pyrimidine nucleotides. Both cytidine triphosphate (CTP) and thymidine triphosphate (TTP) were synthesized as described in the following reaction.

Q.6. Write about the ascorbic acid with structure.

Ans. **Ascorbic Acid or Vitamin C**

Ascorbic acid is also known as vitamin C. It is the vitamin, whose absence gives rise to scurvy. This disease is characterized by a tendency of bleeding, with pathological changes in teeth and gums. In guinea pigs, in which experimental scurvy can be induced by a diet lacking in vitamin C, the joints become enlarged and painful.

Pure ascorbic acid is a white crystalline, solid and freely soluble in water with a pleasant acidic taste. It is a powerful reducing agent and reduces Fehling's solution in cold and itself is converted into dehydroxy-ascorbic acid giving up two hydrogen atoms. This property of the

vitamin is also used for its quantitative estimation. The presence of ascorbic acid in a tissue or even in a cell can be detected by submitting the preparation to a weak solution of $AgNO_3$. Parts containing the vitamin are indicated by deposits of silver. In the presence of traces of Cu and oxygen, the vitamin is rapidly oxidized at pH value above 4.0.

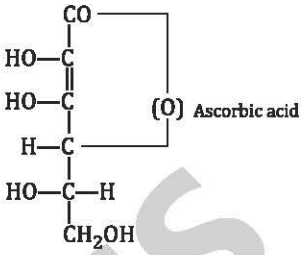


Fig. D-glucose → *D*-glucuronolactone → *L*-gluconolactone → *L*-ascorbic acid.

Ascorbic acid is synthesized by certain moulds, fungi, higher plants and animals except the guinea pig, primates and man. The biosynthetic pathway is as follows :

In the rat the process takes place in the liver, but in man, primates and the guinea pig, the liver lacks the enzyme necessary for the final step. These species, therefore develop deficiency symptoms (scurvy), if the diet is lacking in the vitamin.

Ascorbic acid is present in all body fluids and tissues. In the cells of adrenal cortex and medulla the vitamin is found aggregated near the Golgi apparatus. A high content of ascorbic acid is characteristic, especially of glandular tissues; thus the supra-renal glands contain some 100 to 200 mg/100 g. and the pituitary, corpus luteum and thymus are all rich sources. The total amount of ascorbic acid in the body of a normal man is about 4 to 6 gm. There is normally some 15 to 30 mg. of ascorbic acid per 100 gm. of leucocytes in the blood of healthy persons taking diet rich in the vitamin; but in subjects depleted of ascorbic acid, the vitamin C content of the leucocytes falls progressively to reach very low values, 3 to 6 weeks before the signs of scurvy appear.

Deficiency of ascorbic acid leads to defective formation of the collagen fibres of connective tissue. Since the laying down of new connective tissue is essential to the healing of wounds, this process is retarded in guinea pigs, made deficient in ascorbic acid. Formation of bone is also abnormal, partly because of the abnormal formation of collagen and partly because without ascorbic acid the specialized cells that lay down bone (osteoblasts) become functionless. The teeth of guinea pigs, made deficient in ascorbic acid, become soft and spongy but they are quickly restored to normalcy by giving the animals ascorbic acid.

In man, scurvy results because of the deficiency of ascorbic acid. Its main features are bleeding in the skin and deeper tissues and swollen bleeding gums. In young children, there is bleeding under the periosteum of the bones and in the joints. The reason of the haemorrhage is not known, but it has been attributed to deficiencies of the intercellular cementing substance between the endothelial cells of the capillaries. The disorder is rapidly and completely cured by giving ascorbic acid.

The vitamin is found is nearly all fruits (specially citrus) and vegetables. A daily intake of about 10 mg. is sufficient to prevent scurvy.

Q.7. Write a short note on toxicity of ammonia.

Ans. **Toxicity of Ammonia**

Even a marginal elevation in the blood ammonia concentration is harmful to the brain. Ammonia, when it accumulates in the body, results in slurring of speech and blurring of the vision and causes tremors. It may lead to coma and, finally, death, if not corrected.

Hyperammonemia : Elevation in blood NH_3 level may be genetic or acquired. Impairment in urea synthesis due to a defect in any one of the five enzymes is described in urea synthesis. All these disorders lead to hyperammonemia and cause mental retardation. The acquired hyperammonemia may be due to hepatitis, alcoholism etc. where the urea synthesis becomes defective, hence NH_3 accumulates.

Explanation for NH_3 toxicity : The reaction catalysed by glutamate dehydrogenase probably explains the toxic affects of NH_3 in brain

$$\alpha\text{-ketoglutarate} + NH_3 \xleftrightarrow[NADP^+]{NADPH + H} \text{Glutamate}$$

Accumulation of NH_3 shifts the equilibrium to the right with more glutamate formation, hence more utilization of α-ketoglutarate. α-ketoglutarate is a key intermediate in TCA cycle and its depleted levels impair the TCA cycle. The net result is that production of energy (ATP) by the brain is reduced. The toxic effects of NH_3 on brain are, therefore, due to impairment in ATP formation.

Q.8. What do you mean by phylloquinone? Write in brief.

Ans. **Vitamin K**

Dam and later **Almquist** described a haemorrhagic disease in chickens, due to food deficiency. The disease is associated with a decrease in the amount of prothrombin in the blood. The factor missing from such a diet, which is associated with fat soluble fraction, has been given the name vitamin K.

There are at least two naturally occurring forms of the vitamin. Phylloquinone (vitamin K_2) is synthesised in green parts of the plants while farnoquinone by certain micro-organisms. Vitamin K is fat soluble and its absorption from the alimentary tract therefore, depends upon bile salts.

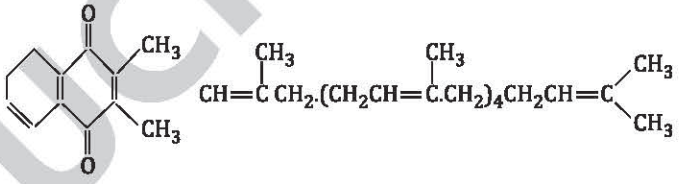


Fig. Structure of vitamin-K

Vitamin K and coagulation of blood : The theory of the blood clotting process as understood at present is that thromboplasts liberated from injured tissue cells or from disintegrated blood platelets, together with Ca ions, convert prothrombin into thrombin and once the thrombin is formed, it converts the fibrinogen of the plasma into insoluble fibrin (blood clot). Vitamin K is necessary for the formation of prothrombin, a process which occurs in the liver.

SECTION-C LONG ANSWER TYPE QUESTIONS

Q.1. Describe the metabolism of amino acids with the suitable structures.

Ans. **Metabolism of Amino Acids**

The amino acids obtained from dietary source or body protein turnover are utilized for protein biosynthesis and the production of a wide range of nitrogen-containing compounds (creatine, amines, porphyrin etc.)

The amino acids undergo certain common reactions like transamination followed by deamination for the liberation of ammonia. The amino group of the amino acids is utilized for the formation of urea which is an excretory end product of protein metabolism. The carbon skeleton of the amino acids is first converted to keto acids (by transamination) which meet one or more of the following fates :

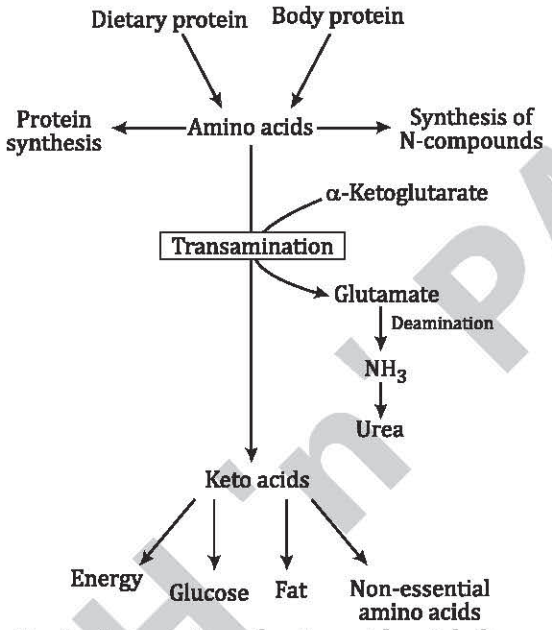


Fig. 1 : An overview of amino acid metabolism.

1. Utilized to generate energy.
2. Used for the synthesis of glucose.
3. Diverted for the formation of fat or ketone bodies.
4. Involved in the production of non-essential amino acids.

The details of general and specific metabolic reactions of amino acids are described as follows :

Transamination

The transfer of an amino ($—NH_2$) group from an amino acid to a keto acid is known as transamination. This process involves the interconversion of a pair of amino acids and a pair of keto acids, catalysed by a group of enzymes called **transaminases** (recently, **aminotransferases**).

Transamination, quantitatively, is the most important reaction in the amino acid metabolism. The salient features of transamination are :

1. All transaminases require **pyridoxal phosphate** (PLP), a coenzyme derived from vitamin B_6.
2. Specific transaminases exist for each pair of amino and keto acids. However, only two-namely, aspartate transaminase and alanine transaminase make a significant contribution for transamination.

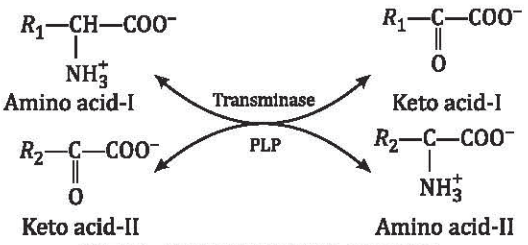


Fig. 2 : Transamination reaction

3. There is no free NH_3 liberated, only the transfer of amino group occurs.
4. Transamination is **reversible**.
5. In the cells, all the amino acids are not readily available in a proportion needed for protein biosynthesis. Transamination is very important for the redistribution of amino groups and **production of non-essential amino acids**, as per the requirement of the cell.
6. It involves both catabolism (degradation) and anabolism (synthesis) of amino acids. Transami nation is ultimately responsible for the synthesis of non-essential amino acids.
7. Transamination diverts the excess amino acids towards **energy generation**.
8. The amino acids undergo transamination to finally concentrate nitrogen in glutamate. **Glutamate** is the only amino acid that undergoes oxidative deamination to a significant extent to liberate free NH_3 for urea synthesis.
9. All amino acids except lysine, threonine, proline and hydroxyproline participate in transamination.
10. Transamination is not restricted to α-amino groups only. For instance, δ-amino group of ornithine is transaminated.
11. Serum transaminases are important for diagnostic and prognostic purposes. Serum glutamate pyruvate transaminase (SGPT) or alanine transaminase (ALT) is elevated in all liver diseases. Serum glutamate oxaloacetate transaminase (SCOT) or aspartate transaminase (AST) is increased in myocardial infarction.

Mechanism of transamination : Transamination occurs in two stages :

1. Transfer of the amino group to the coenzyme pyridoxal phosphate (bound to the coenzyme) to form pyridoxamine phosphate.
2. The amino group of pyridoxamine phosphate is then transferred to a keto acid to produce a new amino acid and the enzyme with PLP is regenerated.

All the transaminases require **pyridoxal** phosphate (PLP), a derivative of vitamin B_6. The aldehyde group of PLP is linked with ε-amino group of lysine residue, at the active site of the enzyme forming a **Schiff base** (imine linkage). When an amino acid (substrate) comes in contact with the enzyme, it displaces lysine and a new Schiff base linkage is formed. The amino acid-PLP Schiff base tightly binds with the enzyme by non covalent forces. Snell and Braustein proposed a **Ping Pong Bi Bi** mechanism involving a series of intermediates (aldimines and ketimines) in transamination reaction.

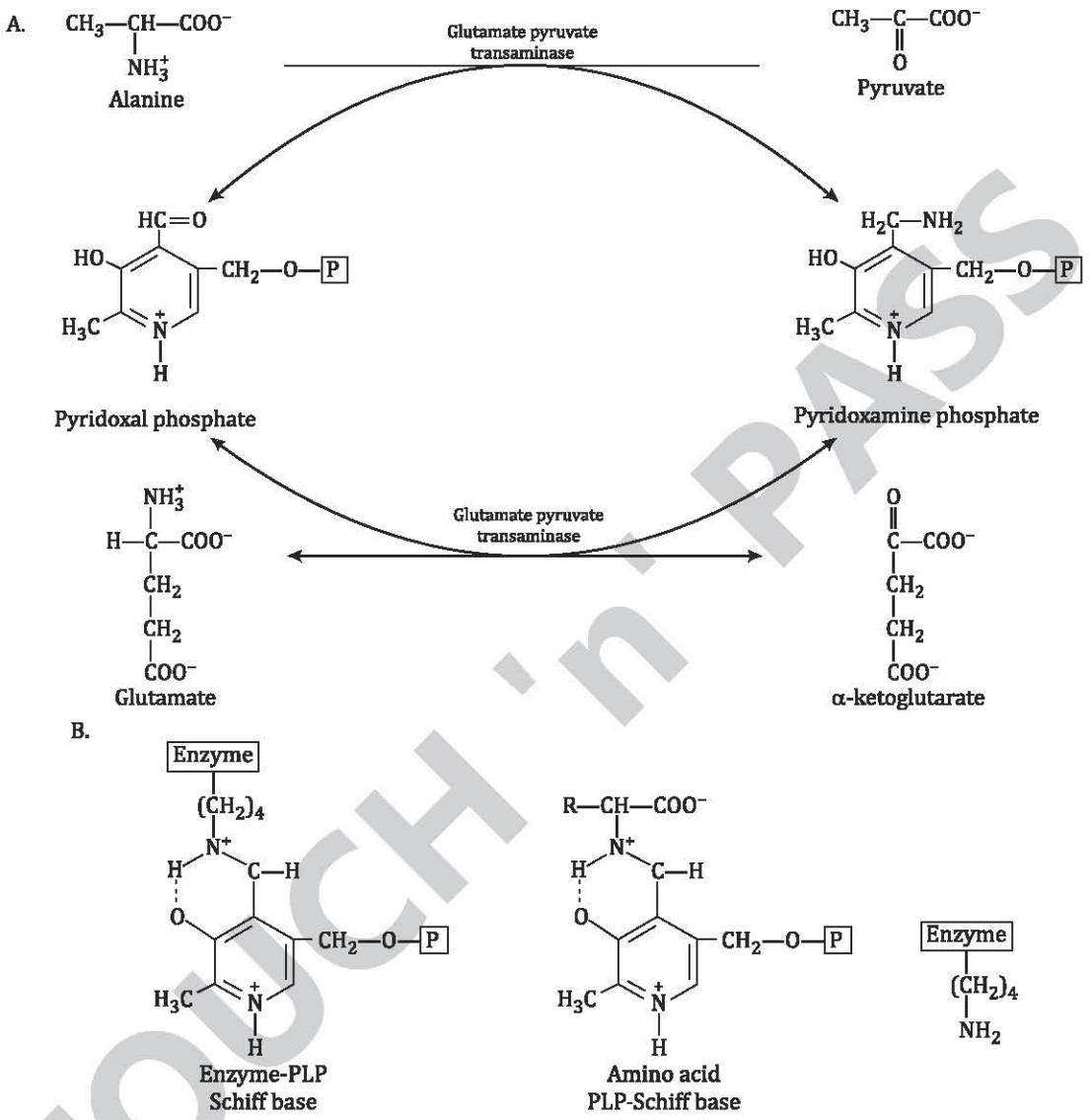


Fig. 3 : Mechanism of transmination : (A) Involvement of pyridoxal phosphate (PLP) in the transfer of amino group, (B) Formation of enzyme-PLP-Schiff base and amino acid-PLP-Schiff base. Note that when the amino acid binds, enzyme separates

Deamination

The removal of amino group from the amino acids as NH_3 is deamination. Transamination (discussed above) involves only the shuffling of amino groups among the amino acids. On the other hand, deamination results in the liberation of ammonia for urea synthesis. Simultaneously, the Carbon skeleton of amino acids is converted to keto acids. Deamination may be either oxidative or non oxidative.

Although transamination and deamination are separately discussed, they occur simultaneously, often involving glutamate as the central molecule. For this reason, some authors use the term transdeamination while describing the reactions of transamination and deamination, particularly involving glutamate.

1. Oxidative deamination

Oxidative deamination is the liberation of free ammonia from the amino group of amino acids coupled with oxidation. This takes place mostly in liver and kidney. The purpose of oxidative deamination is to provide NH_3 for urea synthesis and α-keto acids for a variety of reactions, including energy generation.

Role of glutamate dehydrogenase : In the process of transamination, the amino groups of most amino acids are transferred to α-ketoglutarate to produce glutamate. Thus, glutamate serves as a 'collection centre' for amino groups in the biological system. Glutamate rapidly undergoes oxidative deamination, catalysed by glutamate dehydrogenase (GDH) to liberate ammonia. This enzyme is unique in that it can utilize either NAD^+ or $NADP^+$ as coenzyme. Conversion of glutamate to α-ketoglutarate occurs through the formation of an intermediate, α-iminoglutarate.

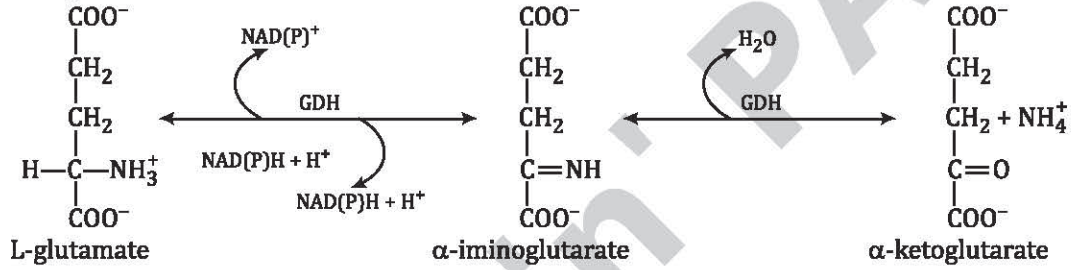


Fig. 4 : Oxidation of glutamate by glutamate dehydrogenase (GDH).

Glutamate dehydrogenase catalysed reaction is important as it reversibly links up glutamate metabolism with TCA cycle through α ketoglutarate. GDH is involved in both catabolic and anabolic reactions.

Regulation of GDH activity : Glutamate dehydrogenase is a zinc containing mito chondrial enzyme. It is a complex enzyme consisting of six identical units with a molecular weight of 56,000 each. GDH is controlled by allosteric regulation. GTP and ATP inhibit-whereas GDP and ADP activate—glutamate dehydrogenase. Steroid and thyroid hormones inhibit GDH.

After ingestion of a protein-rich meal, liver glutamate level is elevated. It is converted to α ketoglutarate with liberation of NH_3. Further, when the cellular energy levels are low, the degradation of glutamate is increased to provide α ketoglutarate which enters TCA cycle to liberate energy.

Oxidative deamination by amino acid oxidases : L-Amino acid oxidase and D-amino acid oxidase are flavoproteins, possessing FMN and FAD, respectively. They act on the corresponding amino acids (L or D) to produce α-keto acids and NH_3. In this reaction, oxygen is reduced to H_2O_2, which is later decomposed by catalase.

The activity of L-amino acid oxidase is much low while that of D-amino acid oxidase is high in tissues (mostly liver and kidney). L-Amino

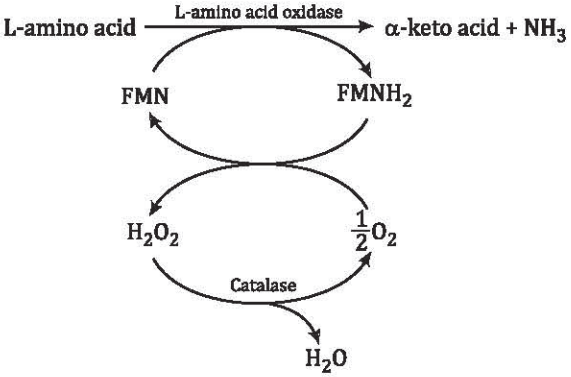


Fig. 5 : Oxidative deamination of amino acids

acid oxidase does not act on glycine and dicarboxylic acids. This enzyme, due to its very low activity, does not appear to play any significant role in the amino acid metabolism.

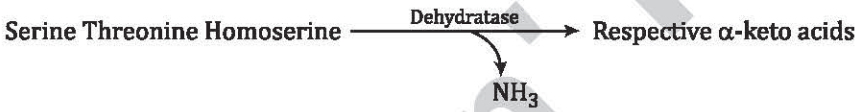
Fate of D-amino acids : D-Amino acids are found in plants and micro-organisms. They are, however, not present in the mammalian proteins.

But D-amino acids are regularly taken in the diet and metabolised by the body. D-Amino acid oxidase converts them to the respective α-keto acids by oxidative deamination. The α-keto acids so produced undergo transamination to be converted to L-amino acids which participate in various metabolisms. Keto acids may be oxidized to generate energy or serve as precursor for glucose and fat synthesis. Thus, D-amino acid oxidase is important as it initiates the first step for the conversion of unnatural D-amino acids to L-amino acids in the body.

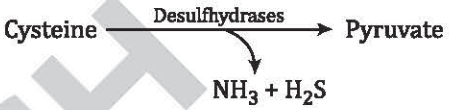
2. Non-oxidative deamination

Some of the amino acids can be deaminated to liberate NH_3 without undergoing oxidation :

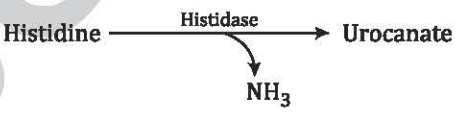
(i) **Amino acid dehydrases :** Serine, threonine and homoserine are the hydroxy amino acids. They undergo non-oxidative deamination catalysed by PLP-dependent dehydrases (dehydratases).



(ii) **Amino acid desulfhydrases :** The sulfur amino acids, namely cysteine and homocysteine, undergo deamination coupled with desulfhydration to give keto acids.



(iii) **Deamination of histidine :** The enzyme histidase acts on histidine to liberate NH_3 by a non oxidative deamination process.



Q.2. Describe the urea cycle.

Ans.

Urea Cycle

Urea is the end product of protein metabolism (amino acid metabolism). The nitrogen of amino acids converted to ammonia (as described above) is toxic be to the body. It is converted to urea and detoxified. As such, urea accounts for 80-90% of the nitrogen containing substances excreted in urine.

Urea is synthesized in liver and transported to kidneys for excretion in urine. Urea cycle is the first metabolic cycle that was elucidated by Hans Krebs and Kurt Henseleit (1932), hence it is known as, Krebs-Henseleit cycle. The individual reactions, however, were described in more detail later on by Ratner and Cohen.

Urea has two amino ($—NH_2$) groups, one derived from NH_3 and the other from aspartate. Carbon atom is supplied by CO_2 Urea synthesis is a five-step cyclic process, with five distinct enzymes. The first two enzymes are present in mitochondria while the rest are localized in cytosol. The details of urea cycle are described in given figure 1.

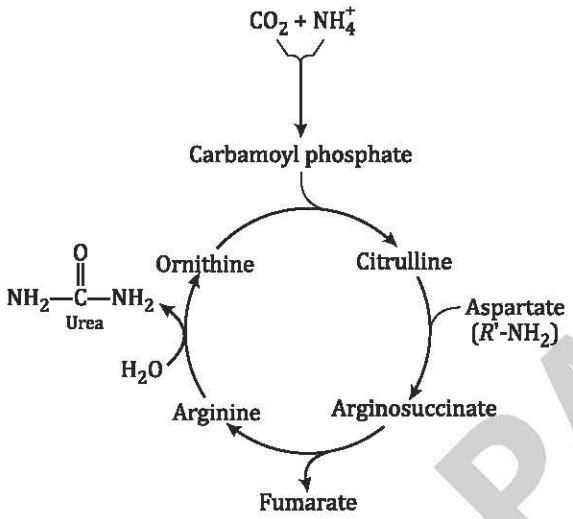


Fig. 1 : Outline of urea cycle. (Note: In the synthesis of urea one amino group comes from ammonium ion while the other is from aspartate; carbon is derived from CO_2. This is represented in colour).

1. **Synthesis of carbamoyl phosphate :** Carbamoyl phosphate synthase I (CPS I) of mitochondria catalyses the condensation of NH_4^+ ions with CO_2 to form carbamoyl phosphate. This step consumes two ATP and is irreversible and rate-limiting. CPS I requires N-acetylglutamate for its activity. Another enzyme, carbamoyl phosphate synthase II (CPS II)—involved in pyrimidine synthesis—is present in cytosol. It accepts amino group from glutamine and does not require N-acetylglutamate for its activity.
2. **Formation of citrulline :** Citrulline is synthesized from carbamoyl phosphate and ornithine by ornithine transcarbamoylase. Ornithine is regenerated and used in urea cycle. Therefore, its role is comparable to that of oxaloacetate in citric acid cycle. Ornithine and citrulline are basic amino acids. (They are never found in protein structure due to lack of codons). Citrulline produced in this reaction is transported to cytosol by a transporter system.
3. **Synthesis of arginosuccinate :** Arginosuccinate synthase condenses citrulline with aspartate to produce arginosuccinate. The second amino group of urea is incorporated in this reaction. This step requires ATP which is cleaved to AMP and pyrophosphate (PP). The latter is immediately broken down to inorganic phosphate (Pi).
4. **Cleavage of arginosuccinate :** Arginosuccinase cleaves arginosuccinate to give arginine and fumarate. Arginine is the immediate precursor for urea. Fumarate liberated here provides a connecting link with TCA cycle, gluconeogenesis etc.
5. **Formation of urea :** Arginase is the fifth and final enzyme that cleaves arginine to yield urea and ornithine. Ornithine, so regenerated, enters mitochondria for its reuse in the urea cycle. Arginase is activated by CO^{2+} and Mn^{2+}. Ornithine and lysine compete with arginine (competitive inhibition). Arginase is mostly found in the liver, while the rest of the enzymes (four) of urea cycle are also present in other tissues. For this reason,

arginine synthesis may occur to varying degrees in many tissues. But only the liver can ultimately produce urea.

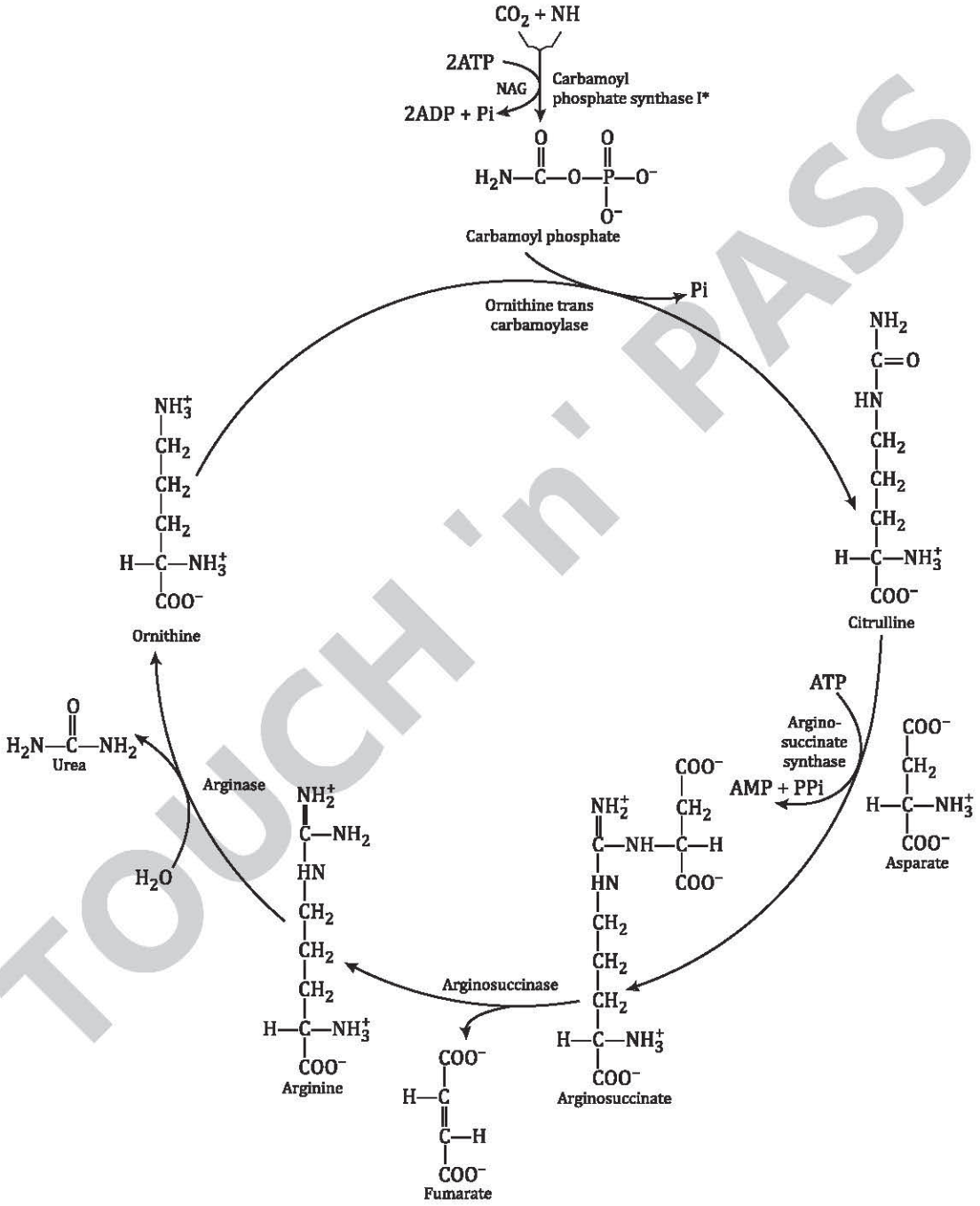


Fig. 2 : Reactions of urea cycle (NAG—N—acetylglutamate (in the formation of urea, one amino group is derived from free ammonium ion while the other is from aspartate; carbon is obtained from CO_2, *mitochondrial enzymes, the rest of the enzymes are cytosomal).

Overall reaction and energetics : The urea cycle is irreversible and consumes 4 ATP. Two ATP are utilized for the synthesis of carbamoyl phosphate. One ATP is converted to AMP and PPi to produce arginosuccinate which equals 2 ATP. Hence 4 ATP are actually consumed.

$$NH_4^+ + CO_2 + \text{Asparate} + 3ATP \longrightarrow \text{Urea} + \text{Fumarate} + 2ADP + 2Pi + AMP + PPi$$

Q.3. What are vitamins? Discuss the role played by B-complex groups of vitamins.

Ans. **Vitamins**

The term 'Vitamin' refers to an essential dietary factor which is required by the organism in small amounts and whose absence results in deficiency diseases. The word "Vitamine" was coined by the Polish Biochemist, Funk in 1911 for the antiberiberi factor. 'Vita' means the essential nature or the vital nature of the substance and "amine" indicates its chemical nature. However, this word has been later used to a heterogenous group of substances which are all not amines in structure. Therefore, in 1919 the letter "e", from vitamine was removed to signify the non-amine structure of the vitamins. Thus, vitamins now include a special group of substances which are chemically unrelated. They may be amines, aminoacids, organic acids, esters, alcohols, steroids, flavoproteins, etc.

Vitamins are divided into two subgroups on the basis of their solubility properties, the water soluble and fat soluble vitamins. The fat soluble vitamins are A, D, E and K occurring with fats, mostly with animal fats. The water soluble vitamins are the B-complex group and vitamin C. Vitamins are not stored in the body and excess amounts are excreted in the urine. In the following account, for the sake of convenience, they are described in the alphabetical order.

Vitamin-B Complex

In 1926 vitamin B, as it was then called, was shown to consist of a heat labile component having the properties formerly ascribed to vitamin B and a heat stable component. Further investigations have shown that the vitamin B contains about 11 different substances.

Substances comprising the vitamin B complex :

1. Thiamine (vitamin B_1).
2. Riboflvain (vitamin B_2, growth factor).
3. Biotin (vitamin H).
4. Inostol.
5. Choline.
6. Niacin.
7. Pyridoxin (vitamin B_6).
8. Pantothenic acid.
9. Para-amino benzoic acid
10. Folic acid.
11. Cobalamine (vitamin B_{12})

1. **Thiamine (B_1) :** The principal constituents of the heat labile component of vitamin B complex are thiamine and pantothenic acid. Thiamine consists of a pyrimidine and a thiazole ring system joined by a methylene bridge. It is freely soluble in aqueous solutions but insoluble in fat solvents. The pure substance is quite stable in acid solutions and can be stabilized for 30 minutes at 120°C without appreciable loss of activity. In alkaline and neutral solutions the vitamin is rapidly destroyed, because here it is hydrolysed into its two main components - the pyrimidine and thiazole ring.

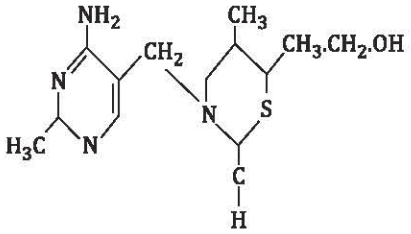


Fig. 1 : Thiamine (B_1)

The concentration of the thiamine in biological fluids and tissues can be measured by first converting the vitamin into thiochrome with potassium ferricyanide and then estimating the thiochrome by its bluish fluorescence in ultraviolet light.

The physiologic actions of thiamine are due to its pyrophosphoric ester: thiamine pyrophosphate (TPP), which is formed by the phosphorylation of the vitamin under the influnce of ATP and magnesium ions.

TPP, often in association with lipoic acid forms the enzyme system needed for the decarboxylation of α-keto acids, such as pyruvic acid. In the deficiency of thiamine, pyruvic acid cannot be metabolized and so accumulates in the fluids and tissues of the body. In man too, the daily requirement for thiamine is related to the consumption of carbohydrate. A person eating a high carbohydrate diet requires more thiamine than one consuming mainly fat and protein.

Pigeons suffering from thiamine deficiency have gross muscular weakness and incoordination (polyneuritis). The O_2 consumption of the brain is reduced and lactic acid and pyruvic acid accumulate in the brain, which, however, are rapidly abolished by the addition of thiamine to the diet. Such experiments suggest that thiamine is in some way responsible for proper functioning of nervous tissuse in pigeons.

Prolonged deficiency of vitamin B_1 in man results in the disorder known as beri beri, which is incorporated with polyneuritis—muscular weakness and incoordination, enlargement of the heart and cardiac failure etc.

2. **Riboflavin** : Riboflavin, an allaxozine derivative, functions in flavine mononucleotide (FMN) or flavine adenine dinucleotide (FAD) as the prosthetic group of flavoprotein enzymes which act in cellular respiration between dehydrogenases and either oxygen or cytochrome. It is a constituent of Warburg's "yellow enzyme", xanthine oxidase, D-amino oxidase and cytochrome reductase.

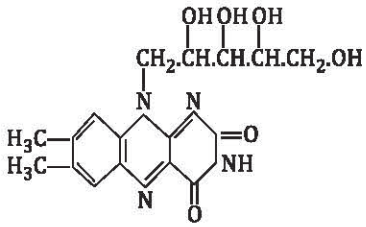


Fig. 2 : Riboflavin

Riboflavin is readily absorbed from the upper aliminatry tract. It is present in blood mainly in combination with plasma globulin to the extent of about 0.5 micrograms/100 ml. High concentrations of the vitamin are found in liver, heart and kidneys. It is eliminated in the urine in the form of pigment, uroflavin, the excretion of which fluctuates with the intake of vitamin. Riboflavin must be phosphorylated before it aquires biological activity. This probably occurs in the cells of the intestinal mucosa and in the liver.

The vitamin is relatively stable in acid soultion kept in dark. Ordinary cooking processes cause little destruction of riboflavin, although a certain amount may be lost be extracting the cooking water. Considerable loss of riboflavin may occur in milk exposed to bright sunlight.

Riboflavin is synthesized by many microorganisms, yeasts, bacteria and probably flagellates. It stimulates multiplication of *Chilomonas*. It is also required by numerous insects. Some insects appear to get sufficient riboflavin from intestinal symbionts (*Lasioderma* and *Blatella*) but others require it in diet (*Drosophila*). Trout needs about

0.5 mg. of riboflavin per kg body weight per day. Rats deficient in riboflavin develop skin disease, shedding of hair. etc. Fur-bearing mammals such as fox require riboflavin for normal sleekness and colour of fur. The vitamin is synthesized by intestinal micro-organisms in many mammals, Rabbits excrete it in faeces 10 to 15 times their intake, so grow without dietary riboflavin either because of caecal absorption or from eating faeces. A true requirement by man is not established, although the recommended daily allowance is 1.5-1.8 mg. per day and a more generous intake is advised during pregnancy.

3. **Biotin :** Biotin was isolated from egg yolk in 1936. The mode of action of biotin is not so clearly established as that of other vitamins. But it is believed to act as a coenzyme in relation to the fixation of CO_2 in carboxylation reactions, such as conversion of pyruvic acid to oxaloacetic acid. It is also required in the enzymatic deamination of some amino acids. It is known to be a growth factor for plants and for many animals.

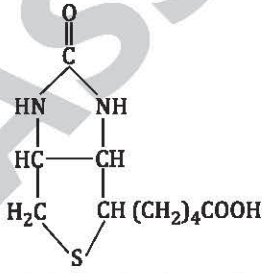


Fig. 3 : Structure of Biotin

It has been known for a long time that a high concentration of uncooked egg white in experimental diets is toxic to rats and man. The reason is, that the protein avidin of egg white forms with biotin a stable compound, which is not hydrolysed in the intestine, and therefore cannot be absorbed. Biotin may, therefore, be described as an essential food factor in man. Biotin is found in foods along with other vitamins of the B group.

4. **Inositol :** This is mouse anti-alopecia factor. We owe to Woolley the addition of inositol to the vitamin B complex. Working with young mice and using a synthetic diet containing all the known vitamins, Woolley discovered that the mice failed to grow and that their hairs were affected. Addition of pantothenic acid—absence of which may also give rise to hair changes—proved useless. The addition of biotin of para-aminobenzoic acid made no change. Cures were observed by the addition of inositol isolated from liver.

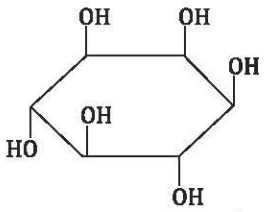


Fig. 4 : Structure of inositol

It has been claimed that the "spectacle eye" condition in rats can be cured with inositol. This claim has also been made for biotin. Inositol is found in muscles, liver, kidneys, brain and other animal tissues.

5. **Choline :** Its role in nutrition was pointed out by Best, who presented evidence to show that choline prevented the development of fatty livers in depancreatized dogs. On a diet low in choline, many animals develop fatty livers and haemorrhagic renal changes, and if such a diet continues, cirrhosis of the liver appears in the earlier stages of degeneration inclusion of choline in the diet is followed by marked improvement of the condition.

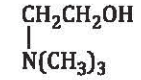


Fig. 5 : Structure of choline

Choline may function in several ways to stimulate the production of phospholipids, to produce acetylcholine, or to supply labile methyl groups.

The richest source of choline is egg yolk. Liver and kidneys are other good sources.

6. **Nicotinic acid :** Nicotinic acid or niacin and the corresponding amide, nicotinamide, are curative factors for dog's black-tongue disease and for human pellagra, and a deficiency of which results in dermatitis, diarrhoea etc.

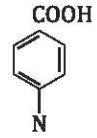


Fig. 6 : Nicotinic acid

Nicotinic acid amide combines with adenine, a pentose and phosphate to form DPN (diphosphopyridine nucleotide) and TPN (triphosphopyridine nucleotide) which are coenzymes for many dehydrogenases. The conversion of nicotinic acid to nicotinamide takes place in kidney and brain slices, as well as in liver slices in the presence of glutamine. Niacin in a variety of animals and man is derived from the amino acid, tryptophan which is also active in curing pellagra. It is evident that in the body the amino acid is converted to anthranilic acid and through a series of intermediates to nicotinic acid.

Nicotinic acid is present in almost all tissues, the greater proportion being present as coenzyme. The highest concentration is found in liver. Blood normally contains some 0.30 to 0.83 mg. per 100 mg, mainly as coenzyme. The daily reuirement of nicotinic acid is of the order of 50 mg. per day, but very much larger doses are given to patients with pellagra.

7. **Pyridoxine (B_6) :** Vitamin B_6 includes pyridoxine, pyridoxal and pyridoxamine. A deficiency of this vitamin in young rats results in the development of dermatitis with swelling and edema. This skin disturbance, at first thought to resemble pellagra, cannot be cured with nicotinic acid.

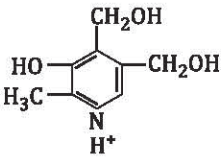


Fig. 7 : Pyridoxine

The three members of the group B_6 are present in tissues as phosphate esters. The active coenzyme form is believed to be pyridoxal phosphate. This is the conezyme for transamination of α-amino acids; hence it is important in protein metabolism. Pyridoxine stimulates growth in *Chilomonas*. The rumen contents of sheep, also the milk of cows, may contain 10 times as much pyridoxine as the food. Pyridoxine deficiency shows retarded growth and anaemia.

8. **Pantothenic acid :** Pantothenic acid was isolated in 1939. In the living cell pantothenic acid combines with mercaptoethylamine to form pantotheine, which in turn is built up into the important substance, coenzyme, to play an essential role in the metabolism of both fat and carbohydrate.

Lack of vitamin in the diet of rats results in marked loss of weight, symmetrical greying of the fur (achromotrichia), loss of fur and irritation of the nose and eyes, together with haemorrhage into, and necrosis of the adrenal glands. Lack of pantothenic acid in man may be responsible for the phenomenon of "burning feet" complained of by patients suffering from beriberi and pellagra.

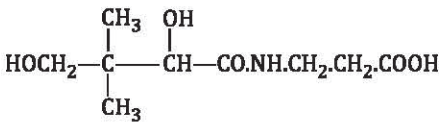


Fig. 8 : Pantothenic acid

Liver, kidney, meat, peas and yeast are good sources of pantothenic acid.

9. **Para-amino benzoic acid (PABA) :** Ansbacher demonstrated that in mouse achromotrichia (lack of hair pigment) could be cured by feeding a diet with p-amino benzioc acid. It appeared to be essential for growth and for the maintenance of a normal fur coat for the rat.

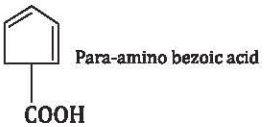


Fig. 9 : Para-amino benzoic acid

10. **Folic acid (Pteroylglutamic acid) :** It is a combination of glutamic acid, para-amino benzoic acid and a pteridine nucleus. This pteridine nucleus together with para-amino benzoic acid is known as pteroic acid, so that folic acid itself is also called pteroylglutamic acid (PGA).

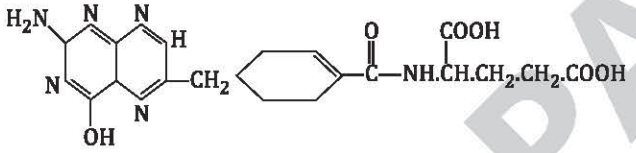


Fig. 10 : Folic acid

Folic acid is needed for growth and blood formation by chicks and monkeys. Rats and dogs, as a rule, do not need the vitamin, since sufficient quantities are synthesized by intestinal bacteria. This probably applies to man also. Folic acid thus plays an essential role in cellular metabolism. It is necessary especially for production of red cells in the bone marrow (haemopoiesis) and the deficiency is, therefore, characterized by anaemia. This kind of anaemia usually occurs in pregnancy, perhaps because of great demands made upon the bone marrow at that time.

The daily requirement of folic acid is probably less than 1 mg. a day.

11. **Cyanocobalamin (Vitamin B_{12}) :** Folken, Smith and others isolated a factor from liver which is curative in pernicious anemia and is now termed vitamin B_{12}. It is found in animal tissues in the form of a conjugate with a polypeptide. The vitamin induces an increased reticulocyte rise and an increase in haemoglobin and red cells count.

Vitamin B_{12} and its family of compounds appear to be involved in a large number of biochemical reactions, although little is known of the mechanism of their action. One example of the action of the cobalamine coenzymes is their specificity for the conversion of glutamic acid to β-methylaspartic acid in micro-organisms.

Normally about 45 per cent of a 1 μg dose of cyanocobalamin given orally is absorbed in the lower part of ileum which, however, is reduced (usually to 20 per cent) in pernicious anaemic condition and mal-absorptive disease of ileum.

After absorption cobalamins (especially hydroxycobalamin) becomes bound to β-globulin, although small amounts ramain free in plasma. If not utilized in cell metabolism, cobalamines are stored and bound to β-globulin in liver, which may contain as much as 1 to 2 mg.

The vitamin is required for the biosynthesis of methyl groups from one carbon precursor and for the synthesis of thymidine and other deoxyribosides. Its action on the red cell maturation is unknown. It has also been implicated in protein synthesis, in

the activation of SH enzymes, and for the adequate storage of folic acid. Vitamin B_{12} affects myelin formation and one of the symptoms of B_{12} deficiency is demyelinization.

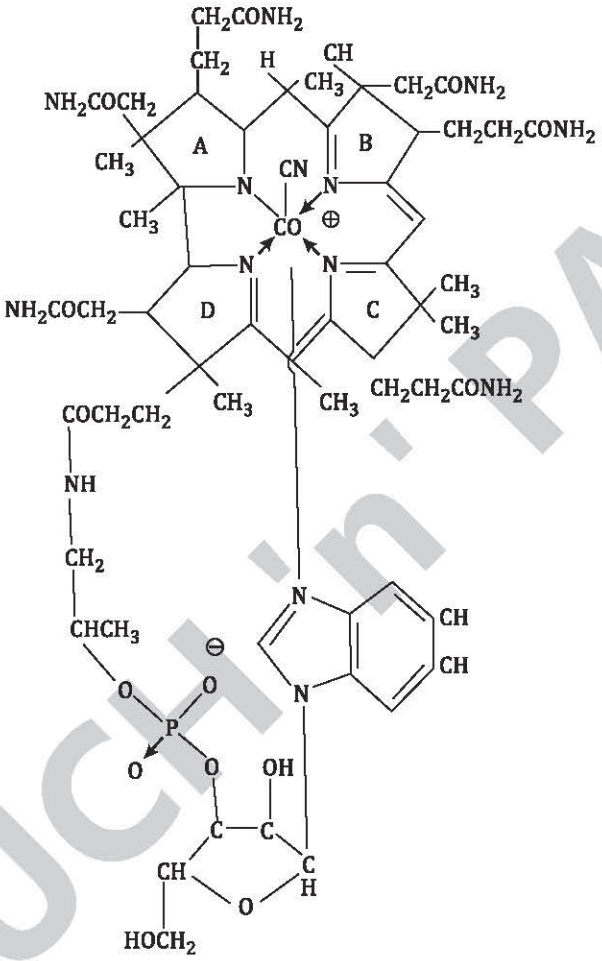


Fig. 11 : Cyanocobalamine

Not more than about 1 μg per day is required to maintain normal health, provided there is no interference with absorption. Vitamin B_{12} is widely distributed in foods. Beef, kidney and liver are the best sources (15-20 μg/100 g).

❑❑❑

UNIT-V

Digestion and Respiration in Humans

SECTION-A VERY SHORT ANSWER TYPE QUESTIONS

Q.1. Which glands are associated with the alimentary canal?

Ans. The salivary glands, the liver and the pancreas are the lists of glands associated with the alimentary canal.

Q.2. What is the functions of bile?

Ans. Bile is a dark yellowish-green or brown colour fluid produced by the liver and stored within the gall bladder. It comprises organic molecules such as bile acids, slats, bilirubin and cholesterol and water.

Q.3. What is the process of elimination?

Ans. Elimination is a final process of digestion. In this process, the food residues that cannot be digested or absorbed are excreted or egested from the body as semi-solid faeces.

Q.4. What is glycogenesis?

Ans. The process of conversion of glucose into glycogen is called glycogenesis. Glucose is the free sugar occuring in blood. After a meal the level of glucose in blood is elevated after absorption. The excess of glucose is converted into glycogen as a reserve food both in liver and muscles.

Q.5. What is constipation?

Ans. Constipation is defined as the digestive disorders, associated with the irregular and difficult bowel movement characterised by hardened faeces.

Q.6. What is the difference between digestion and absorption?

Ans. **Digestion** is the process of crushing or digesting large and insoluble food molecules into smaller and soluble molecules for easy absorption into the blood stream.

Absorption is the mechanical and digestive process of absorbing or assimilation of substances into the cells or across the tissues and organs through the process of diffusion or osmosis.

Q.7. What is chyme?

Ans. Chyme is partially digested mass of food that is forced into the small intestine.

Q.8. Write very short note on anti-sterility vitamin.

Ans. Vitamin-E is known as anti-sterility vitamin or fertility vitamin. Chemically vitamin-E is tocopherol.

Q.9. What is indigestion?

Ans. Indigestion, also known as dyspepsia, is a medical term. Which describes the pain and discomfort in the upper abdomen. It is a type of a functional disorder, caused by the abnormal functioning of the digestive system or gastrointestinal organs.

Q.10. What is the difference between alveolar and inspired air?
Ans. Alveolar air : The air present in the alveoli.
Inspired air : The amount of air inspired at a time.

Q.11. What is respiratory quotient?
Ans. Respiratory quotient (RQ) : The ratio of the amount of O_2 (volume) used up and the amount of CO_2 (volume) produced simultaneously during respiration in any animal is called respiratory quotient. This ratio is different for the oxidation of different food substances.

$$RQ = \frac{\text{Volume of } CO_2 \text{ formed}}{\text{Volume of } O_2 \text{ formed}}$$

Q.12. Define vital capacity.
Ans. The value of air exhaled by a maximum strong expiration is referred to as vital capacity.

Q.13. What is cori cycle?
Ans. Due to inadequate supply of O_2 excess lactic acid accumulates in the muscles, it diffuse into the blood. Major part of this blood locate is taken up by the liver where it is converted into glycogen. The liver glycogen is converted into glucose which enters the blood and it transported to muscles. In muscles this glucose is then converted into muscles glycogen. This cycle is called Cori cycle.

Q.14. What is the role of carbonic anhydrase in RBCs?
Ans. In the presence of the enzyme carbonic anhydrase, about 70% of CO_2 interacts with water to generate carbonic acids in RBCs.

Q.15. Define the partial pressure of a gas.
Ans. Partial pressure of a gas is the pressure contributed by an individual gas in a mixture of gases and it is denoted as PO_2 for O_2 and PCO_2 for O_2.

Q.16. How many O_2 molecules can be carried out by one haemoglobin molecule?
Ans. Four molecules of O_2 can be carried by one haemoglobin molecule.

Q.17. How is the entry of food pivoted in the respiratory tract?
Ans. During swallowing, the epiglottis, a cartilaginous flap-like structure, covers the glottis and prevents food from entering the respiratory tract.

Q.18. What is percentage of O_2 in inspired and expired air?
Ans. Inspired air has 20% O_2 and expired air has 16% O_2.

Q.19. What is functional residual capacity?
Ans. The volume of air that remains in the lungs after a person inhales and exhales normally is known as functional residual capacity (FRC). The residual volume, as well as the expiratory reserve volume are included which is

$$FRC = RV + ERV$$

Q.20. What is the difference between carbaminohaemoglobin and oxyhaemoglobin?
Ans. The differences between carbaminohaemoglobin and oxyhaemoglobin is as follows :

Carbaminohaemoglobin	Oxyhaemoglobin
It is generated when oxygen reacts with the Fe^{2+} component of haemoglobin.	It is created when carbon dioxide reacts with the amine radical of haemoglobin.
The alveolar surface is where it forms.	It is made up of cells that are found in the tissues.

Q.21. What do you mean by hypoxia, artificial hypoxia and anaemic hypoxia?

Ans. **Hypoxia** is a situation in which there is a lack of oxygen in the tissues.

Artificial hypoxia is caused by a lack of oxygen at elevations above 2400 metres. Mountain sickness is characterised by headaches, dizziness, nausea, vomiting, mental exhaustion and a lack of breath, among other symptoms. **Anaemic hypoxia** is caused by a decrease in blood O_2 capacity as a result of low Hb levels or carbon monoxide poisoning.

SECTION-B SHORT ANSWER TYPE QUESTIONS

Q.1. Write a short note on vitamins.

Ans. **Hopkins** discovered that there are certain important organic substances found in the food which are very essential for the proper health. First of all **Funk** (1912) used the term-**Vitamins** for these components. (*L. vita* = vitally essential for life + amine). Study of vitamins is called **Vitaminology**. **Vitamins** are relatively simpler organic components synthesized mostly by plants and certain intestinal bacteria. Hence, animals obtain most of these in traces from their food.

About 20 different types of vitamins have been properly discovered.

These fall into two main categories—those soluble in water and those soluble in fats.

I. Water-Soluble Vitamins

1. **Vitamin B Complex :** This group consists of several water soluble vitamins, most of them have been isolated in pure form. It includes following vitamins;
   (i) **Thiamine (B_1) Antinuretic :** It is found in yeast, cereals (wheat, peanuts, seeds), egg yolk, liver, pork, etc. It regulates the Carbohydrate metabolism. It keeps tone of gastro intestinal tract and causes appetite. Deficiency of this vitamin causes Beri-beri, loss of appetite, cessation of growth.
   (ii) **Riboflavin (B_2) :** It can be obtained from green leaves, milk, eggs, yeast, liver, cheese, etc. Its adequate quantity is essential for growth. It forms active group of several enzymes which cause intermediate metabolism of food. If it is in deficiency, it causes chelosis (inflammation and cracking at corners of mouth) and checks growth. It also causes paralysis in Chicks.
   (iii) **Nicotinic Acid or Niacin (B_5) or Antepellagric :** It is found in green leaves, wheat, egg yolk, yeast, liver and meat. It is essential for the activity of cellulose. It acts as coenzyme in tissue reactions. Its deficiency causes a severe disease called pellagra (rough skin), characterized by dermatitis (inflammation of skin), cracked or scaly skin, diarrhoea, dementia. Muscle atrophy and severe inflammation of mucous membrane of mouth and gut causing haemorrhage.
   (iv) **Pyridoxine (B_6) :** It is found in milk, cereals, yeast and liver. It accelerates metabolism and serves in transmission and decarboxylation of amino acids. Its effects are little known in man. Its deficiency causes anaemia dermatitis, (convulsions, nausea, vomiting, mental disorders and retarted growth).
   (v) **Folic Acid Group or Pteroylglutamic Acid :** This group of vitamins is essential for growth, because these play significant roles in synthesis of DNA during cell division, and maturation of blood corpuscles in bone marrow. Deficiency causes

retarted growth and anaemia. These are found in green leaves, soyabean, yeast, kidneys, liver, etc. and are also synthesized by intestinal bacteria.

(vi) **Pantothenic Acid (B_3) :** It is obtained from grains, yeasts, sugarcane, egg yolk, milk, liver, malasses and fresh fruits. It maintains, serves and preserves skin health. It also produces co-enzyme which catalyses addition of acetyl group to **cholino** and other substances. It deficiency causes haemorrhagic lesions in adrenal cortex. **Achro motrichia** (premature greying of hair) may result due to its deficiency.

(vii) **Biotin or Vitamin-H :** It is richly found in yeast, meat, cereals, grain, sugarcane, vegetables and fresh fruits. It is essential for growth and Carbohydrate metabolism. It deficiency causes muscular pain and heart distress.

(viii) **B Complex (B_{12}) or Cyanocobalamin :** It is richly found in fish, liver, meat and egg yolk, it can also be synthesized by intestinal bacteria. It is essential for formation of blood and cell growth. Its deficiency, causes **pernicious** anaemia in human.

2. **Vitamin C or Ascorbic Acid :** It can be obtained from citrus fruits, tomatoes, apples, green vegetables. It keeps integrity of capillary walls and produces 'inter-cellular cement' for teeth and jaw bones. Its deficiency causes scurvy (bleeding of mucus membrane under skin and joints). Along with this it results in loss of weight and fatigue. In its absence wounds do not heal properly.

II. Fat-Soluble Vitamins

1. **Vitamin-A or Retinol :** It is present in yellow maize, peas, carrots, beans, milk, fish liver oil, butter, cream, egg, etc. The deficiency causes abnormalities in the epithelial lining of alimentary canal and respiratory tract. The cornea becomes dry due to absence of tear secretion and causes xerophthalmia. It also causes night blindness or Nyctalopia and keratomalacia (Ulceration causing blindness and softening of cornea).
2. **Vitamin-D or Ergocalciferol or Antirachitic Vitamin :** It is found in fish liver oil, egg, beef, fat and also from exposure of skin to ultra-violet radiation (sun-light). It regulates the metabolism of calcium and phosphorus. It is required for normal growth and mineralisation of bones. Deficiency causes rickets in children in which bones become soft and deformed. It also causes osteomalacia in females in which pelvic bones are deformed that affects child-birth.
3. **Vitamin E or Tocopherol :** It is richly found in green vegetables, vegetable fats, wheat, gram oil, etc., its deficiency causes sterility both in males and females. Along with this it causes degenerative change in muscles. This vitamin helps in the utilization of vitamin A and functions as Antioxidant *i.e.,* prevents the oxidation of vitamin A in digestive tract.
4. **Vitamin-K or Phylloquinone or Naphthoquinone :** It can be obtained from green leaves, liver, eggs and soyabeans. It is also found in certain bacteria of intestinal flora. It is essential for the production of prothrombin in liver which is essential for the clotting of blood. Its deficiency causes haemorrhages as blood fails to clot.

Q.2. Write about the action and functions of saliva.

Ans.

Action of Saliva

Saliva is a very important liquid, which takes part in the digestion of food. It is regularly secreted by the salivary glands under the regulation of autonomic nervous system. Salivary glands secrete 1 to $1\frac{1}{2}$ litre of saliva per day.

Functions of Saliva

1. Saliva contain 99.5%, water rest mucus and potassium and bicarbonate ions, it moistens, softens and lubricates the food. Due to saliva food could easily moved around in buccal cavity by the tongue.
2. Saliva is acidic (pH-6.8) in nature. It contains enzyme called ptyalin, which splits carbohydrates of food into maltose. In man, it accounts for splitting of about 30% to 40% of food carbohydrates.
3. Saliva keeps the tongue moist. It helps in speaking and free movements of the tongue in the cavity.
4. Taste buds of the tongue can taste the food only when the food is moistened by saliva.
5. It dissolve the small bits of food. It destroys the bacteria that enter into the cavity in large numbers with or without food. It is possible due to ions of thiocyanate and lysozyme enzyme present in the saliva.

Q.3. What is the structure of liver? Describe in brief.

Ans.

Structure of Liver

Liver is a collective mass of numerous lobules formed of hepatic cells liver is reddish brownish structure which has five lobes. The lobes are polygonal and are separated by interlobular septa. The compact mass of hepatic cells is tunneled through intrinsic system of narrow space carrying fine blood capillaries, the liver sinusoids.

In transverse section of liver following structure are visible :

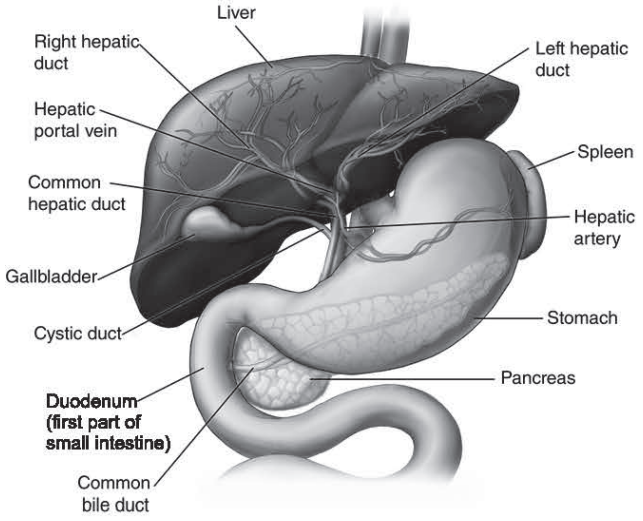


Fig. Structure of liver

1. **Hepatic Cells :** These are polygonal with centrally situated nucleus and granular cytoplasm. These contain fat, protein and glycogen in the form of granules. The

pigment granules are also found scattered in the cytoplasm. The hepatic cells synthesize hepatic juice and carry out a number of other physiological activities.

2. **Bile Capillaries :** Between the adjacent lines of hepatic cells run **bile capillaries** or **bile passages**. These capillaries unite to form large ductuless which finally combine on the surface of lobules forming **interlobular channels**. These act as drainage ducts for the bile juice and convey it to the gall bladder by hapatic ducts.
3. **Blood Capillaries :** The hapatic portal vein forms interlobular veins at the surface of the lobules. These after traversing through the lobules between hepatic strands enter the sinusoids end empty into the intralobular veins, all of which join to form the hepatic vein. The blood capillaries supply blood to the hepatic cells.
4. **Nerve Fibres and Connective Tissue :** The hepatic cells are held together in the connective tissue fibres. The nerve fibres of sympathetic system are found scattered in the connective tissue mass.

Q.4. Write a short note on partition hypothesis of Frazer and Pfluger for absorption of fats in intestine.

Ans. During digestion the fats are hydrolysed into fatty acid, glycirol and into mono, di- and tri-glycerides. Their absorption is accomplished in the intestine. There are two theories regarding the absorption of fats :

1. **Partition hypothesis of Frazer :** (i) Fats in imulsified form is absorbed into the lymphatic channels and pass into the blood through the thoracic duct.
   (ii) Fatty acids and glycerol produced by hydrolysis of fat are absorbed into the partal blood. The fatty acids with bile salts form complex salts soluble in water and are absorbed by the mucosa cells of intestine wall.
2. **Lipolytic hypothesis of Pfluger :** According to this hypothesis the mucosal epithellial cells of intestine absorb fatty acids and glycerol and from them resynthesize triglycerides. These are transported to lymph spaces where these remain suspended in the lymph as chilomicrones and make lymph milky.

Q.5. What do you mean by Bohr effect? Explain with the help of diagram.

Ans.

Bohr Effect

Changes in pH and CO_2 concentration in blood are important to enhance oxygenation or behinding of haemoglobin with O_2 of blood in the lungs and its deoxygenation (dissociation and release of O_2 from oxyhaemoglobin) in the tissues. This is known as **'Bohr effect'**. It can be explained as follows : As blood passes through the lungs, CO_2 readily diffuses from it into alveolar air. This reduces blood pCO_2 (partial pressure of CO_2) and raises its pH. Both these changes enhance rapid oxygenation of haemoglobin. The net result of this is decreased pCO_2 increased pH and pO_2 and reduced p_{50} (this is an index of pO_2 at which haemoglobin is only half saturated).

Since, there is no question of dissociation of oxygen and haemoglobin in lungs, the curve of this dissociation shifts towards left in a graphic illustration. In the tissues, opposite effect occur. CO_2, entering into the blood from the tissue fluid, increases H^+ ion concentration and both these changes enhance dissociation of oxyhaemoglobin, allowing more and more supply of O_2 to the tissue fluid for body cells. Consequently, pCO_2 increases in the blood, pH and pO_2 decrease and p_{50} rises. All these, conditions naturally shift the oxygen dissociation curve of

haemoglobin towards the right. A rise of body temperature has effects similar to increase pCO_2 and decrease pH.

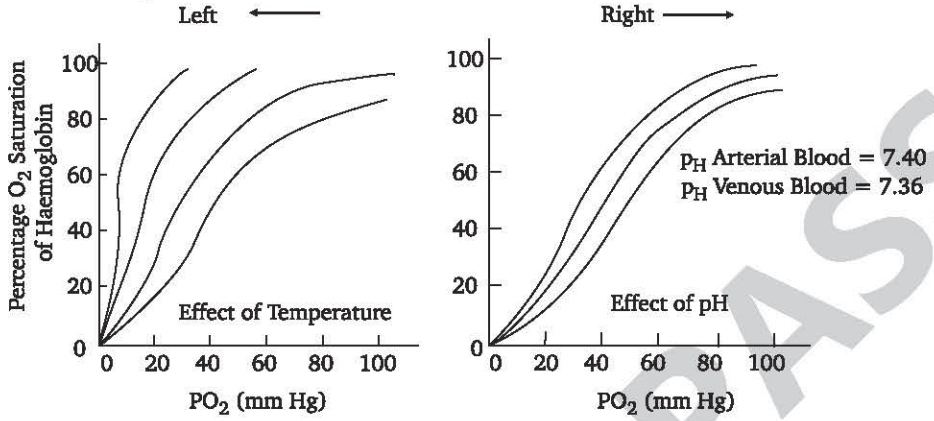


Fig. : Effect of temperature ond pH upon O_2 haemoglobin dissociation curve

Q.6. Write about the functions of liver.

Ans.

Functions of Liver

1. The bluish or greenish bile juice is manufactured by the liver cells. It contains liver salts like **sodium carbonate** (Na_2CO_3) and **cholesterol**.
2. The bile juice is alkaline and reacts against the acidity of food to prepare the alkaline medium necessary for digestion.
3. It destroys bacteria. Inactive lipase of the pancreatic juice is activated by the bile juice.
4. The liver acts as a store-house for nonconsumable sugar. The sugar is stored in the form of glycogen (**glycogenesis**). Whenever needed by the body, the glycogen is converted into glucose (**glycogenolysis**) to be utilized.
5. To overcome the shortage of sugar, glucose is synthesized from proteins (**gluconeogenesis**).
6. Proteins and amino acids are converted into ammonia (NH_3) and urea after chemical decomposition (**deamination**).
7. The fat digested by the alimentary canal cannot be used by all the parts of the body. Hence the **Kupffer cells** of liver pick up the fat granules and convert them into ordinary fat.
8. Liver synthesizes and stores prothrombin and fibrinogen proteins.
9. The bile juice carries a number of excretory products such as calcium phosphate etc. which are discharged into the duodenum and finally excreted out along with the undigested food.
10. The special blood corpuscles of liver act as phagocytes and destroy bacteria. In the embryonic stage of mammals, it manufactures RBCs.
11. A very important substance **heparin** is produced in the liver which avoids clotting of blood in blood vessels.
12. The old and destroyed RBCs are converted by the liver into bile pigments.

Q.7. What do you mean by gaseous exchange? Show it with the help of labelled diagram.

Ans.

Gaseous Exchange

Oxygen of the inspired air diffuses into the blood through the walls of the alveoli and the capillaries. Likewise, carbon dioxide from the blood diffuses into the alveoli. The diffusion of the gases depends upon the difference in partial pressure across the capillary membrane.

In a mixture of gases, each gas exerts its own pressure. The total pressure of dry air in the alveoli is 713 mm Hg, of which oxygen constitutes about 14%. The partial pressure of oxygen (P_{O_2}) in alveoli, therefore, is approximately 100 mm Hg ($P_{O_2} = 713 \times 0.14 = 92.82$). The partial pressure of carbon dioxide (P_{CO_2}) of the alveolar air is 36 mm Hg. The P_{O_2} and P_{CO_2} of venous blood is approximately 40 and 46 mm Hg, respectively. Therefore, the difference in pressure of 60 mm Hg allows the passage of oxygen from the pulmonary alveoli to venous blood which is thus oxygenated. Similarly, there is difference of pressure of carbon dioxide between the venous blood and alveoli. The difference is about 10 mm Hg, and is sufficient to cause the diffusion of carbon dioxide from venous blood to alveoli. After gaseous exchange, blood has a P_{O_2} of 100 mm Hg and P_{CO_2} of 36 mm Hg.

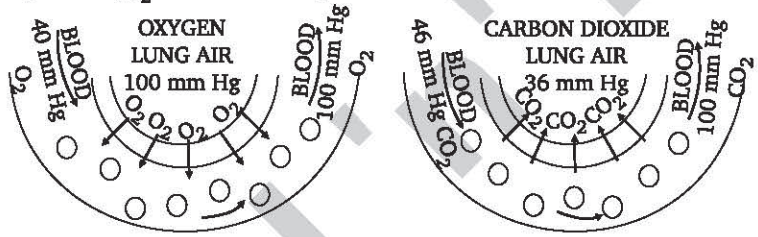


Fig. Diagram showing exchange of gases in the lung. Left, the transport of oxygen from the lung to the blood due to higher partial pressure of O_2 in the lung. Right, the transport of CO_2 from the blood to the lung due to higher partial pressure of CO_2 in the blood.

The diffusion of nitrogen, which forms a considerable portion of the atmospheric air, does not arise because the pressure of nitrogen is the same in blood as in the pulmonary alveoli.

Q.8. Write a short note on mechanism and breathing control in mammals.

Ans.

Breathing

In mammals, the action of respiratory muscles as those of **diaphragm** and the chest, abdominal walls and ribs increase the volume of thoracic cavity and pressure, it reduces, this atmospheric air rushes its way into the lungs and **inspiration** is done. During expiration, the diaphragm, ribs, vertebral column and muscles get relaxed and lungs contract expelling the air out.

Control on Breathing

The respiratory process is involuntary and regulated by a particular group of cells present in the medulla oblongata. These cells from the respiratory centre and discharge impulses to the spinal cord and finally to nerves, which incite the muscles of inspiration. When nerve impulses are stopped expiration is done due to relaxation of diaphragm and muscles of ribs. Respiration is regulated by two ways :

(i) Reflex Control (ii) Chemical Control.

According to **Hering** and **Breuer**, in reflex control respiratory centre sends either spontaneous impulses or in response to the carbon dioxide present in the lungs.

While in chemical control, carbon dioxide concentration of blood which is sensitive to respiratory centre, regulates the respiration. A slight increase in the carbon dioxide concentration in the blood results in deep and fast breathing.

Q.9. Write about the rhythmicity and control of breathing.

Ans. Rhythmicity and Control of Breathing

Breathing is caused by the rhythmic contraction and relaxation of the diaphragm and the external intercostal muscles of the chest. These muscles consist of skeletal muscles and cannot contract unless stimulated to do so by nerves. The movement of these muscles is brought about by the generation of efferent and afferent nerve impulses. The efferent nerve impulses are generated at respiratory centres in the anterior medulla oblongata and posterior pons (part of the brain stem just above the medulla); the afferent form the pulmonary stretch receptors (**Hering-Breuer** receptors) in the lungs.

The respiratory centre consists of three functional units, viz., the pneumotaxic or pontine centre in the rostral-most part of the pons, the expiratory centre in the lower and middle pons, and the inspiratory centre in the ventro-lateral medulla. These units are connected in such a manner that the inspiratory centre both excites and inhibits the expiratory centre, the expiratory centre only inhibits the pneumotaxic centre, and the pneumotaxic centre inhibits the inspiratory centre.

The inspiratory centre (cluster of neurons) sends out efferent nerves (phrenic nerves to the diaphragm and intercostal nerves to the intercostal muscles which cause the contraction of these muscles. This accounts for the inspiratory phase of the breathing cycle. The inspiratory centre simultaneously excites the expiratory centre. This in turn stimulates the pneumotaxic centre; the latter then inhibits the inspiratory centre. This stops the discharge of its inspiratory impulses through the efferent nerves. As a result of this, the diaphragm and the external intercostal muscles relax and the expiratory phase of breathing cycle commences. It is obvious from the above discussion, therefore, that inspiration is an active process while expiration passive. The expiratory centre, nervertheless, is also connected with efferents to the diaphragm and external muscles, which can bring about active expiration.

The inspiratory centre sends out continuous impulses so that if all nerves except the efferents are severed, a continuous inspiration (apneusis) occurs. The rhythmicity of breathing is also influenced by afferent impulses generated by the pulmonary stretch receptors (Hering-Breuer receptors) of the lungs. The stretch receptors discharge impulses when the lungs inflate. These impulses travel upwards in the vagus nerves and inhibit the inspiratory centre. This is known as Hering-Breuer reflex. The Hering-Breuer receptors act like "circuit breaker" and are stimulated only when they are fully stretched. This takes places at the height of the inspiratory phase when the lungs reach a certain threshold tension. The time delay between the onset of inspiration and the simulation of Hering-Breuer receptors allows successful completion of the inspiratory phase.

However, even if the vagus nerves are cut, the breathing continues to be rhythmic, although it comes deeper and slower. Hering-Breuer reflex, therefore, is not the only mechanism that causes rhythmicity of breathing. The respiratory centres along with the Hering-Breuer reflex make the rhythm in breathing more reliable. Voluntary control of breathing is also mediated through the same nervous mechanism as involuntary breathing. In the former case the higher centres of the brain, cerebral cortex, send out impulse to the respiratory centres and control their activity.

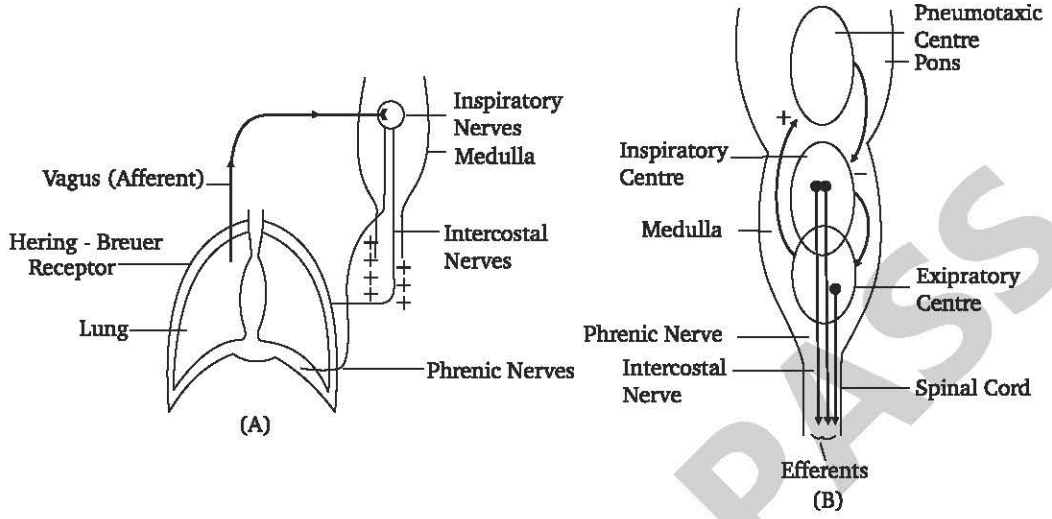


Fig. Diagrams showing regulation of respiratory rhythm : (A) The Hering-Breuer mechanism; (B) The Pontine mechanism.

Strong emotions, fright, excitement, and other mental factors also have a striking influence on the breathing process. Choking and coughing are reflex acts of protective value which are usually caused by stimulation of nerve endings in the lining of the respiratory passages by chemicals or foreign particles. Choking and coughing generally result in expulsion of the irritating substances.

SECTION-C LONG ANSWER TYPE QUESTIONS

Q.1. Describe the physiology of digestion in different parts of mammalian alimentary canal.

Ans.

Digestion

Digestion is the biological process by which the various items of food become broken up into a form that can be assimilated into the blood and lymph. The chemical action in the breakdown is called **hydrolysis**. Whereby water is inserted across the junctions of the initial molecule, making many small units.

Types of Digestion

Digestion in animal is of two types :

1. **Intracellular Digestion :** By which the food particles are taken directly into the cell lining the gut (lower animals).
2. **Extra-Cellular Digestion :** By which the enzymes are liberated into the alimentary canal and the product of the action of the enzymes are absorbed. This is the types of digestion in mammals and all other vertibrates.

The **alimentary canal** of the vertebrates is differentiated into two regions for functions of **digestion** and **absorption**. In mammals, the digestion begins in the buccal cavity where the teeth are differentiated according to the diet of the animal and where salivary enzymes begin their chemical digestion of food.

Physiology of Digestion in Man

The enzymes are organic catalysts which hasten the chemical reaction of the body. Three pairs of salivary glands, viz., the parotid, sub lingual and mandibular open into the buccal cavity.

The presence of food in the mouth stimulate sensory structures in the buccal cavity which in turn stimulates the salivary glands, to secrete salvia. The stimulation is also carried to the stomach via the vagus (X cranial nerve) and the stomach is thus prepared to receive the food.

A. Digestion in Buccal Cavity

1. Saliva contains the enzyme—ptyalin, sodium bicarbonate, mucus and water. With pH 6.7 Ptyalin acts only upon Carbohydrates. It hydrolyses into **maltose** though many steps. The mucus lubricates the food and the teeth and tongue help to mix the food and enzyme. The mastication of the food by teeth aids the subsequent digestion by breaking food into smaller particles on which enzyme acts.
2. **Oesophagus :** No digestion takes place in the oesophagus and it serves merely a passage for food from the buccal cavity to stomach by paristatic movements.

B. Digestion in Stomach

The lining of the stomach consists of a number of gastric pits where gastric juice is secreted. It contains :

1. **Mucus :** Its function is to protect the tissues from the action of the enzymes, to neutralise the medium and to provide a mechanical buffer between the substrates and living tissue.
2. **Hydrochloric Acid :** It is secreted by **oxyntic** cells. It makes the medium **acidic** which is suitable for action of **pepsin** and to **kill** a majority of bacteria taken with the food.
3. **Pepsin :** It is the enzyme, which acts on proteins. It is and endopeptidase which converts protein into peptone molecules.

   Pepsin is secreted in an inactive state called pepsinogen and it is activated by HCl and then by its own hydrolyses, it is converted into pepsin.
4. **Rennin :** It is found only in mammals. In the presence of Ca^{++} salts, the soluble **milk protein** or **Caseinogen** is converted into in soluble casein. The solubility of casein depends on pH and it is curdled in the presence of rennin and Ca^{++}.

C. Co-ordination of the Stomach

Impulses, caused by food in the buccal cavity pass through vagus and prepare the stomach for receiving food. Smell or sight of food may also stimulate the stomach. Once the food reaches the stomach, the hormonegastrin is secreted by the gastrine epithelium which is discharged into the blood and through circulation it reaches the **gastric pits** to increase their activity. The action of sympathetic nerves to the stomach depresses the enzyme secretion.

The food stays in the stomach for about 4 ot 5 hours during which, pepsin and rennin have done their work in the presence of HCl. The warmth in the stomach melts fatty substrates and the churning action of stomach breaks the largest particles into smaller bits to facilitate enzymatic action later.

D. Digestion in Intestine

The terminal narrow end of the stomach is called **pylorus** which leads into the small intestine. The first section of intestine is duodenum which is a wide tube. As soon as the food (chyme) enters the duodenum, its mucosa secretes three hormones :

1. **Secretion :** It stimulates the floro of pancreatic juice from pancreas.
2. **Cholecystokinin :** It stimulates the contraction of gall bladder.

3. **Enterocrinin :** It stimulates the secretion of intestinal juice. The bile juice from the liver, pancreatic juice from the **pancreas** and intestinal juice from the intestinal glands are mixed in the small intestine and complete the digestive process.

   (i) **Bile Juice :** It is an alkaline fluid which is formed in the hepatic cells of the liver and stored in **gall bladder** through fine hepatic ducts. The gall bladder contracts and the bile passes to the duodenum. The **bile** neutralises the acidity of chyme. It contains proteins, water, inorganic salts, bile salts, lipids and **bile pigments.** However, enzymes are absent.

   Bile salts like sodium glycocholate, sodium taurocholate, and **cholesterol** emulsify fat and break it into small particles. These reduce the surface tension and help in the digestion of fats and fat soluble vitamins.

   The **bile pigments** are bilirubin and **bilverdin.** These are formed by the decomposition of haemoglobin. These are excretory substances and are expelled out along with undigested food.

   (ii) **Pancreatic juice :** It is alkanine (pH 8) and contains following digestive enzymes which are secreted inactive or in zymogen state.

   (a) **Trypsin and Chymotrypsin :** These are secreted in inactive form called **trypsinogen** and **chymotrypsinogen.** In the presence of enterokinase and intestinal juice trypsinogen is activated to trypsin, which in turn activates chymotrypsinogen into chymotropsin. Both of these enzymes hydrolyse protein into polypeptides :

$$\text{Trypsinogen} \xrightarrow{\text{Enterokinase}} \text{Trypsin}$$

$$\text{Chymotrypsinogen} \xrightarrow{\text{Trypsin}} \text{Chymotrypsin}$$

   (b) **Carboxypeptidase :** It hydrolyses the polypeptide chain into amino acids.

   (c) **Amylopsin :** It hydrolyses the remaining starch and glycogen into maltose like disaccharides.

   (d) **Steapsin or Lipase :** It hydrolyses the remaining fats into fatty acids and glycerol.

   (e) **Nucleases and Nucleotidases** like ribonuclease and deoxyribonuclease hydrolyse **nucleic acids.**

Physical Changes in food in duodenum : The food is converted into a very fine paste, called **chyle.**

E. Digestion of food in Ileum (Small Intestine)

The Brunner's glands and the crypts of Leiberkuhn secrete intestinal juice or Succus entericus. It is alkaline in nature (pH 8.3). It contains following enzymes :

1. **Enterokinase or Enteropeptidase :** It activates the inactive trypsinogen into trypsin.
2. **Erepsin :** It is a group of peptidase enzymes which hydrolyse polypeptides, tripeptidase and dipeptidase into amino acids. These enzymes are known as tripeptidase and amino peptidase.
3. **Arginase :** It converts amino acids into urea.
4. **Maltose :** Hydrolyses maltose (disaccharide) into Monosaccharide glucose.

5. **Sucrose :** Hydrolyses sucrose into (monosaccharides) glucose and fructose.
6. **Lactose :** Converts lactose into glucose and galactose.
7. **Lipase :** Emulsifies remaining fat into fatty acids and glycerol.

Succus Entericus also contains nuclease, nucleotidase, nucleosidase and amylase, which hydrolyse nucleic acids, nucleotides nucleosides and starch, respectively. The Brunner's glands also secret mucus which lubricates the intestinal cavity.

F. Digestion of Food in Caecum

In herbivorous animals food is rich in cellulose. The caecum contains bacteria which can digest cellulose and hydrolyse into sugars, which are absorbed by the intestinal wall.

Rectum is the last part which stores and propels the faecal matter through the anus.

Q.2. Describe the organisation of gastrointestinal tract with suitable diagrams.

Ans. Organisation of Gastrointestinal Tract

Gross Structure : The mouth is followed by a muscular tube called pharynx. The latter leads to a spacious chamber, the stomach, through a narrow tube known as oesophagus. The passage from the oesophagus to the stomach is guarded by a valve known as the cardiac sphincter. The stomach is followed by small intestine which can be divided into three parts. The distal end of the stomach opens through pyloric sphincter into the duodenum which is first part of the small intestine. The ducts from the liver and pancreas pour their secretions into the duodenum. The middle part of the small intestine is called the jejunum, and the last ileum. The last section of the alimentary canal is known as large intestine. Ileum opens into the first part of large intestine, the colon through another valve known as ileo-colic valve. A vermiform appendix is present at the site of ileo-colic valve which is vestiginal in human beings. The colon leads into the last tubular part of large intestine—rectum. The latter, whose distal end is guarded by anal spincters, opens outside through the anus.

The wall of the entire alimentary canal is typically made up of four layers. These are the mucosa, submucosa, muscularis and the serosa.

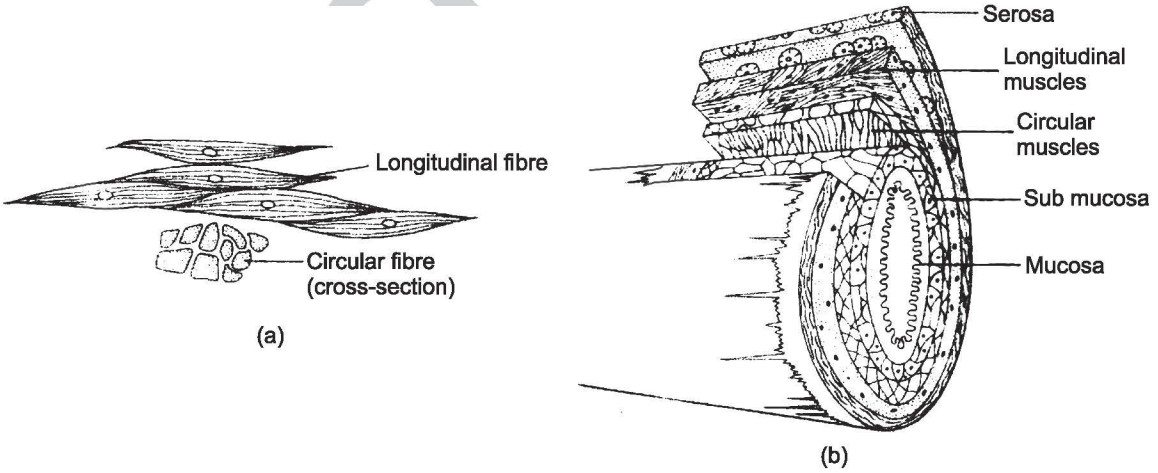


Fig. (a) Microscopic appearance of intestinal smooth muscles; (b) Diagrammatic representation of arrangement of layers of the intestinal wall

The innermost layer of the alimentary canal is known as mucosa. It is made up of a single layer of stratified or columnar epithelial cells. Throughout its lengths, the epithelium is provided with gland cells. The epithelium rests upon a thin membrane known as basement membrane. The submucosa contains blood and lymph vessels, and a nerve plexus held together by loose

connective tissue. The muscularis consists of an inner circular and an outer longitudinal layer of muscles. This layer is also provided with nerves forming another plexus. The serosa is the outermost layer of the alimentary canal. It is continuous with mesenteries and contains blood and lymph vessels, and sometimes adipose tissue. In oesophagus, however, the serosa is absent and the outermost cost is made up of fibrous tissue known as fibrosa.

Properties of Intestinal Smooth Muscles

The muscular is layer of gastro-intestinal tract is made up largely from smooth muscle fibres. The muscle fibres are arranged in circular and longitudinal layers. The circular muscle fibres run circumferentially whereas the longitudinal muscle fibres run parallel to the longitudinal axis of the gut. Contraction of the circular muscle fibres reduces the diameter whereas that of longitudinal muscles shortens the length of the alimentary canal. The simultaneous contraction of these two muscle layers brings about the characteristic intestinal movements called peristalsis. This movement mixes the food as well as propels it forwards. Normally, the food moves only towards the rectum. Under abnormal conditions the food may be propelled towards the mouth by antiperistaltic movements causing vomiting.

The smooth muscles of the alimentary canal are plasitc in nature, as the tension exerted on the muscles due to stretching disappears within a very short period. This allows large quantities of food to be stored in stomach and intestine for long periods without causing any damage. The disappearance of tension caused by stretching saves energy which would otherwise be required to keep the muscles in a state of active tension (stretch). The muscles also exhibit automaticity and tonicity. Automaticity means that the muscles may contract even without nervous stimuli. This results in involuntary peristaltic movement of the alimentary canal. The muscles of the alimentary canal are always in a state of partial tension, a property referred as tonicity.

Innervation of Gastrointestinal Tract

The muscles of the gastrointestinal tract (alimentary canal) are under the control of the autonomic nervous system; the parasymphathetic nerves, which are cholinergic accelerate whereas the sympathetic nerves which are adrenergic inhibit their contractions. Acetylcholine, therefore, increases the tonus and magnitude of active contraction. A drenalin, on the other hand, has an opposite effect. However, the valves (sphincters) of the alimentary canal are innervated in an opposite manner. These are relaxed by parasympathetic stimuli and contracted by sympathetic sensations.

There are two nerve plexuses present in the intestine; the one present in the sumucosa is called the plexus of Meissner, and the other between the circular and longitudinal muscles is known as the plexus of Auerbach. These nerve plexuses form a local system of conduction within the muscles of the intestine. These two plexuses make synaptic connections with the parasympathetic nerve only. The sympathetic nerve sends out branches directly without making connections with these plexuses.

The autonomic nerve supply of the gastro-intestinal tract has a regulatory function only. The normal contractions of the alimentary canal, however, are dependent on the automaticity of smooth muscles and the local nerve plexuses.

Q.3. What do you understand by digestion? Describe the process of digestion of carbohydrates, facts and proteins in different parts of alimentary canal.

Ans.

Digestion

Digestion is the hydrolysis of macromolecules of food components into small molecules or monomers by the assistance of enzymes at normal body temperature. After digestion, food substances are easily absorbed by the intestinal wall and are utilized by the cell for cell metabolism.

Digestion of Carbohydrates

1. In Buccal Cavity : In buccal cavity digestion of carbohydrates starts. Salivary amylase enzyme which is present in saliva hydrolyses starch into sugar (maltose sucrose and lactose). In the stomach carbohydrates are not digested completed in the small intestine where intestinal lipase hydrolyses the remaining fats. The mono and diglycerides are absorbed in emulsified form while the hydrolysed fats are absorbed as glycerol and fatty acids.

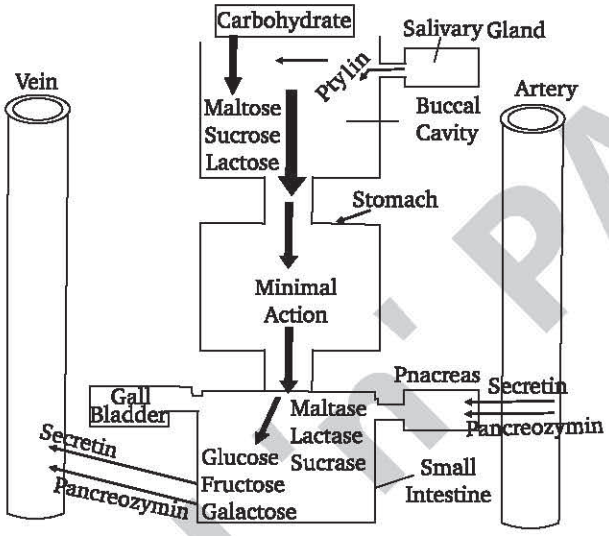


Fig. 1 : Schematic respresentation of carbohydrates digestion and absorption

Digestion of Proteins : Digestion of proteins begins in stomach. Gastric juice contains enzyme pepsin which hydrolyses proteins into **proteoses** and **peptones.**

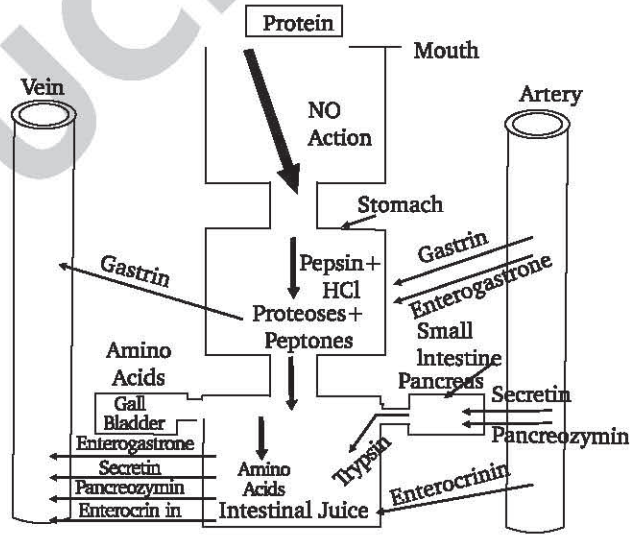


Fig. 2 : Schematic representation of digestion of proteins.

$$\text{Proteins} \xrightarrow{\text{Pepsin}} \text{Proteoses} + \text{Peptones}$$

Inside duodenum, the pancreatic juice contains proteins digestive enzyme **trypsin** and **chymotrypsin**. Both of them hydrolyse proteins and proteoses into peptones and polypeptides.

$$\text{Proteins} \xrightarrow{\text{Trypsin}} \text{Peptones} + \text{Polypeptides}$$

$$\text{Proteins} \xrightarrow{\text{Chymotrypsin}} \text{Peptones} + \text{Polypeptides}$$

The enzyme carboxypeptidase hydrolyses polypeptide chains into constituent **amino acids.**

The digestion of proteins is completed inside small intestine. The intestinal juice or saccus entericus contains protein digesting enzymes **tripeptidase, dipeptidase** and **aminopeptidase**. These enzymes complete hydrolysis of polypeptide chains into amino acids.

$$\text{Polypeptide chain} \xrightarrow{\text{Tripeptidase}} \text{Tripeptides}$$

$$\text{Polypeptide chain} \xrightarrow{\text{Dipeptidase}} \text{Dipeptides}$$

$$\text{Tripeptides} + \text{Dipeptides} \xrightarrow{\text{Amino peptidase}} \text{Amino acids}$$

2. In Duodenum : The digestive enzyme amylopsin or intestinal amylase present in the pancreatic juice, takes up the digestion of carbohydrates in alkaline medium and hydrolyses remainder starch and all carbohydrates to maltoses, sucrose and glucose.

3. In Small Intestine : The intestinal juice or saccus entericus, secreted by the intestinal glands contains enzymes maltase, lactase and invertase or sucrase. These enzymes act on maltose, lactose and sucrose respectively and hydrolyse them into monosaccharides :

(i) $\text{Sucrose} \xrightarrow{\text{Sucrase}} \text{Glucose} + \text{Fructose}$

(ii) $\text{Maltose} \xrightarrow{\text{Maltase}} \text{Glucose}$

(iii) $\text{Lactose} \xrightarrow{\text{Lactase}} \text{Glucose} + \text{Galactose}$

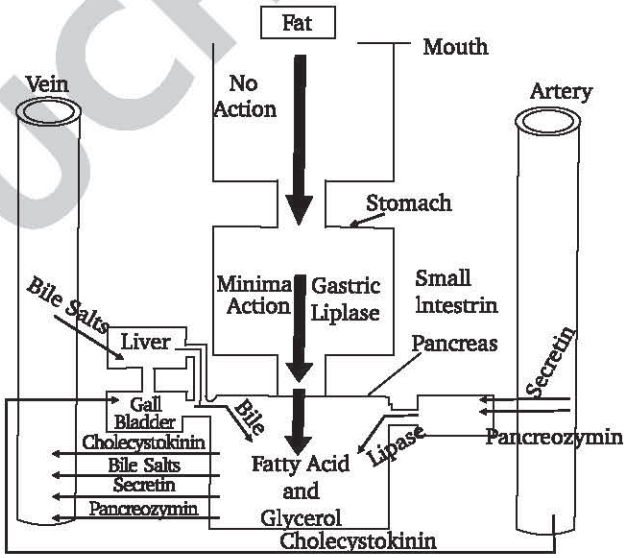


Fig. 3 : Schematic representation of fat digestion

Digestion of Fat : Fats remain unchanged in buccal cavity. These are partially hydrolysed in stomach into **fatty acids** and **glycerol** by the action of gastic lipase. In duodenum, the bile

juice secreted by liver, emulsifies fat into small particles (mono and diglycerides) and enzyme steapsin or pancreatic lipase of pancreatic juice hydrolyses remaining fats into fatty acids and glycerol.

Q.4. Explain the mechanism of breathing. Describe how is breathing regulated in the mammalian body.

Ans.

Breathing

For continued gaseous interchange in lungs a constant renewal of air is essential *i.e.*, fresh air enters the lungs and exhausted or used air is expelled out alternately. This process of taking fresh air from the atmosphere into the lungs and expelling out the used air from lungs to the exterior is known as breathings.

The process of breathing can be separated into two distinct steps :

1. **Inspiration** or breathing air into the lungs.
2. **Expiration** or expelling out air from the lungs.

The movement of air in and out of the lungs occurs because of alternate changes in intrapulmonary pressure, which is brought about both during inspiration and expiration by the contraction and relaxation of **diaphragm** and the **intercostal muscles**.

1. Inspiratory Mechanism

During inspiration the size of the thoracic cavity increases in all directions. The enlargements is brought about by the flattering of **diaphragm** and lifting up of the thoracic basket.

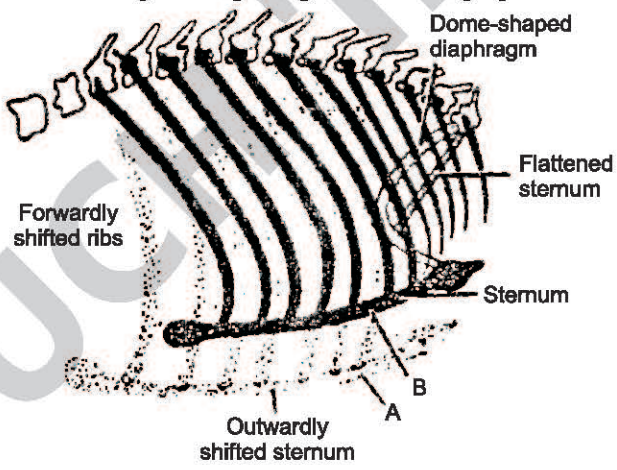


Fig. 1 : Position of ribs during expiration and inspiration

The diaphragm is formed of a thin sheet of radial muscles present on the floor of thoracic cavity. Its margins are attached to lumbar vertebrae posteriorly and laterally and to the sternum anteriory. In resting position it is dome-shaped. During inspiration, when the radial muscles contract, the diaphragm flattens and descends down into the abdominal cavity. As a result thoracic cavity enlarges in antero-posterior direction.

The ribs are provided with two sets of muscles—**external intercostal muscles** and **internal intercostal muscles**. During inspirations the external intercostal muscles and the intercartiginous portion of the internal intercostal muscles contract pulling, the ribs forward and outward and thereby bringing about the enlargement of thoracic cavity. When the thoracic cavity increases in size, the pleural cavities expand and negative pressure is

increased in it. Now the lungs enjoy greater space and expand. As a result pulmonary pressure is lowered below the atmospheric pressure. Therefore, a suction force is created and the atmospheric air rushes in through the respiratory passage.

2. Expiratory Mechanism

During expiration, the changes occur in opposite direction. Due to relaxation of radial muscles of diaphragm and contraction of internal intercostal muscles the diaphragm and ribs are brought to their original position and form. The diaphragm assumes domeshaped appearance. Therefore, the volume of thoracic cavity is reduced and so also the negative pressure of the pleural cavities. This exerts pressure on lungs and the air filled in the lungs is compressed and is squeezed out. As a matter of fact, the expiratory phase is a passive event in breathing.

The extent to which the movements of thoracic cage and diaphragm play part in respiration varies from animal to animal and from year to year in the same animal. The lungs are not totally emptied by any movement of breathing and some air is left in air passages. Therefore, the air is never changed completely during inspiration but is merely freshened up.

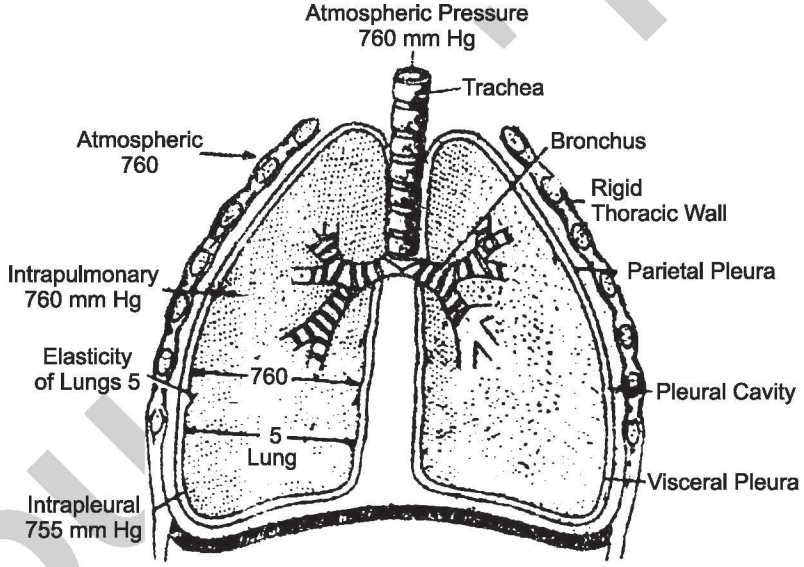


Fig. 2 : Diagram of throacic cavity shwowing intrapulmonary and intrapleural pressures with chest wall in resting position

Regulation of Breathing Reflexes

Respiration is an involuntary process and is carried out automatically at a constant rate under normal conditions. The contraction of various respiratory muscles at proper time and with proper strength to secure adequate gaseous exchanges is coordinated by a complex series of reflexes maintained by the nervous system and also to some extent by CO_2 concentration. The breathing reflexes are controlled in the following ways :

1. **Medullary respiratory centre** (the vital knot of Flourens) is situated in the floor of 4th ventricle present in the medulla. The centre is bilateral and two halves are connected together by commissural neurons. The sides of this centre are connected with the motor respiratory neurons. The neuron cells of the centre are connected to

the breathing apparatus with the motor as well as sensory or afferent and efferent nerves and thus maintain a reflex arc. These cells are sensitive to changes in the chemical organization of blood and concentration of CO_2 in plasma.

Each half of the respiratory centre is composed of two parts : inspiratory centre and expiratory centre. The expiratory centre lies above the inspiratory centre. Out of the two only one works at a time. According to Pitts, Magoun and Ranson, the inspiratory centre worked in normal breathing and expiratory centre during forced expiratory conditions like sneezing, laughing and coughing. The expiratory neurons are excited by the aforesaid stimuli, whereas inspiratory neurons discharge spontaneously.

2. **Stretch Receptors :** In the wall of alveoli of lungs are present stretch receptors baroreceptors, which are stimulated by the expansion and relaxation of lungs and propagate inhibitory impulses to the inspiratory and expiratory parts of the respiratory centre respectively. The receptors are innervated by the branches of vagus nerve.

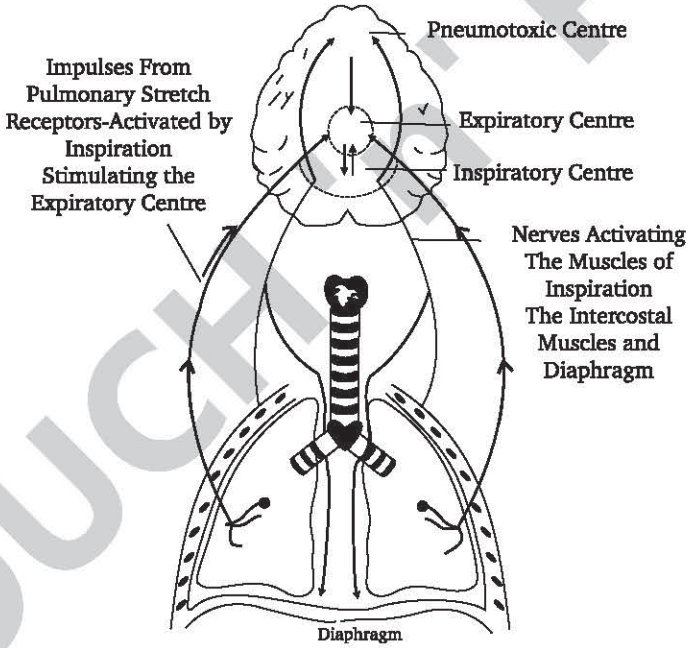


Fig. 3 : Diagrammatic representation of mechanism of breathing rhythm

3. **A Pneumotaxic Centre** is present in the pons, which acts as an inhibitory nerve centre and connected with both inspiratory and expiratory parts of respiratory centre.

The respiratory centre is connected with the lungs, carotid sinuses, aortic arch etc. through afferent nerves with the respiratory muscles through efferent nerves and with the pneumotaxic centre by both afferent and efferent nerves. The inspiratory centre propagates impulse spontaneously to the intercostal muscles. As a result of their contraction, the throax and lungs expand and in doing so stimulate the stretch receptors. The stretch receptors initiate impulses at a very high rate, which are propagated by afferent neurons in the vagus nerve to the pneumotaxis centre. The activated pneumotaxic centre is inhibitory in nature and sends impulses to the

expiratory centre. The activated pneumotaxic centre is inhibitory in nature and sends impulses to the expiratory centre. The expiratory centre then inhibits inspiratory centre. As a result inspiration ends and expiration starts. This reflex was described by Hering and Breuer and is described as Hering and Breuer reflex.

4. **Chemical Control :** Respiration is controlled to some extent by the concentration of respiratory gases in blood. The respiratory centre is very sensitive to CO_2 concentration. If increase in tension is slight, breathing becomes deep and fast permitting more CO_2 to leave the blood. Similarly, O_2 concentration in blood affects the breathing rate but in opposite direction.

Q.5. What is chloride shift or Hamburger's phenomenon? Discuss its importance in the transport of CO_2.

Or **Describe the transport of O_2 and CO_2 during respiration.**

Ans. **Physiology of Respiration**

The respiratory physiological mechanism consists of :

1. Exchange of Oxygen in Lungs

The first step in the supply of oxygen to tissues and the lost step in the discharge of CO_2, both take place in the lungs. It is accomplished by two systems, viz. Circulatory and respiratory one. With the aid of haemoglobin, blood carries to and from the tissue cells large amount of Oxygen and Carbon dioxide.

The ventilation of lungs in external respiration is accompanied with simultaneous gaseous exchange between blood and alveolar air across the alveolar walls, *i.e.*, diffusion of O_2 from alveolar air into the blood and that of CO_2 from blood into the alveolar air. Obviously, it depends upon the concentration gradients. (partial pressures) of the concerned gases in the fluid surface film of respiratory membrane. Both O_2 and CO_2 are highly and equaly soluble in lipid and easily diffusible through cell membrane. In water, however, CO_2 is about 20 times more soluble and diffusible than O_2.

The partial pressures of O_2 and CO_2 in alveolar air are 104 mm and 40 mm Hg respectively. While in the blood the arterial capillaries of alveolar wall, the partial pressure of O_2 and CO_2 are 40 and 45-46 mm Hg respectively. As the blood flows in alveolar capillaries, O_2 from alveolar air diffuses into it due to an initial pressure difference of 64 mm Hg. Which gradually falls, becoming zero at the venous end of alveolar capillaries. Thus, the mean partial pressure of O_2 in these capillaries comes to about 11 mm Hg. In an average young man, the diffusing capacity of respiratory membrane for O_2 under normal conditions average 21 ml per minute per mm Hg. Thus, about 230 ml of O_2 (11×21) should normally diffuse through respiratory membrane from alveolar air into pulmonary blood per minute.

The difference of partial pressure of CO_2 in pulmonary blood and alveolar air is only about 5 to 6 mm Hg, but, since CO_2 diffuses very rapidly through the respiratory membrane, this difference averages less than 1 mm Hg.

The net result of this gaseous exchange in alveoli is that in the blood drained away from alveolar wall, the partial pressures of O_2 and CO_2 are 140 mm Hg, and 40 mm Hg respectively, *i.e.*, equal to those in alveolar air.

2. Transport of O_2 and CO_2 in Blood

Oxygen diffuses across the respiratory epithelium into the blood and combines with the respiratory pigment, haemoglobin, which is red in collor. By binding oxygen, respiratory pigment increases the O_2 centent of blood.

Each haemoglobin molecule can combine with 4 Oxygen molecules.

$$\underset{\text{Haemoglobin}}{Hb} + O_2 \rightleftharpoons \underset{\text{Oxyhaemoglobin}}{HbO_2}$$

The rate of oxygen uptake increases in proportion to the difference in partial pressure across respiratory epithelium. A haemoglobin with high oxygen affinity facilitates the movement of O_2 into the blood from the environment because O_2 is bound to haemoglobin at low PO_2. Thus a large differences in PO_2 across the respiratory epithelium and, therefore, a high rate of oxygen transfer into the blood is maintained until haemoglobin in fully saturated. A haemoglobin of high oxygen affinity favours the uptake of O_2 by the blood, whereas a haemoglobin of low O_2 affinity facilitates the release of oxygen in the tissues.

Haemoglobin Oxygen affinity is unstable. It is reduced either by increase in PCO_2, temperature and organic phsophate ligands like 3-diphosphoglycerate (DPG) or ATP or by a decrease in pH.

Oxyhaemoglobin Dissociation Curve

The haemoglobin behaves in an unique manner under different physiological conditions. This is expressed by plotting the percentage saturation of Hb with oxygen against the PO_2 in the varying physiological ranges. This is know as Oxyhaemoglobin dissociation curve. The percentage of saturation in the ratio of the oxygen combined with the Hb to the oxygen capacity multiplied with 100, where the oxygen capacity is the maximum amount of oxygen that will combine with Hb at a high PO_2.

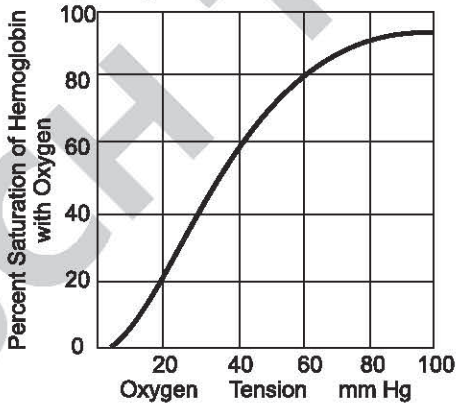


Fig. Graph showing the relationship between the partial pressure of oxygen and the formation of oxyhemoglobin—'Oxyhemoglobin-dissociation curve'.

A study of this curve illustrates the following remarkable properties of Hb :

1. The curve is S-shaped (sigmoid).
2. At PO_2 of 96 mm Hg. Hb is saturated with 97.5% of Oxygen.
3. The dissociation curve is flat at the top, at PO_2 greater than 100 mm Hg, Hb cannot accept more oxygen.
4. There is little change in the amount of oxygen held by haemoglobin, between PO_2 of 100 mm Hg and 70 mm Hg.
5. The low PO_2 (between 10-40 mm Hg) the curve is very steep.

The dissociation curve is not fixed. It changes with temperature. pH and other physiological conditions.

3. The Exchange of Oxygen in the Tissues

The freshly oxygenated blood is supplied to all parts of the body on reaching the tissue capillaries, each 100 ml of blood holds about 19.5 ml of oxygen, corresponding to a percentage haemoglobin saturation of about 97.5% at PO_2 of approximately 96 mm Hg.

Like the gases exchange in the lungs, the exchange of gases in tissues also occurs by passive diffusion of oxygen molecules from the region of high PO_2 to another low PO_2. The dissolved oxygen diffuses out of the plasma through capillary wall to reach the cells. Loss of oxygen from the plasma lowers the PO_2, surrounding the red corpuscles and, inturn, oxyhaemoglobin, dissociates, liberating about 25% of its available oxygen for tissue consumption.

Finally, the venous blood issues from the capillaries with a PO_2 of 40 mm Hg and an oxygen load of about 14.5 ml per 100 ml.

4. Exchange and Transport of Carbon dioxide

In addition to supply O_2, the blood also removes the waste products of cellular activity such as CO_2. It is carried by the venous blood to the lung capillaries where it is discharged in the expired gas.

Carbondioxide is readily soluble and dissolved as it is formed in the tissue cells. In solution, it is transferred to the tissue fluid surrounding the cells, and from there enters the capillaries where a small part of it carried in the plasma as dissolved gas.

The amount of carbon dioxide that goes into solution chiefly depends on the partial pressure (PCO_2). The carbonic acid (H_2CO_3) weakly dissociated, forming hydrogen (H^+) and bicarbonate (HCO_3^-) ions.

$$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

5. Carbon dioxide Exchange in Tissues

Like the interchange of oxygen, the Carbondioxide exchanges in tissues and lungs through simple, passive diffusion brought about by differences in partial pressure. However, since the carbondioxide is more rapidly soluble, it diffuses more quickly than oxygen. Removal of carbondioxide takes place through following ways :

(i) **Formation of Carbonic Acid and Bicarbonates :** Carbondioxide reacts with water of blood to form carbonic acid, which dissociates into bicarbonate, hydrogen and carbonate ions.

$$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

$$HCO_3^- \rightleftharpoons H^+ + CO_3^{2-}$$

The proportion of CO_2, HCO_3^- and CO_3^{2-} in solution is dependent on pH, temperature and the ionic strength of the solution.

H_2CO_3 combines immediately with the potassium salt of haemoglobin :

H_2CO_3	+	KHb	$\rightleftharpoons$	$KHCO_3$	+	H.Hb
Potassium haemoglobinate				Pot. bi. carbonate		free haemoglobin

About 80-85% CO_2 combines with potassium salt to form bicarbonates.

Chloride Shift of Hamburger Phenomenon : The $KHCO_3$ formed in RBC ionises immediately dissociates into :

$$KHCO_3 \rightleftharpoons K^+ + HCO_3^-$$

The bicarbonate ions diffuse out in the plasma and Chloride ions of RBC's combine with K^+ to form KCl.

$$H_2CO_3 + NaCl \rightleftharpoons NaHCO_3 + HCl$$

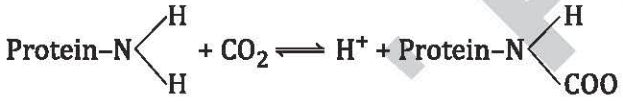
The exchange of Cl^- and HCO_3^- ions between plasma and RBCs is known as Chloride shift.

(ii) The alkaline phosphate present in plasma also combines with carbonic acid to form sodium carbonate.

$$Na_2HPO_4 + H_2CO_3 \rightleftharpoons NaH_2PO_4 + NaHCO_3$$

(iii) **Formation of Carbamino Compounds :** Carbondioxide released in blood, also reacts with NH_2 groups of proteins, and in particular, haemoglobin to form carbamino compounds.

$$HbNH_2 + CO_2 \rightleftharpoons H^+ + HbNHCO_2^-$$



6. Elimination of CO_2 in Lungs

The Haldane effect results from the simple fact that Oxyhaemoglobin behaves as a strong acid. This, in turn, displaces CO_2 from the blood in two ways :

(i) Due to its increased acidity, the haemoglobin losses its capacity to combine with CO_2. Hence all carbamino haemoglobin dissociates to release its CO_2.

(ii) Secondly, the highly acidic oxyhaemoglobin releases an excess of H^+ which binds with bicarbonate ions (HCO_3^-) forming carbonic acid, which soon dissociates into H_2O and CO_2. This CO_2 diffuses into the alveoli.

Thus, in the longs, the Haldane effect increases the release of CO_2 because of O_2 uptake by haemoglobin. But in the tissues, a reverse process occurs. The Haldane effect increases CO_2 uptake because of removal of O_2 from the haemoglobin.

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UNIT-VI

Circulation and Excretion in Humans

SECTION-A VERY SHORT ANSWER TYPE QUESTIONS

Q.1. What happens if the blood does not coagulate?

Ans. Blood coagulates or dots whenever there is an injury or trauma. Coagulation limits unnecessary blood loss from the body. Its absence can cause huge blood loss and can be fatal.

Q.2. What is haemoglobin?

Ans. Haemoglobin is an iron-containing compound and consists of an iron prophyrin (heme) coupled with a protein globulin. Hence, constitutes the active and functionally significant portion of haemoglobin whereas globin serves simple as a carrier of heme.

Q.3. What is the cardiac cycle?

Ans. The cardiac cycle is associated with the complete heart beat from its production to the commencement of the next beat. It comprises of diastole, the systole and the intervening pause.

Q.4. Define the oxyntic cells.

Ans. Parietal cell (also known as oxynetic or delomorphous cells) are the epithelial cells that secrete hydrochloric acid (HCl) and intrinsic factor. These cells are located in the gastric gland found in the lining of the fundus and in the cardia of the stomach.

Q.5. What is the role of the time gap in the passage of action potential from the sino-atrial node to the ventricle?

Ans. It allows ventricles to relax. Thus, the ventricular pressure falls, leading to the closing of semilunar valves, and restricts the backblow of blood ventricles.

Q.6. Define blood and lymph.

Ans. Blood and lymph are two essential fluids of the human body. Blood is a fluid connective tissue that consists of plasma, blood cells and platelets. Lymph is a colourless fluid that circulates inside the lymphatic vessels consisting of lymph nodes and lymph vessels.

Q.7. What is white blood cells?

Ans. White blood cells (WBCs) are nucleated amoeboidal cells which exhibit phogocytosis and amoeboid movement. Their count is higher in children and also during pathological conditions.

Q.8. What is the functional role of the lymphatic system?

Ans. It carries blood from the intestine to the liver before it is surrendered to the systemic circulation. Its importance is as follows :

1. The blood from the alimentary canal is rich in glucose, amino acids, and other nutrients. Excess of glucose and fats are utilized by the liver when blood passes through during starvation.

2. Conversion of toxic ammonia into urea that is later eliminated by the kidney.
3. The liver generates proteins such as fibrinogen which are passed through the circulation of blood.

Q.9. What is the heart beat?

Ans. No circulation of the blood is possible without a driving force. The circulation of blood, brought about by the rhythmic contraction and relaxation of heart muscles is known as the heart beat.

Q.10. What are the two types of the circulatory system?

Ans. The circulatory system is of two types :

1. **Open Circulatory System :** This type of circulatory system is found only in insects. In this system of circulation, blood flows through parts of the body cavity, which not in closed vessels.
2. **Closed Circulatory System :** This type of circulatory system is found in all the vertebrates. In this system of circulation, blood flows through closed tubes called blood like vessels.

Q.11. Write very short note on cardiac output.

Ans. It is the volume of blood ejected from the heart in the aorta in one minute and is also called minute volume. It is calculated as the product of stoke volume and the rate of heart beat.

$$\text{Cardiac output} = \text{Stroke volume} \times \text{Rate of heart beat}$$
$$= 70 \text{ ml} \times 70 - 72 \text{ times/minutes}$$
$$= \text{About } 5 \text{ L}$$

Q.12. What are the symptoms of Hypertension?

Ans. The common symptoms of hypertension are :

1. Dizziness.
2. Heart attack.
3. Visual Changes.
4. Shortness of Breath.
5. Narrowing of blood vessels and the formation of plaques in the blood vessels.

Q.13. How does the excretion of uric acid take place in birds and reptiles?

Ans. In birds and reptiles, uric acid is formed mostly in the liver transported to the kidney through blood. It is separated by renal tubules and temporarily stored in cloacae. Water is absorbed by cloacal walls needing only a minimum amount of water for excretion. In birds, urine is eliminated in a past-like form along with feces.

Q.14. What is systole?

Ans. The time period when the heart is contracting. The period specificially during which the left ventricle of the hear contracts.

Q.15. Differentiate between ureotelism and uricotelism.

Ans. The difference between ureotelism and uricotelism are as follows :

S.No.	Ureotelism	Uricotelism
1.	The process of elimination of main urea.	The process of elimination of mainly uric acid.
2.	Water moderately required for excretion.	Much less water required for excretion.
3.	Synthesis of urea requires less energy expenditure.	Synthesis of uric acid needs more energy expenditure.

Q.16. What is haemophilia?

Ans. Haemophilia is a mostly inherited genetic disorder that impairs the body's ability to make blood clots, a process needed to stop bleeding.

Q.17. What is the importance of counter-current systems in renal functioning?

Ans. Vasa rectal is responsible for the concentration of urine. The vase rectal is in the form of loops. Therefore, the blood flows in the opposite directions in two limbs of each vasa Fecta; the blood entering its descending limb comes into close contact with the outgoing blood in the ascending limb. This is called a Counter-Current System. The two limbs of the loops of Henle form another Counter-Current System.

Q.18. What is the position and function of the juxtaglomerular apparatus (JGA)?

Ans. This is a specialized cellular apparatus located where the distal convoluted tubule passes close to the Bowman's capsule between the afferent and efferent arterioles. JGA cells secrete substance like renin that modulates blood pressure and renal blood flow and thus, glomerular filtration rate (GFR) is regulated.

Q.19. What is the role of the liver in excretion in mammals?

Ans. The liver changes ammonia into urea which is less toxic than ammonia. Urea is eliminated from the body by the kidneys through urine. The liver is the principal organ of excretion of cholesterol, bile pigments (bilirubin and biliverdin) some vitamins, drugs, and inactivated products of steroid hormones. The liver excretes these substances in the bile which carries them to the small intestine. Ultimately, these substances get eliminated along with feces.

Q.20. What is hemopoiesis?

Ans. Hemopoiesis is the formation of blood cellular components. All cellular blood components are derived from haemotopoietic stem cells (HSCs). In a healthy adult person, approximately $10^{11} - 10^{12}$ new blood cells are produced daily in order to maintain steady state levels in the peripheral circulation.

Q.21. What is MN blood group in humans?

Ans. The MN blood group system is under the control of an autosomal locus found on chromosome 4, with two alleles designated LM and LN. The blood type is due to a glycoprotein present on the surface of red blood cells, which behaves as a native antigen. Phenotypic expression at this locus is codominant because an individual may exhibit either one or both antigenic substances. Frequencies of the two alleles vary midely among human populations.

SECTION-B SHORT ANSWER TYPE QUESTIONS

Q.1. Write about the functions of blood.

Ans.

Functions of Blood

1. **Transport of Food Materials :** Plasma transports digested food to different organs and tissues of the body.
2. **Removal of excretory substances :** Waste substances from the tissues are removed and carried to the kidneys for elimination.
3. **Disposal of CO_2 :** Major portion of CO_2 from the tissues is removed by plasma, where it remains dissolved in the form of bicarbonates.

4. **Transport of oxygen :** Certain percentages of O_2 is also transported by plasma. Even the oxygen which is bounded by the red blood cells is first dissolved in the plasma before reaching the cell.
5. **Blood Clotting :** The plasma protine fibrinogen, prothrombin and some other blood clotting factors are present in the plasma which help in the clotting of blood in case of injury.
6. **Protection Against Diseases :** Immuno globulins of plasma act as antibodies and neutralize the harmful effects of foreign agents.

Q.2. Describe various blood groups in human. Also explain their significance in blood transfusion.

Ans.

Blood Groups

Dr. Landsteiner (1900) discovered that when the red blood cells of one person were mixed with the serum of another person, the agglutination (Clumping of cells) sometimes occurs. When a foreign protein is injected into the blood, the cells produce a substance which reacts with the foreign protein. This produced substance is known as antibody, and the foreign protein responsible for the formation of antibody is known as antigen. Two antigens have been discovered in human red cells and the two corresponding antibodies in the serum. Thus, all human beings of the world can be identified into four categories as regard to the two antigens. These for possibilities are known as blood groups :

S.No.	Blood Group	Antigen in Cells	Antibodies in Plasma
1.	O	None	A, B
2.	A	A	B
3.	B	B	A
4.	A-B	A, B	None

Whatever antigen a person has in his blood, the corresponding named antibody must be absent in his plasma. Instead, he must have other of the two antibodies of none if he is to live.

Blood Transfusion

The knowledge of blood groups is a must for transfusion (the process of introducing the blood of one person into the body of other). Result of mixing cells and serum of human blood groups are shown in the following table :

Blood Groups	Donor	O	A	B	AB	Can receive Blood from	Can given to	Remarks
Acceptor	O	–	+	+	+	O	O, A, B, AB	Universal donor
	A	–	–	+	+	O, A	↓ A & AB	
	B	–	+	–	+	O, B	↓ B & AB	
	AB	–	–	–	–	O, A, B, AB	↓ AB	Universal recepient

***Note :** [– Compatible, no agglutination, + not compatible (death) aggultination]*
It is now known that ABO incompatibility is responsible for death of unborn children, and this often the cause why married couples have not children.

Determination of Blood Group

To determine ABO blood groups, blood of a person is taken out and allowed to clot. The residual liquid plasma left behind is called serum, which contains all the plasma antibodies. To this sera antibodies a and b are prepared.

A small drop of blood is drawn from the body of person whose blood group is to be determined and mixed separately with the sera upon a glass slide. The blood group is revealed by (clumping or no clumping) of the RBCs in the drops of respective sera.

The combination of antigens and antibodies in human blood is such that there is no antigen antibody clumping there by no agglutination takes place. During blood transfusion, it is necessary that the RBCs of donor's blood do not have these antigens which get agglutinated by antibodies present in the serum of recipient.

Q.3. Write a short note on Rh-factor.

Ans. **Rh Factor**

Rh factor or (Rhesus factor), a substance found in the human blood, is an example of inheritance by Mendel's laws. The factor so named because of the Rhesus monkeys blood from which was used in the experiments of its discovery.

An Rh antigen is present in the RBCs of the majority of people. The person having this antigens are called Rh-positive (Rh is a dominant gene), the remaining persons, without Rh antigen are called Rh-negative. About 85% of the world population and 97% of India are Rh-positive.

If Rh-positive blood is repeatedly transfused into an Rh-negative individual, the antigen, stimulates production of anti-Rh agglutination which is usually fatal. A more serious situation may result if an Rh-positive man and Rh-negative woman marry. Their offspring will be Rh-positive and will produce the antigens. Some of this antigen will pass from the embryo into the mother's blood and will produce antibodies. These antibodies will then enter the foetus and destroy its erythrocytes, causing anamia and death of new born babies.

Q.4. What is pacemaker? Write in brief.

Ans. **Pacemaker**

As said earlier cardiac cells have an innate rhythmicity or myogenecity which enables them to contract without nervous stimuli. Myogenecity is most highly developed in specialised structures which are called nodes, and less so in modified myocardial cells known as conducting tissue. As a matter of fact there is a gradient in the myogenic capability, in a descending order, starting from the nodes, conducting tissue, and the myocardial cells. Both the nodes and the conducting tissue are formed by anastomosed muscle elements showing an apparently embryonic undifferentiated structure, of which the sarcoplasm is particularly rich in glycogen. These are unique type of muscle elements of fundamental importance in cardiac physiology of contraction.

The heart of human body contains the node of Keith and Flack or sinoatrial node (S-A node) in the region where the superior vena cava opens into the right atrium. There is another nodal tissue, the node of Aschoff and Tawara or atrioventicular node (A-V node), situated above the point of insertion of the tricuspid valve. Both these nodes are capable of generating spontaneous electrical currents at regular intervals. The S-A node has a faster intrinsic rate of generating impulses as compared to the A-V node. The conducting system carries the impulses from the node to the entire heart and causes the myocardial cells to contract. Since the S-A node sends impulses at a much higher rate than the A-V node, it controls the rate (pace) of the heart beat. The S-A node is, therefore, known as the pacemaker of the heart. If the S-A node is experimentally destroyed the A-V node takes over the role of a pacemaker, and the heart beats at a rate at which the A-V node fires its impulses. Since the pacemaker originates from muscles cells, it is known as a myogenic pacemaker in contrast to neurogenic pacemaker which is in the form of nerve cells present in the heart. Neurogenic pacemakers are found in all adult invertebrates except molluscs.

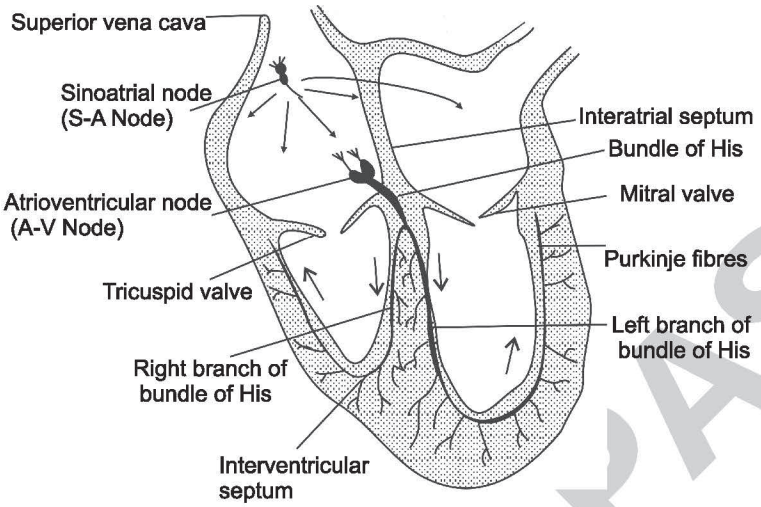


Fig. Cut-away view of the heart showing the nodes and the Purkinje system

Q.5. What is the O_2 dissociation curve? Explain briefly.

Ans. The oxygen-hemoglobin dissociation curve also called the oxyhemoglobin dissociation curve or oxygen dissociation curve (ODC) is a curve that plots the proportion of hemoglobin in its saturated (oxygen-laden) form on the vertical axis against the prevailing oxygen tension on the horizontal axis. The curve is an important tool for understanding how our blood carries and releases oxygen. Specifically, the oxyhemoglobin dissociation curve relates oxygen saturation (SO_2) and partial pressure of oxygen in the blood (PO_2), and is determined by what is called "hemoglobin affinity for oxygen", that is how creadity hemoglobin acquires and releases oxygen molecules into the liquid that surround it.

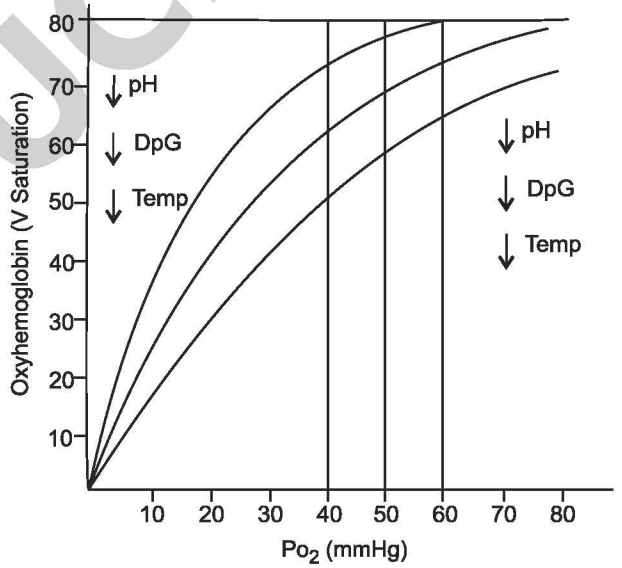


Fig.

Q.6. Write a short note on blood pressure.

Ans. **Blood Pressure**

The force of the blood against the walls of the blood vessels is known as blood pressure and depends on several factors such as blood volume, blood vessel space, force of the heart beat, and blood viscosity etc. Blood pressure varies considerably in different parts of the circulatory system. The maximum pressure is encountered in the *aorta* where it normally reaches to 140 mm of mercury. Then it gradually decreases in the arteries and arterioles, becoming lower in the capillaries and still lower in the veins. the arterial blood pressure undergoes a rhythmic change reaching a maximum during ventricular systole when blood in pumped into the arteries and decreasing during ventricular diastole. The former is called systolic pressure and the latter, the diastolic pressure. The normal systolic pressure in humans ranges from about 120 to 140 mm of mercury, whereas the diastolic pressure ranges from about 75 to 90 mm of mercury.

Q.7. Write a short note on Electrocardiogram.

Ans. **Electrocardiogram (ECG)**

A heart beat can also be analysed in terms of electrocardiogram (ECG) obtained by electrocardiograph. The conduction of the excitatory impulse from the pace maker to and within the muscles of the heart is manifested by an action potential wave. The complex ECG of vertebrates represents a wave spreading over the heart. The ECG is similar whether ventricular conduction is in purkinje tissue (mammals and birds) or in muscle (poikilotherms) and whether there is a ventricular septum. Typically the normal ECG consists of a series of slow waves, including upward (negative) deflections called P, R and downward positive deflections Q and S. Of them, (i) the P wave represents atrial depolarization, which precedes the contraction of the atria. The PQ interval represents the delay at the auriculo-ventricular junction. (ii) The QRS complex represents preceding ventricular contraction. A normal QRS complex lasts about 0.06 sec. (iii) The T wave represents ventricular repolarization. It is much smaller than the QRS depolarization complex. There is no comparative atrial repolarization visible, for it is obscured by the large QRS depolarization of the ventricles, occurring at the time.

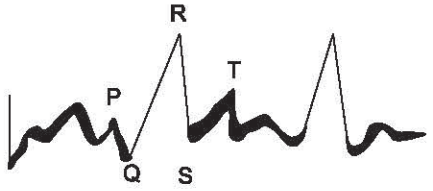


Fig. Electrocardiogram from man, P = first upward deflection due to contraction of auricles, Q, R, S, T = deflection due to action of ventricles

An important parameter of the ECG is the PR interval, which indicates the length of time between the beginning of the atrial contraction and the beginning of the ventricular contraction and thus the conduction time through the heart. A normal PR interval is 0.16 sec or less. In incomplete heart block, when conduction through the AV bundle is slowed, the PR interval may be almost doubled, and there may be 2 to 3 p waves for each QRS-T complex. In complete heart block, the ventricles 'escape' from SA and atrial control, and the P waves may be completely dissociated from the ORS-T complexes. Prolongation of the QRS complex, which normally lasts about 0.06 sec., indicates delayed conduction through the ventricles, often

caused by ventricular hypertrophy. The QT interval coincides with the beginning and the end of ventricular contraction. It lasts about 0.03 sec. The electrocardiogram reflects the activity of various part of the heart and thus aids in diagnosis of different heart ailments.

The percent of time occupied by the different phases of the ECG (as P-R interval and Q-T interval) is almost similar in mammals having different heart beats per minute. In fishes and amphibians a wave arising in the sinus venosus precedes the P or the auricular contraction. The electrocardiogram is different is myogenic heart with muscular contraction from the ECG in neurogenic heart with nervous conduction.

Q.8. What do you mean by coronary blood flow and nutrition of the heart?

Ans. Coronary Blood Flow and Nutrition of the Heart

The cardiac muscles are nourished through coronary circulation. Blood enters into the coronary arteries through openings just ahead of the semilunar valves of the aorta. This opening is not guarded by valves, therefore, blood continuously flows through the coronary system during the entire cardiac cycle. Most of the blood in the coronary anteries flows during diastole; during systole, the blood flow is, however, reduced because the developing tension of the cardiac muscle compresses the walls of coronary blood vessels. The coronary veins drain the blood into the right ventricle through coronary sinus, and some of the veins even directly open into the ventricle. The total coronary blood flow is about 3 to 10% of cardiac output.

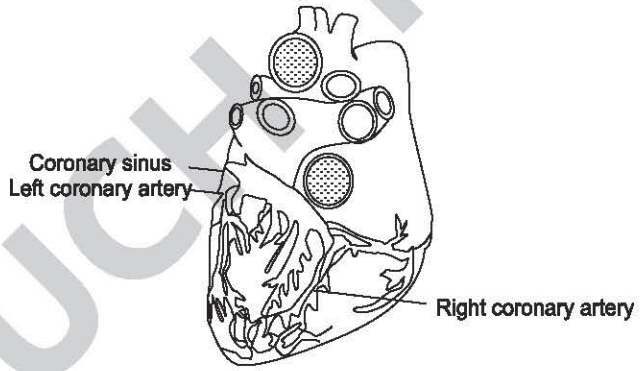


Fig. Coronary circulation in man

Coronary Occlusion : Interruption of circulation in any coronary vessel is called a coronary occulison. The normally occurs due to deposition of fatty substances and cholesterol in the coronary arteries (arteriosclerosis), or an obstruction caused by a blood clot or thrombus (thrombosis). Coronary occlusion deprives the heart of its oxygen and it soon stops functioning. Cardiac muscle has no physiological mechanism to incur oxygen debt, since it does not utilize anaerobic metabolism. When occlusion occurs, the cardiac muscles receiving blood from the affected vessel dies, and a scar is formed and becomes non-functional. This area is called a cardiac infarction. If infraction covers a large area, the heart stops, and death occurs by heart failure.

Besides oxygen, other factors such as balanced electrolytes in the cardiac muscles, pH, availability of glucose, and temperature are equally important for the proper functioning of the heart. An excess of Na^+ is toxic for the heart, and it is the reason why intake of table salt is

reduced in cardiac patients; excess of K^+ may cause complete stoppage of heart in diastole; and excess Ca^{++} can result in heart failure during systole.

Q.9. Write about the general characteristics of urine.

Ans. **General Characteristics of Urine**

1. It is a pale—yellow in colour due to the presence of a pigment urochrome, which is a breakdown product of haemoglobin.
2. It is aromatic in odour when fresh. The odour becomes ammonical after bacterial decomposition of urea.
3. It is slightly acidic in reaction (pH = 6.0).
4. Its specific gravity ranges between 0.015-1.025 in man.
5. In a healthy adult man both the kidneys receive 1300 ml of blood per minute, out of this 700 ml is the part of blood-plasma and form 120 ml filtrate per minute. Thus total filtrate formed by both the kidneys is 24 hours is about 170 litre. Out of this 168.5 litre filtrate is reabsorbed in the blood through the nephrone's body. Hence, a healthy adult man passes about 1.5 litre urine in 24 hours. Urine volume is less in summer.

Q.10. Write a short note on ornithine cycle.

Ans. **Ornithine Cycle or Kreb's Henseleit Cycle**

Ammonia is liberated by the deamination of amino-acids during protein metabolism. Free ammonia is toxic to the body, hence, inside the liver, it is converted into nontoxic urea. The process involved in the formation of urea constitutes ornithine arginine cycle.

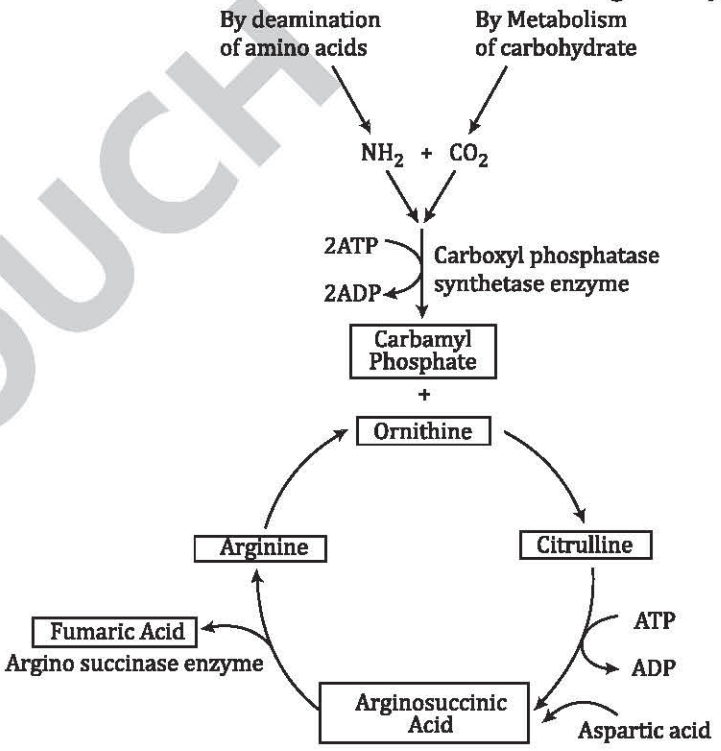


Fig. Ornithine cycle

The cyclic chain of chemical reactions involved in the ornithine arginine cycle leading to the formation of urea can be summarised as under :

An important aminoacid-ornithine occurs freely in the liver cells.

1. It forms the starting point in the chain of ornithine cycle.
2. Ornithine combines with NH_3 and CO_2 and forms citrulline and releases one molecules of water.
3. Citrulline combines with large quantities of NH_3 and water to form arginine.
4. Arginine is catalysed by enzyme arginase present in the liver. This breaks arginine into arnithine and urea, thus completing the cycle.

Ornithine combines again and again with ammonia to repeat the ornithine cycle. Thus arginase play an important role. It is found in all the tissues in elasmobranch fishes and in liver cells of mammals. Ornithine cycle was describe by Krebs and Henseleit (1932). They demonstrated the action of arginase in urea formation by using slices of rat liver.

Q.11. Write a short note on the hormonal feedback circuits in controlling renal functions.

Ans. Two important hormonal control of the kidney function by negative feedback circuits can be identified:

1. **Control by Antidiuretic Hormone ADH :** ADH produced in the hypothalamus of the brain and released into the blood from the pituitary gland, enhances fluid retention by making the kidneys reabsorb more water. The release of ADH is triggered when osmoreceptors in the hypothalamus detect an increase in the osmolarity of the blood. The osmoreceptors cells also promote thirst. Drinking reduces the osmolarity of the blood which inhibits the secretion of ADB, thereby completing the feedback circuit.
2. **Control by Juxtaglomerular Apparatus (JGH) :** It operates a multihormonal Renin Angiotensin-Aldosterone System (RAAS). JGA responds to decrease the blood pressure and release enzyme renin into the blood. In the blood, the enzyme initiates chemical reactions that convert a plasma protein called angiotensinogen to a peptide called angiotensin II which works as a hormone. Angiotensin II increases blood pressure and stimulates the adrenal gland to release aldosterone, a hormone. This leads to an increase in blood volume and pressure completing the feed-back circuit by supporting the release of renin. Still another hormone, a peptide called Atrial Natriuretic Factor ANF, opposes the regulation by RAAS.

Thus, ADH, the RAAS, and ANF provide an elaborate system of checks and balance that regulate the kidney functioning to control body fluid, osmolarity, salt concentration, blood pressure, and blood volume.

Q.12. Write about the role of skin and lungs in excretion.

Ans. **Role of Skin in Excretion**

Human skin possesses glands for secreting sweat and sebum (from the sebaceous gland). Sweat contains NaCl, lactic acid, urea, amino acids, and glucose. The volume of sweat various negligible to 14 L a day. The principal function of sweat is the evaporative cooling of the body surface. Sebum is a waxy protective secretion to keep the skin oily and this secretion eliminates some lipids, such as waxes, sterols, other hydrocarbons, and fatty acids. Integument in many animals is excreting ammonia into the surrounding by diffusion.

Role of lungs in excretion : Human lungs eliminate around 18 L of CO_2 per day and about 400 ml of water in normal resting conditions. Water loss via lungs is small in hot humid climates

and large in cold dry climates. The rate of ventilation and ventilation pattern also affects the water loss through the lungs. Different volatile materials are also readily eliminated through the lungs.

Q.13. Write a short note on haemodialysis.

Ans. **Haemodialysis**

In case of renal failure, an artificial kidney is used for removing excess urea from the blood of the patient by a process called hemodialysis. Blood is taken out from the artery of the patient, cooled to 0°C, mixed with an anticoagulant such as heparin, and then pumped into the apparatus called artificial kidney. In this apparatus, blood flows through channels.

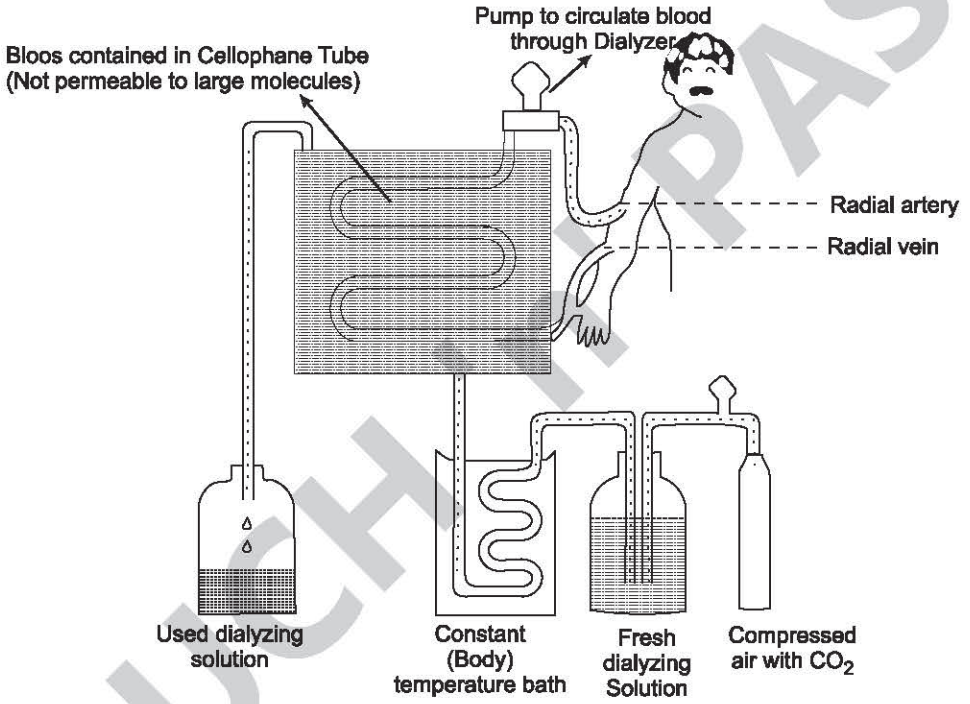


Fig. Working of artificial kidneys for haemodialysis

Q.14. What are the diseases associated with the urinary system?

Ans. Diseases associated with the urinary system :

1. **Polynephritis :** It is a bacterial infection, which causes inflammation of renal pelvic nephrons and medullary tissues of the kidney. It affects the counter-current mechanism. Its main symptoms are frequent and painful urination, fever, and pain in the lumbar region.
2. **Uremia :** It causes the presence of a high concentration of urea, uric acid, creatinine, etc, in the blood due to some bacterial infection or some obstruction in the passage of the urinary system. Urea poisons the cells. It is not passed in the urine and accumulates in the blood.
3. **Renal stones :** When uric acid precipitates and accumulates in the nephrons of kidneys in the form of renal stones or when calcium phosphates and oxalates accumulate in the nephrons of the kidneys in the form of renal stones. It causes

blockage or frequent painful urination along with blood in the urine. Renal stone causes severe colic pain starting in the back and radiating down to the front of the thigh or vulva or testicle on that side.

4. **Glomerulonephritis :** It is characterized by the inflammation of Glomeruliduct, some injury to the kidney, abnormal allergic reaction, or by some streptococci bacteria infection. Proteins and red blood corpuscles become filtered into the glomerular filtrate. It may lead to kidney failure in severe infection.
5. **Oedema :** It is characterized by the increased volume of interstitial fluid mainly caused by retention of excess Na^+ ions which in turn causes water retention. Blood pressure increases dining edema.

Q.15. Differentiate between ureter and urethra?

Ans. **Differences between Ureter and Urethra**

S.No.	Ureter	Urethra
1.	It is a muscular tube.	It is a membranous tube.
2.	It is long.	It is short.
3.	It arises from the renal pelvis of the kidney.	It arises from the urinary bladder.
4.	It carries urine to the urinary bladder.	It eliminates stored urine of the exterior.
5.	No muscular splincter.	Muscular splinter keeps urethra-closed except for maturation.

Q.16. What do you mean by the Rh-incompatibility in humans?

Ans. Rh antigen is seen on the RBC surface of majority humans, these are called Rh-positive individuals and when the antigen is absent they are Rh-negative individuals. Both these individuals are phenotypically normal individuals. However, in these individuals, a problem emerges during pregnancy or transfusion of blood. The first blood transfusion from Rh-positive blood to the RI-T individual leads to no harm as the Rh-negative person acquires antibodies or Rh factors in their blood. During the second transfusion of blood, from Rh-positive blood to the Rh-negative individual, the antibodies already formed attack to destruct the RBC of the donor. In pregnancy, if the father's blood is Rh-positive and the mother's blood is Rh-negative, the blood of the fetus will be Rh-positive, which leads to serious issues. The Rh antigens of the fetus are not exposed to the Rh-positive blood of the mother during the first pregnancy, as they are separated from the placenta. But in the succeeding Rh-positive fetus, the anti-Rh factors from the mother destruct the RBCs of the fetus as the blood mixes which causes hemolytic disease in the newborn(HDN) known as erythroblastosis fetalis. This can be prevented through the administration of anti-Rh antibodies to the mother after the delivery of the first child.

SECTION-C LONG ANSWER TYPE QUESTIONS

Q.1. What is blood coagulation? Describe various steps of blood coagulation.

Ans. **Coagulation of Blood**

Blood, whenever comes out of the vessels, quickly changes from a fluid state into a thick jelly-like material. This is known as clot and the process of separation of clot from the plasma (the serum) is known as clotting or coagulations. The process of clotting involves the

conversion of soluble blood protein, the fibrinogen (which is normally dissolved in plasma) into insoluble fibrous protein fibrin (which is in the form of long delicate fibres).

But due to the involvement of a variety of factors of different nature the process is much complicated and can be separated under following steps :

Step 1. Liberation of thromboplastin or origin of thromboplastic activity in blood : In the circulating blood thromboplastin is present. Thromboplastic activity arises only at the time of clotting by the combination of certain factors. These factors are : a phospholipid furnished by rupturing of the platelets, Ca^{++} ions and antithemophilic factor.

Step 2. Conversion of prothrombin into thrombin : The prothrombin is the inactive form of the enzyme thrombin, which is essential for blood clotting. In presence of Ca^{++} ions the accelerator globulin *i.e.,* the prothrombin is converted into thrombin by thromboplastic activity of thromboplastin.

Step 3. Conversion of fibrinogen into fibrin : Thrombin is proteolytic enzyme, whose action converts the soluble plasma protein, fibrinogen, into insoluble protein fibrin. According to recent view, fibrin molecules initially obtained are soluble but in presence of cation and the fibrin stabilizing factor (F-XIII), it is converted into insoluble fine threads, which separate from the blood plasma and settle down in the form of a fibrous net.

***Step 4.* Role of blood platelets :** The blood platelets are presumed to contain thromboplastin. It is liberated, when blood platelets rupture. The rupture of blood platelets occurs when capillaries or blood vessels are damaged and blood flows out. This also liberates a number of other factors, which activate the process of clotting.

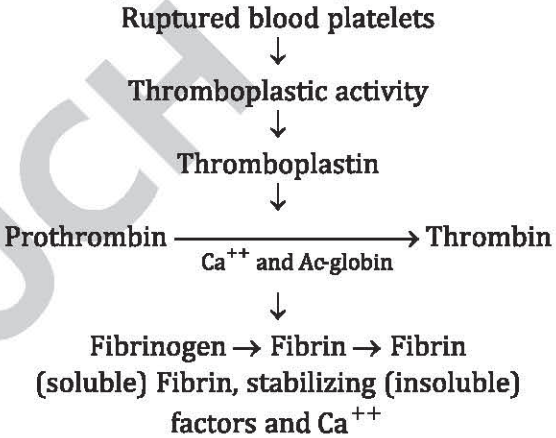


Fig. Clotting of blood

Factors of Blood Clotting

1. **Factor 1 (Fibrinogen) :** It is a soluble plasma-protein, which is present in circulating blood-plasma. It takes active part in blood clotting and produced by liver cells.
2. **Factor II (Prothrombin) :** It is also a plasma-protein and present in inactive form in the blood plasma. Its normal concentration in blood about 10 to 15 mg per 100 ml. of blood. It is synthesized by liver cells in presence of vitamin K.
3. **Factor III (Thromboplastin) :** It is a lipoprotein, present in the cytoplasm of blood platelets corpuscles and tissue cells. It is also called thrombokinase.

4. **Factor IV (Calcium) :** It most important factor for blood clotting. Its normal concentration in blood is about 10 mg per 100 ml of blood.
5. **Factor V (Proaccelerin or labil factor) :** It is a specific protein called as accelerator globulin or Ac-globulin. In blood-plasma, it is present in minimum concentration. During blood clotting it activates prothrombin and also releases the thromboplastin from blood platelets.
6. **Factor VI (Proconvertion or Stable factor) :** It is present in blood serum and helps in conversion of prothrombin into active thrombin.
7. **Factor VII (Antihaemophilic globulin = AHG) :** It is a glycoprotein. Its plasma concentration is 1-6 mg per 100 ml of blood. This factor is required for the formation of prothrombin activator from blood constituents.
8. **Factor VIII (Christmas factor or Plasma Thromboplastin Component PTC) :** This factor is also required for the formation of prothrombin activator or formation of thromboplastin. It is a globulin protein, which occurs in inactive form in blood plasma.
9. **Factor IX (Stuart factor or Power factor) :** It is present in inactive form in plasma, but during blood clotting with the help of active christmas factor, calcium ions and anti haemophilic factor converted to active form.
10. **Factor X (Plasma Thromboplastin Antecedent or PTA factor) :** It also occurs as inactive form in the plasma. It activates the christmas factor and takes part in the formation of thromboplastin.
11. **Factor XI (Hageman factor or Contact factor) :** It occurs as inactive form in the plasma. When it comes in contact with injured walls of blood vessels, it becomes active and takes active part in the formation of thromboplastin.
12. **Factor XII (Fibrin Stabilizing factor or FSF factor) :** This is glycoprotein. Its plasma level is 2 mg per 100 ml, of blood. This active factor, alongwith calcium ions causes polymerization of soluble fibrinogen so that insoluble fibrin is formed. This leads to the formation of a solid fibrous clot. Congenital deficiency of this factor leads to a poor wound healing.

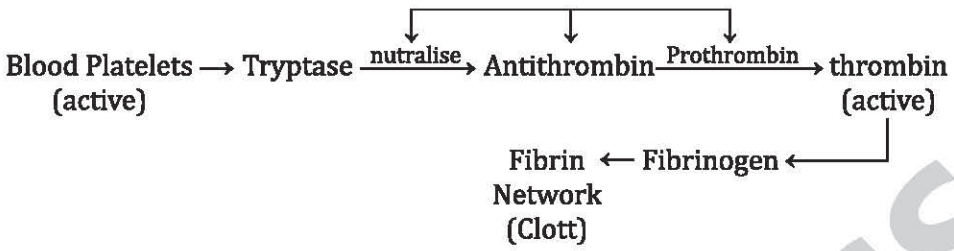
Significance of Clotting

Clotting or Coagulation is very essential for blood in the life of an organism. It is a protective device against any damage caused to the blood capillaries. If any blood vessel is ruptured, its blood immediately starts Oozing out. The usefulness of this property is that it prevents excessive haemorrhage from small wounds and this helps in retaining the blood inside the body.

Theories of Blood Coagulation

Malpighi (1666) was the first to considered the problem of coagulation. Some of the important theories of blood coagulation considered are :

1. **Morawitz Theory (1905) :** According to this theory presence of thrombokinase, prothrombin, Ca^{++} ions and fibrinogen are essential for coagulation.
2. **Howell's Theory :** According to this theory, thromboplastic substances (Cephalin), liberated by platelets, neutralises, heparin, which normally maintains fluidity of blood. Ca^{++} ions act on prothrombin to convert it to thrombin.



3. **Best and Taylor's Theory :** According to this theory, following four chemicals are required for Coagulation :
   (i) **Prothrombin :** Synthesized in liver.
   (ii) **Thromboplastin :** Found in tissues.
   (iii) **Calcium Ions :** Inorganic constituents of plasma.
   (iv) **Fibrinogen :** Soluble plasma protein.

   When, due to some injury blood is shed, the thromboplastin is released by the injured cells, which acts on prothrombin. This prothrombin (in active form) is converted into thrombin in presence of Ca^{++} ions. Now the active thrombin converts the soluble fibrinogen (protein/into insoluble firbin.) The fibrin in turn, makes the clott with erythrocytes and leucocytes.

$$\text{Prothrombin} \xrightarrow[\text{Thromboplastin}]{Ca^{++}} \text{Thrombin (active)}$$

$$\underset{\text{(soluble)}}{\text{Fibrinogen}} + \underset{\text{Active}}{\text{Thrombin}} \longrightarrow \underset{\text{(Insoluble threads)}}{\text{Fibrin}}$$

Fibrin + RBC + WBC = Blood Clott.

   Intra vascular clotting is prevented by the presence of anti thrombin. This anti thrombin is neutralized during injury by the liberation of thromboplastin or Heparin.

4. **Fuld and Spiro's Theory :** According to this theory an enzyme Tryptase is produced by the injured blood platelets, which converts prothrombin into thrombin in the presence of Ca^{++} ions. Thrombin converts soluble fibrinogen into insoluble fibrin threads to form clott.

Q.2. What is cardiac cycle? Describe different phases of the cardiac cycle.

Ans.

Myogenic Heart

The heart which contraction and relaxation is not under the control of nervous system is called as myogenic heart.

Cardiac Cycle

The heart contracts rhythmically and ceaselessly throughout life. Each heart beat consists of systole (contraction of heart) and diastole relaxation of heart). The total duration of the same is about 0.8 sec. The duration for ventricular systole and diastole is 0.3 and 0.5 sec respectively. The atria and ventricles do not contract stimultaneously, the atria contract first followed by ventricular systole.

In this way, the action of heart in pumping blood follows a cyclic pattern and the various changes during the course are described below :

1. **Atrial Systole :** The atrial contraction or systole begins when the atrial chambers are full of blood. A wave of contraction is initiated at the sino-atrial node (S.A. node) which spreads to all parts of the atria, thereby forcing blood into the ventricles. This is accompanied by opening of the atrioventricular valves. The atrial systole lasts for about 0-15 sec. When this wave of contraction reaches the atrio-ventricular node (A.V. node), it is also excited. It takes some time and accounts for a brief pause after the atrial systole, before ventricular contraction or systole begins.
2. **Ventricular Systole :** Once the atrioventricular node is excited the wave of contraction spreads to all the parts of the ventricles through the bundle of His. Because of this, both the ventricles and their parts contract stimultaneously. Due to ventricular systole the pressure increases inside the ventricular cavities. Because of the increase in pressure, the tricuspid and bicuspid valves close. The closure of these valves produces first heart sound.

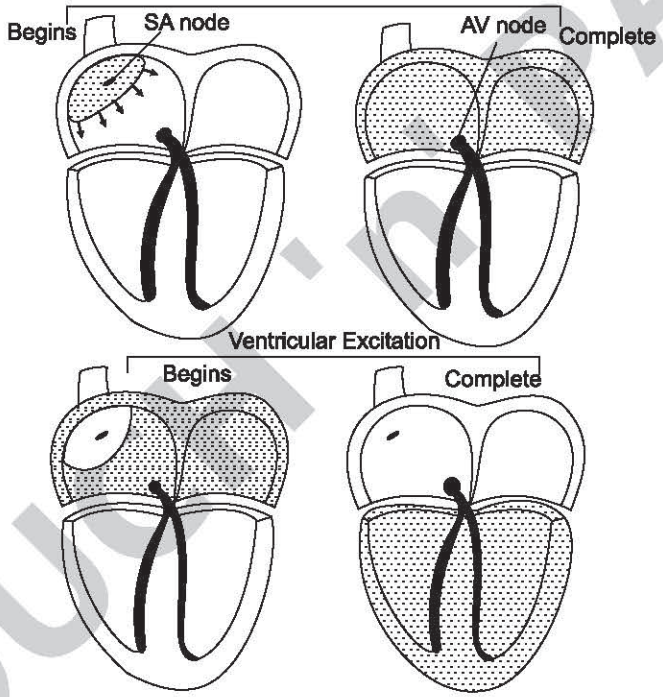


Fig. 1 : Path of exitation and contraction and relaxation of heart chambers during heart beat in a myogenic heart

When the pressure inside the ventricles exceeds that in the arteries, the semilunar valves open and blood spurts into the pulmonary artery and aorta from right ventricle and left ventricle respectively. Ventricular systole lasts for about 0-3 second. As the blood is ejected from the ventricular cavities into the arteries their pressure begins to fall and when it becomes lower than that of the arteries, the semilunar valves close and this causes second heart sound. This indicates end of ventricular systole and beginning of ventricular diastole.

During ventricular systole and atrioventricular valves remain closed because, the pressure within the ventricles is still greater than that within the atria. During this stage, the atria remain in a relaxed state (atrial diastole) and blood flows from the veins into the relaxed atrium.

3. **Ventricular Diastole :** After ventricular systole, the ventricles undergo relaxation and increase in size. As they relax, the pressure within the ventricles decreases. Once, it falls sufficiently, atrioventricular valves open and blood rushes from atria into the ventricles.

Heart Sounds

Each heart beat is accompanied by two heart sounds, first heart sound and second heart sound. The first heart sound marks the beginning of ventricular systole and is due to closure of atrioventricular valves. This is followed by second heart sound, which marks the end of ventricular systole and beginning of its diastole. It is produced by the closure of semilunar valves.

Regulation of Heart Beat : The normal rate of heart beat is maintained by two regulating mechanisms :

1. **Nervous Control :** Although, the heart beat is automatic but, it is regulated by a regulating centre located in the medulla oblongata. This is known as cardiac centre. Functionally, this centre is composed of two parts—cardio-inhibitor and cardio accelerator, cardio inhibitor continuously sends impulses to S. A. node of heart by vagus nerve, whereas the cardio-accelerator sends its impulses through the sympathetic nerve to S. A. node. Both have continuous effect but while the former decrease the rate of heart beat, the latter accelerates it. The decrease in the activity of inhibitory centre, of course, increases the heart beat.

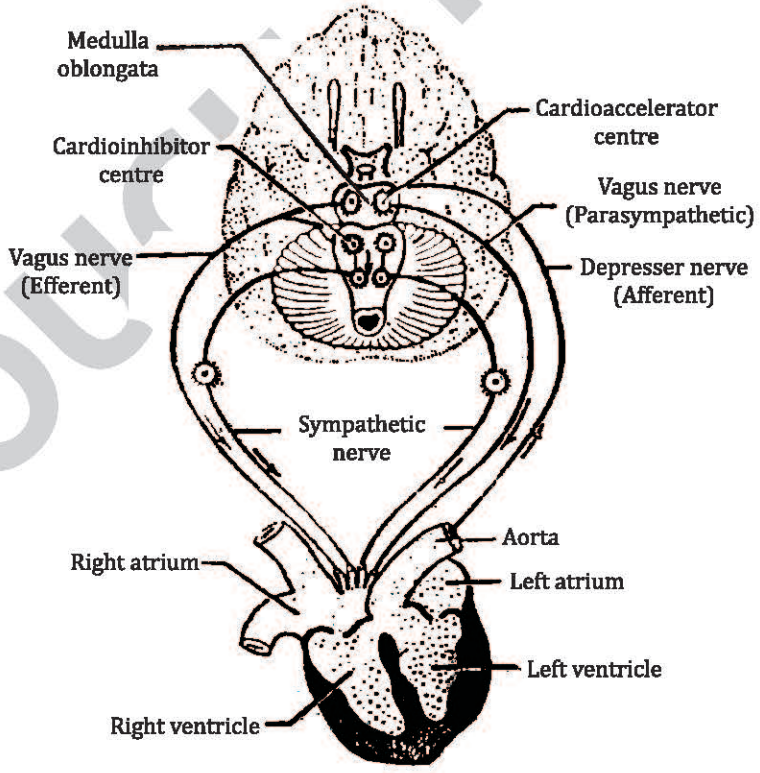


Fig. 2 : Diagrammatic representation of maintenance of heart beat

Thus the impulses are brought to the heart by a pair of vagus nerves (efferent or inhibitory nerves) and two accelerator nerves. If the vagus on each side is cut, keeping the accelerator; infact, the heart beat increases and heart remains beating faster.

The heart beat centre sends out accelerator or brake signals in response to specific sensory nerve impulses. These impulses may reach the centre from any part of the body. All emotions affect heart beat. Their sensory impulses are transmitted into specific parts of brain and from there the interconnected pathways relay these impulses to other parts of brain.

2. **Hormonal Control :** Adrenalin and thyroxin influence the heart rate independent of nervous system. Adrenalin acts directly on S. A. node increasing the frequency. Thyroxin increases the oxidative metabolism of body cells and this causes rapid contraction of heart for proper adjustment.
3. **Other Chemical Agents :** Carbon dioxide lowers the pH of blood and increases the rate of heart beat. Similarly, acidity accelerates the heart beat but alkalinity retards it.

Thus, at any given moment, the actual rate of heart beat is a net result of many simultaneous nervous and non-nervous factors.

Q.3. What is excretion? And also describe structure, functions and the process of urine formation in mammalian kidney.

Ans. **Excretion**

During metabolic activities in the body several waste products such as ammonia, urea, uric acid, etc. are formed which may cause harm to the body. The removal of these nitrogenous wastes from the body is termed as excretion.

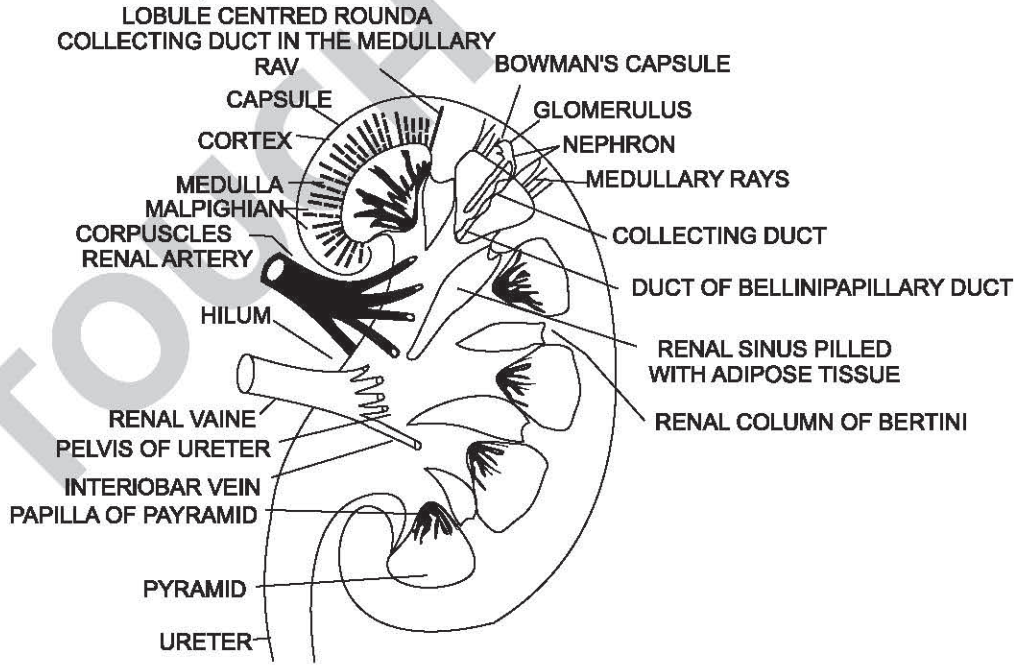


Fig. 1 : The gross anatomy of mammalian kidney

Structure of Kidneys : In the rabbit and man there are two metanephros kidneys, which are dark red, bean-shaped, placed one on either side of median vertebral column in lumber region

(abdominal cavity), but not on same level. In the rabbit, the right kidney is about 25 mm anterior to the left one (in man the left kidney is anterior in position than right one). In man each kidney is about 12 cm in length, 5-8 cm broad and 2.5 cm in thickness. Outer surface of each kidney is convex and inner concave. A depression called hilus is present on the concave side from where ureter takes its origin. The renal artery and renal vein pass in and out at the hilus.

Internal Structure of Kidney

Internally each kidney is distinguished into two zones :

1. **Cortex :** It is outer part of the kidney. Cortex is granular in appearance because the tubules here are much convoluted and it also contains the Malpighian corpuscles.
2. **Medulla :** It is the inner part of the kidney. The medulla looks striated as the tubules run through it in a straight course radiating towards the pelvis. The medulla consists of 10 to 12 conical masses, the renal pyramids, whose apices form the papillae which are project into hilus. Renal pyramids contain the collecting and discharging tubules and related to calyces, the calyces open into funnel-shaped pelvis which is actually a expanded part of ureter in the kidney. The parts of cortex, which are narrow and column like, present between the renal pyramids, called renal column of Bertini.

Structure of Uriniferous Tubules or Nephrons

Histologically each kidney consists of a net of numerous coiled tubules called nephrons or uriniferous tubules. In the rabbit, each kidney contains about two lacs nephrons, while in man their number in each kidney is about one million. In man each nephron is about 35 mm. in length and consists of following parts :

(i) **Malpighian or Renal Corpuscle :** A dilated blind end, the Bowman's capsule which is invaginated to enclose a tuft of convoluted blood capillaries, the glomerulus. The whole structure is called a Malpighian or Renal corpuscle.

(ii) **Proximal Convoluted Tubule :** The tubule leaves the capsule by a constricted neck, passing into the proximal convoluted tubule, which makes a few foils and is restricted to the cortical region of the kidney. The free surface of an cuboidal epithelial cells lining the tubular lumen bears a prominent brush border for reabsorptive activities.

(iii) **Loop of Henle :** It is the middle part of secretory tubule, which is 'U-shaped' in structure and situated in the medulla. It is divided into following three parts :

(a) **A thick descending segment or loop** which is actually straight part of proximal convoluted tubule.

(b) **A thin segment,** which runs a direct, radial course in the medulla; it makes a sharp hair-pin bend and extends past the apex of **Henle's loop**.

(c) **A thick ascending segment or loop,** which is a straight radial tubule. The epithelial cells of this sement are relatively impermeable to water and salts.

(iv) **Distal Convoluted Tubule :** The ascending segment of Henle loop leaves the medullary ray and enters the cortical tissue again, forms the coils like proximal convoluted tubule and becoming the distal convoluted tubule. It lies near its own Malpighian Corpuscle. This segment is short in comparison to the proximal convoluted tubule. It is lined internally with cuboidal epithelium, which are not ciliated.

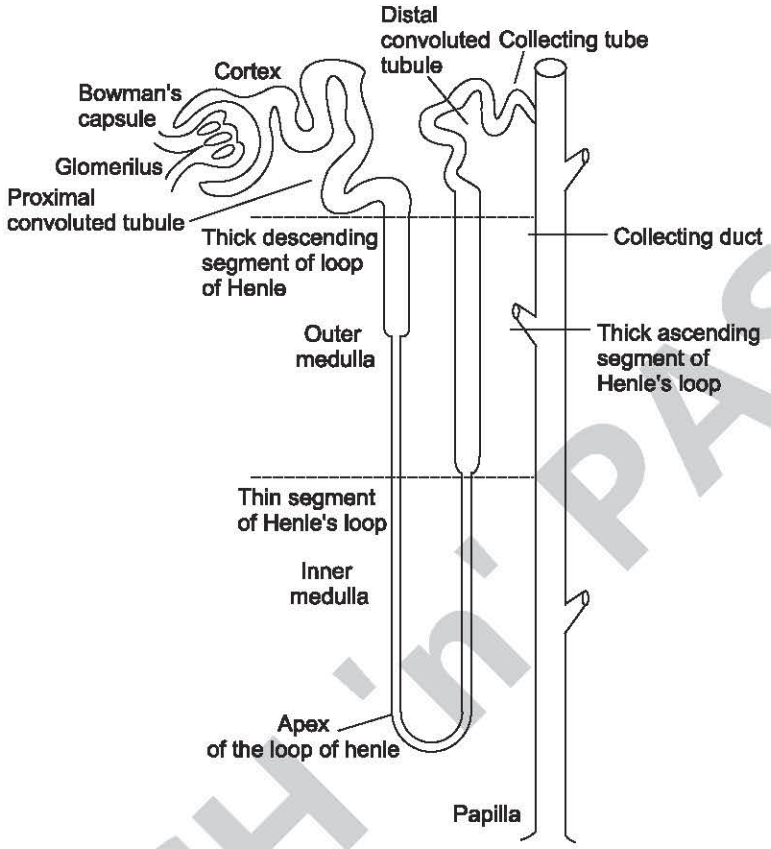


Fig. 2 : The structure of a urinferous tubule

Collecting Duct : The last portion of secretory tubule straightens out again, and by a short junctional tubule joins a straight collecting tubule, which passes down in a medullary ray, to enter a medullary pyramid. On the way, it receives other junctional tubules and forms a tree-like system and finally, a large straight tubule, the papillary duct or duct of Bellini opens into the pelvis at the apex of the papilla.

Functions of the Kidney

1. It excretes waste products, especially the nitrogenous and sulphur containing end products of protein metabolism.
2. It helps to maintain the normal hydrogen-ion concentration of body fluids and electrolytes.
3. It helps to maintain water balance of the body and thereby plasma volume..
4. It helps to maintain the optimum concentration of certain constituents of blood (by the process of selective reabsorption).
5. It eliminates drugs and various toxic substances from the body.
6. It manufactures certain new substances like ammonia, hippuric acid and inorganic phosphates. Ammonia helps in keeping the acid-base equilibrium.
7. It helps in maintaining the osmotic pressures in blood and tissues.

8. It helps in the regulation of blood pressure during hypoxia in condition of emergency, through the liberation of renin from the juxtaglomerular apparatus.
9. It helps in the regulation of erythropoiesis (formation of erythrocytes) through the formation of erythropoietin by REF (Renal Erythropoietin Factor) secreted from the glomerular cells.
10. The glomeruli of the kidney tubules act as ultra filters.

Urine is alemon-coloured, yellow acidic fluid having pH value of 4.6-7.3 and specific gravity about 1.903-1.029 in normal condition.

Composition of Urine : Constituents of urine are grouped as follows :

1. Nitrogenous Organic Constituents :
   (i) Urea (ii) Creatinine
   (iii) Uric acid (iv) Ammonia
   (v) Hippuric acid (vi) Allantoin
   (vii) Urinary indican.
2. Organic Constituents Without Nitrogen :
   (i) Carbohydrates and related compounds (ii) Oxalates
   (iii) Phenolic compounds (iv) Lactates
   (v) Glucuronates (vi) Ketones
3. Inorganic Constituents :
   (i) Sodium (ii) Potassium
   (iii) Phosphates (iv) Sulphates
   (v) Calcium (vi) Magnesium
   (vii) Iron.
4. Water
5. Other Constituents :
   (i) Purine derivatives *e.g.,* Xanthine and proxanthines
   (ii) Amino acids. (iii) Proteins
   (iv) Sulphur Compounds *e.g.,* Chondroitin thiocynates, ethereal sulphates.
   (v) Urinary pigments, *e.g.,* Urochrome, urobilin.

Chemical composition of urine is :

1.	Water	95%
2.	Ammonia	0.05%
3.	Urea	2%
4.	Uric acid	0.03%
5.	Na	0.6%
6.	K	0.15%
7.	Ca	0.015%
8.	Mg	0.01%
9.	Cl	0.6%
10.	PO_4	0.12%

11.	SO_4	0.18%
12.	Creatinine	0.1%
13.	Protein	—
14.	Glucose	—

Physiology of Excretion and Urine Formation

The urine is an aqueous solution of organic nitrogenous wastes, inorganic salts and certain other metabolic substances. The formation of urine involves three processes : filtration, reabsorption and tubular secretion. All these steps take place before the urine reaches the form in which it is eliminated from the body. Briefly, this means that a certain fluid containing wastes is separated from the blood into the kidney tubules, that certain substances from this fluid are then returned to the blood by selective absorption, and that finally other substances are added to the fluid before it is actually called the urine.

1. Ultra Filtration : The Bowman's capsules of kidney act as ultra filters and lie in close contact with the glomerulus. The blood flowing through the afferent arterioles contains urea, water, several salts and blood protein dissolved in the plasma. It is separated from the cavity of renal tubule of Bowman's capsule only by two very thin membranes—the endothelial layer of blood capillaries and the epithelial layer of Bowman's capsule. These two layers are one cell thick and lie in close contact. The diameter of afferent arteriole is more than the efferent arteriole. Therefore, the amount of blood which enters the afferent arteriole in a definite time is not drained out, so the hydrostatic pressure of blood in the capillary network of glomerulus increases.

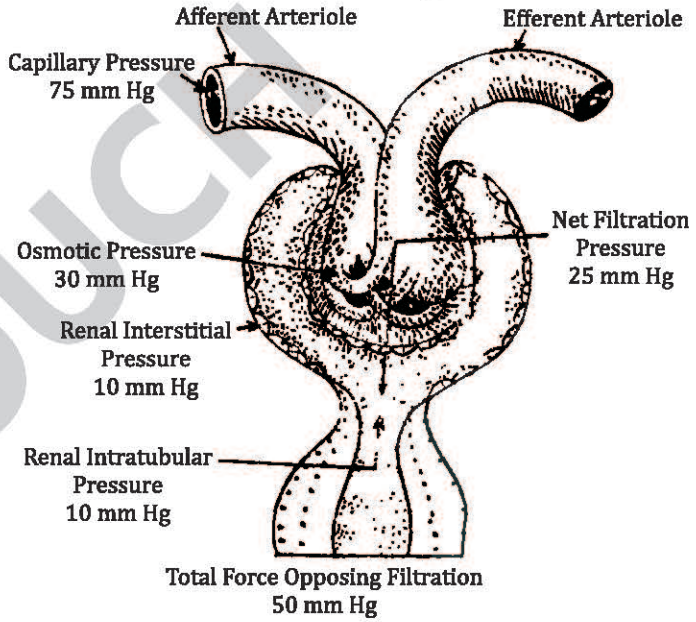


Fig. 3 : Diagrammatic representation of ultra filtration in Bowman's capsule of uriniferous tubule

This capillary pressure in glomerulus is about 75 mm. Hg. This pressure has to overcome the osmotic pressure of the plasma, which works to retain constituents within the capillary walls. The osmotic pressure of plasma is about 30 mm Hg. The renal interstitial pressure on the capillaries together with the resistance to flow in the uriniferous tubules (*i.e* intratubular

pressure) contribute a pressure of about 20 mm. Hg. This also works against the capillary pressure. Therefore, the net filtration pressure responsible for the filtration is about 25 mm Hg. As a result, water and diffusible solute molecules are forced across the membrane from the blood plasma into the Bowman's capsule. This process is known as ultra filtration. As a result of ultra filtration almost all the substances dissolved in plasma filter out into the cavity of Bowman's capsule alongwith water except the blood corpuscles, colloids and certain proteins. This filtered liquid is known as nephric filtrate or glomerular filtrate.

2. Selective Reabsorption : The glomerular filtrate contains many substances necessary for normal metabolism, such as water, glucose, amino acids, fatty acids, vitamin C and various salts or electrolytes like-sodium chloride (NaCl) and sodium carbonate (Na_2CO_3), as well as substances to be excreted and removed, such as urea, uric acid and creatinine.

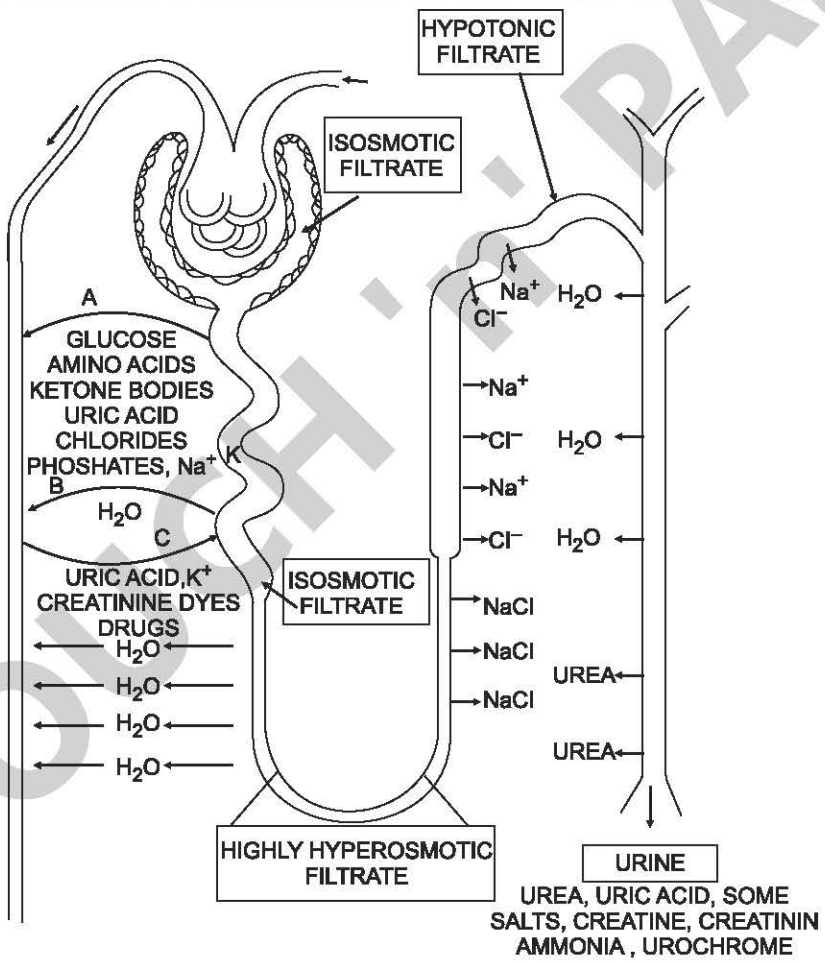


Fig. 4 : Urine Formation in Uriniferous Tubule

Selective reabsorption is the process by which essential constituents of the glomerular filtrate are reabsorbed into the body fluid or blood, during its passage through the different parts of kidney tubules or nephrons. It is also significant in the maintenance of fluid and electrolyte balance and the alkalinity or pH of the blood.

The glomerular filtrate first collects within the Bowman's capsule and then due to continuous beating of cilia of the neck cells, it continuously pushed into the proximal convoluted tubule of the nephron. The inner epithelial cells of the proximal tubule has well developed brush border (microvilli) against the lumen. The microvilli greatly increase the surface area exposed to the glomerular filtrate. The efferent arteriole around the proximal tubule forms a dense net of arterial capillaries, called peritubular blood capillaries.

All the essential constituents like sodium chloride, glucose, amino acids, vitamin C and water etc., from the glomerular filtrate through the cells of proximal tubule are passively reabsorbed into the blood of peritubular blood capillaries net. About 80% of water from the glomerular filtrate is reabsorbed by the proximal part. This reabsorption of water in the proximal part is called obligatory water reabsorption with is a passive process.

In the distal convoluted tubule, a more selective, accurately regulated reabsorption of substances takes place. Here more water, about 13% is reabsorbed with the help of a pituitary hormone ADH, which increases the permeability of the cells of distal tubule to water. Distal tubular reabsorption is called the facultative water reabsorption, a process aided by the hormone. In addition, the distal tubules help to preserve a constant pH in the blood (7.4) by exchanging hydrogen ions for sodium ions (by active transport) whenever the acidity of the blood tends to rise. An adrenocorticosteroid aldosteron hormone promotes the reabsorption of Na^+ in this case.

3. Secretion : It is third step in the urine formation. As the glomerular fluid or filtrate flows through the distal convoluted tubule, the unwanted substances like uric acid and creatinine or other substances like K^+ and H^+ etc., which could not be filtered out in the glomerulus are actively secreted by the distal tubular wall into the filtrate from the blood. As a result of this entire process, homeostasis of the blood is maintained.

Urine : As a result of all the above three steps which occur in uriniferous tubules, all the waste products remained in the tubular fluid or filtrate constitute urine (which contain excess of water urea and unwanted salts) which is ready for excretion from the body.

❑❑❑

UNIT-VII

Nervous System and Endocrinology in Humans

SECTION-A VERY SHORT ANSWER TYPE QUESTIONS

Q.1. Which are the neurons found mostly in the central nervous system?

Ans. Central nervous system consists mostly of multipolar neurons. A multipolar neuron consists of a single axon and many den drites that allow for integration of a large number of impulses with surrounding nerve cells.

Q.2. What is the function of sensory division of the peripheral nervous system?

Ans. The sensory division is a part of the peripheral nervous system (PNS). The PNS travels from the sensory organs to the nervous system (CNS). The sensory division carries the information for touch, pain, pressure, vision, taste etc., to the CNS.

Q.3. Define autonomic nervous system.

Ans. Autonomic nervous system consists of visceral sensory and visceral motor fibres and their cell bodies. Autonomic nervous system concerned with the maintenance and regulation of internal environment. It controls the activities of heart blood vessels, intestine, stomach, uterus, urinary bladder, lungs, sweat glands, salivary glands gastric glands liver pancreas, certain endocrine glands and other organs.

Q.4. What is somatic nervous system?

Ans. The part of the peripheral nervous system which controls voluntary actions of the body *via* skeletal muscles is called somatic nervous system.

Q.5. What is nervous system function?

Ans. The nervous system helps all the parts of the body to communicate with each other. It also reacts to changes both outside and inside the body. The nervous system uses both electrical and chemical means to send and receive message.

Q.6. Which direction do nerves travel?

Ans. Electrical nerve impulses usually travel in one direction-dendrites-cell body-axon-synapse.

Q.7. What is action potential?

Ans. The changed electric potential of the neurilemma is known as action potential. The initial change produces on ionic imbalance in the membrane on the either side of point of stimulus producing local electric current. These areas of negative depolarization in turn initiate change in the membrane adjacent to them.

Q.8. What are neuron cells?

Ans. Neurons are cells within the nervous system that transmit information to other nerve cells, muscle or gland cells. Most neurons have a cell body, an axon and dendrites. The cell body contains the nucleus and cytoplasm.

Q.9. Why are nerve impulses unidirectional?

Ans. Transmission of nerve impulses through nerve fibre occurs unidirectionally because axon of one neuron linked to the dendrite of another neurone through synapse. Synaptic vesicles are filled with a neurotransmitter (*e.g.*, acetylcholine) released by axon ending not by dendrites.

Q.10. Write very short note on sodium-potassium pump.

Ans. Sodium Potassium pump : The cell membrane is impermeable to complex protein and other organic molecules of cytoplasm but selectively permeable for simple organic and inorganic molecules. In resting condition, it is moderately permeable to Na^+ but quite permeable to K^+ and Cl^- ions. Concentrations of Na^+ and Cl^- ions in ECF are respectively about ten and fourteen times more than in the cytoplasm. The concentration of K^+ ions cytoplasm is about thirty times more than in ECF. Obviously, there is a continuous influx of Na^+ and Cl^- into the cytoplasm from ECF and a continuous out flux of K^+ from the cytoplasm. This passive exchange is a potential danger for osmotic equilibrium all cells continuously expel out Na^+ ions ECF and take in K^+ from it against diffusion gradients by active transport. It is called the Na-K pump.

Q.11. What is Schwann cell?

Ans. Schwann cells serve as the myelinating cell of the peripheral neurons cells. A Schwann cell forms a myelin sheath by wrapping its plasma membrane concentrically around the inner axon.

Q.12. What is a node of Ranvier?

Ans. The nodes of Ranvier are characterized by short (1 μm) specialised regions in the axonal membrane that are not insulated in myelin. Although it is bare of myelin at the node, the axon is in direct contact with the microvilli of the Schwann cells in the PNS or with processes of astrocytes in the CNS.

Q.13. Define the saltatory nerve conduction or Transmission.

Ans. Saltatory nerve conduction : A sheath of a Schwann cells occurs around each axon. In most but not in all nerve cells particularly in mammals its sheath. It becomes coiled around the axon to form a thick sheath. It contain a myelin so it is called Myelinated but without it is called non-myelinated nerve fibres. At short intervals called nodes of Ranvier relay of impulses in myelinated fibres jumps from node to node. It is called saltatory transmission of impulses.

Q.14. Where are astrocytes found?

Ans. Astrocytes are star-shaped cells found in the brain. Similarly to other neuronal cells, astrocytes are comprised of synapses or cell ends that allow for chemical and electrical communication between cells.

Q.15. Which was the first hormone discovered?

Ans. The English physician E.H. Starling discovered in collaboration with the physiologist W.M. Bayliss secretion, the first hormone, in 1902. Three years later they introduced the hormone concept with recognition of chemical regulation early regulatory physiology took a major step forward.

Q.16. What is diabetes mellitus?

Ans. Diabetes mellitus is a condition of glycosuria accompanied with hyperglycemia due to lack of insulin. It is caused by the degeneration or hypoactivity of β-cells of islets of

Langerhans. In this condition the patient has high level of blood glucose and excretes glucose with urine.

Q.17. Why is adrenaline called emergency hormone?

Ans. A drenaline is known as the emergency hormone because it is released by the adrenal glands under the conditions of stress or excitement. This hormone is also a part of the body's stress response called the fight or flight response.

Q.18. What is vasopressin?

Ans. Vasopressin : It stimulates water absorption by the cell of distal convulated tubule. Its deficiency causes diabetes insipidus. It enhances blood pressure by constricting peripheral blood vessels. Vasopressin is used clinically in treating gaspains, after surgery.

Q.19. Which hormone controls the blood pressure?

Ans. Renin controls the production of two other hormone, angiotension and aldosterone. And these hormones control the width of your arteries and how much water and salt is moved out of the body. Both of these affect blood pressure.

Q.20. Write very short note on addison's disease.

Ans. Addison's Disease : Addison's disease is caused due to chronic insufficiency of the secretion of hormones from adrenal cortex. Persons with Addison's disease are highly susceptible to various types of stress. They exhibit symptoms like vomiting, diarrhoea, collapse and pyrexia with vigour, hypoglycemia, low blood pressure, dehydration, acidosis, renal failure, progressive loss of weight, mental clouding and pigmentation of the skin (bronzing).

Q.21. What is a hypothalamus gland?

Ans. The hypothalamus is a gland in our brain that controls hormone system. It releases hormones to another part of our brain called the pituitary gland, which sends hormones out to our different organs. These include : adrenals, thyroid.

Q.22. Who discovered vasopresin?

Ans. Although it was known by the late 18th and early 19th century that certain substances from the pituitary body have 'pressor action' it was oliver kamm in 1928 who started the isolation and purification of vasopressin.

Q.23. What is action potential?

Ans. In physiology, an action potential occures when the membrane potential of a specific oxon location rapidly rises and falls.

Q.24. What inhibits ADH?

Ans. ADH release is inhibited by atrial natriuretic peptide (ANP), which is released by stretched atria in response to increases in blood pressure, as well as alcohol and certain medications.

SECTION-B SHORT ANSWER TYPE QUESTIONS

Q.1. What is synap? How does an impulse transmitted across the synapse?

Ans. **Synapse**

Synapse is the functional connection between two neurons. At a synapse, the terminal branches of the axon of one or more neurons lie in contact with the cyton (cell body) or dendrites of other neuron. Therefore, a synapse may be :

1. between the terminal branches of axon of presynaptic neuron and the cyton of postsynaptic won.
2. between the presynaptic fibres of an axon with the dendrites of post synaptic neuron.
3. between terminal branches of axons of pre and post synaptic neurons.

Anatomy of Synapse : The terminal branches of axon *i.e.,* the presynaptic terminals end in the knobs or buttons. These are called synaptic knobs. The membrane of the synaptic knob is the presynaptic membrane and that of dendrites of cyton of the postsynaptic neuron is the postsynaptic or sub synaptic membrane. The two membranes are separated by a synaptic cleft. The synaptic knob consists of a large number of synaptic vesicles. These enclose the excitatory transmitter material acetyl choline) which mediates transmission of impulses from the presynaptic neurons to the post synaptic neurons.

Mechanism of Synaptic Transmission

Transmission of impulse across a synapse is known as synaptic transmission. This is brought about either by chemical, electrical or by both process.

1. **Theory of Electrical Transmission :** Electrical transmission implies that despite the apparent morphological separation of two neurons, an effective local circuit connection exists which permits enough current to pass from the first to the second, to stimulate it. Beet this possibility is ruled out on the basis that synapse permits one way transmission of the impulses whereas nerve fibres can conduct impulses in either direction.

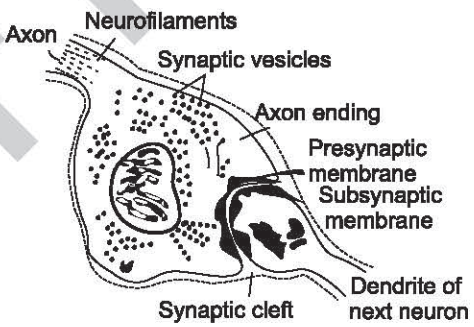


Fig. : Electron microscopic structure of synapse

2. **Theory of Chemical Transmission :** According to this theory synaptic transmission of an impulse is a chemical process. This mechanism was discovered by Henry Dale (1936), which is the most accepted view regarding the transmission of nerve impulse across the synapse. According to this view, the membrane of synaptic knobs possesses some sympatic vesicles containing acetyl choline sterase.

   As soon as the impulse reaches the synaptic knob, there is a sudden influx of Ca^{++} ions from the surrounding interestitial fluid into the synaptic knob. The Ca^{++} ions trigger the release of acetyl choline into the fluid of synaptic cleft, which acts as a chemical transmitter in carrying the nerve impulse across the synapse to the next neuron.

   Chemical transmission of the synapse, involves two processes :

   (i) **Neurosecretion :** The release by the arrival of a nerve impulse of the specific chemical from its storage space at the tip of the axon into the narrow space between the adjacent neurons; and

   (ii) **Chemoreception :** In this, the specific transmitter substance is attached to specific molecular sites in the dendrite and produces a change in the properties of its cell membrane so that a new nerve impulse is set up.

Q.2. Write about the structure and functions of islets of Langerhans.

Ans. **Position and Structure**

These cells are found in acinous form lying between the connective tissue of pancreas the digestive gland. These endocrine parts are called the islets of Langerhans. These contain two types of cells *viz,* α-cells and β-cells.

Hormone Produced : The alpha cells produce glycagon while the beta cells produce insulin. Both the hormones are secreted into the blood of the hepatic portal vein and are carried directly to the liver where they produce their major effects. Some of the hormone passes on through the liver into the general body circulation. This influences the utilization of sugars by all the cells of the body.

1. **Insulin :** Insulin is the protein which containing 51 amino acids.

Action of Insulin : Insulin promotes the transport of glucose through the cell membranes of muscles and especially of the liver. Liver, normally has large stores of glucose in the form of glycogen. It maintains proper levels of blood glucose by either taking it up or releasing it as required. Insulin facilitates this exchange as well as the uptake and utilization of glucose by the muscles and other tissues. The level of blood glucose, normally acts in a feedback manner to control the rate of insulin release from the Islets of Langerhans.

Deficiency of insulin causes inhibition of storage and utilization of sugar and urea as a result of glucose accumulation in the blood until its level may exceed the renal threshold. Glucose appears in the urine (diabetes millitus). When insulin levels are low, fat catabolism is increased and fats are converted into glucose. This further increases blood glucose levels and results in the accumulation of ketone bodies.

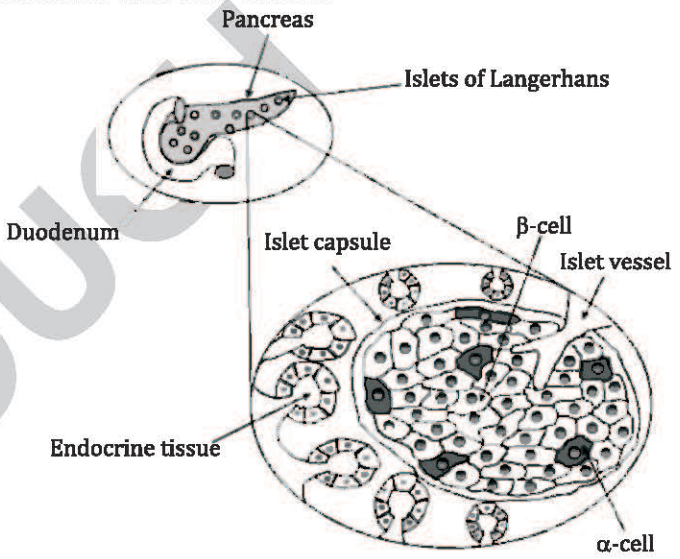


Fig. T.S. Pancreas showing islets of Langerhans

Hypersecretion of insulin may lead to lowered blood glucose levels since, the effect of insulin on glucose uptake by muscles exceeds its effect on liver to release of glucose. Such lowered blood glucose levels may have serious consequences.

2. **Action of Glucose :** Its effects on blood glucose levels is generally reverse to that of insulin. Glucogen favoures the release of glucose from the glycogen stored in the liver and thus, raises blood glucose levels.

A proper balance between insulin and glucagon production is therefore necessary to maintain proper blood glucose concentrations.

Q.3. What is reflex action? Describe the reflex arc with the help of a diagram.

Ans.

Reflex Action

There are certain actions of the body which are performed without the involvement of thinking or brain. These actions are immediate and spontaneous and may be described as automatic response to stimuli or reflexes. Some examples of reflex actions are mentioned as under :

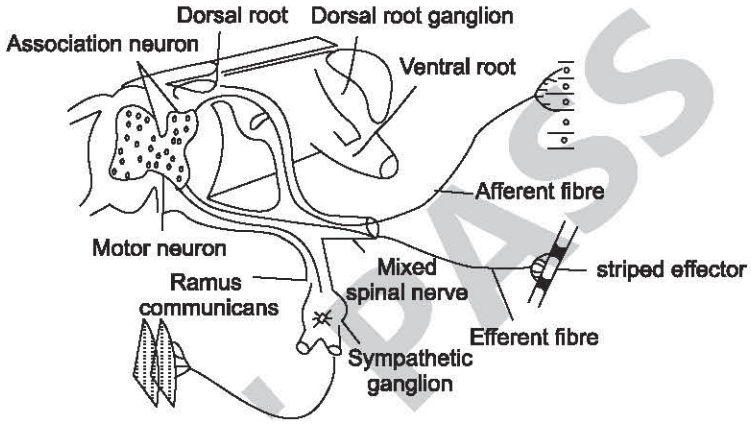


Fig. Reflex arc

1. Mouth starts watering (more or salvia is produced) at the taste, sight or smell of good food.
2. A person immediately withdraw his hand if some hot thing is touched to it.
3. While walking, leg is withdrawn if a nail comes on the way.
4. We immediately blink our eyes if something is seen entering it.

All these reflex actions are usually conveyed through spinal cord by a path called a reflex arc. Reflex are consist of the following parts :

(i) **Receptor :** It is represented by a single sensory cell or a group of cells which receive stimuli.

(ii) **Afferent or Sensory Neuron :** It connects the receptor to the spinal cord. Its cell body is situated in the dorsal root ganglion of the spinal nerve. It conveys impulses from receptor to the spinal cord.

(iii) **Association Neuron or Inter Neurons :** It present in the spinal cord. It connects the afferent and efferent neurons and passes impulses from afferent to efferent neuron, Generally, there is only the association neuron in the reflex arc but sometimes two of them may be present in one reflex arc.

(iv) **Efferent or Motor Neuron :** It is situated within the ventral root of spinal cord. It transmits impulses to the effector organ which may be muscle or gland.

(v) **Effector organ :** a responds to the impulses received and may be muscle or gland.

5. On this basis, two types of reflex arcs have distinguished : Monosynaptic and Polysynaptic.

Types of Reflexes

1. **Unconditioned Reflexes :** These are inborn reflexes transmitted through heredity. These are elicited in response of definite stimuli. The reflex arcs of unconditioned reflexes are constant. *e.g.,* Knee jerk, ankle jerk, blinking of eyelids, rapid withdrawal of hand when pricked or burnt etc.

2. **Conditioned Reflexes :** These are acquired during life time of an animal through learning or experience to stimuli which originally failed to elicit a reaction. The conditioned reflexes involve the establishment of new reflex arc and those close into the cerebral cortex. These are of temporary nature and may disappear or reappear again.

Physiology of Reflex Action : The stimulus takes the following course through the reflex arc :

1. The stimulus is detected by the receptors.
2. These stimuli initiate nerve impulses in the sensors neurons. These impulses pass through the axons of these neurons. The axons collectively form the sensory or afferent nerves, leading from there to the spinal cord.
3. These impulses enter the spinal cord and initiate impulses in one or more interneurons or association neurons.
4. Association neurons initiate impulses in the appropriate motor neurons.
5. When these impulses reach the junction between the motor neurons and the muscles or the glands (the effectors) via motor or efferent nerve, the latter are stimulated to discharge their function.

Q.4. Write a short note on structure and functions of parathyroid gland.

Ans.

Parathyroid Gland

Position : There are four small, yellowish, oval bodies embedded in the posterior surface of thyroid gland, *i.e.* two on each lobe. These have their own blood supply. These are derived from third and fourth branchial pouches.

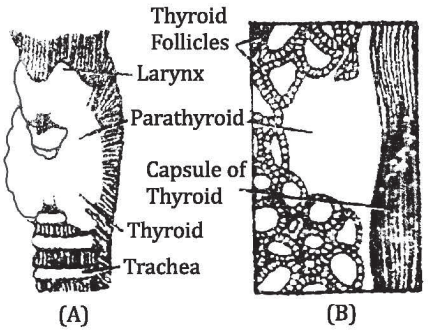


Fig. 1 : Location of parathyroid

Structure : Each gland is surrounded by a connective tissue sheath. It shows densely packed masses of cells usually arranged in cords enclosing sinuses. There are two types of cells :

1. **Principal Cells** form the greater part of gland. These are pale with clear cytoplasm having large nucleus. These cells secrete parathyroid hormone (parathormones).

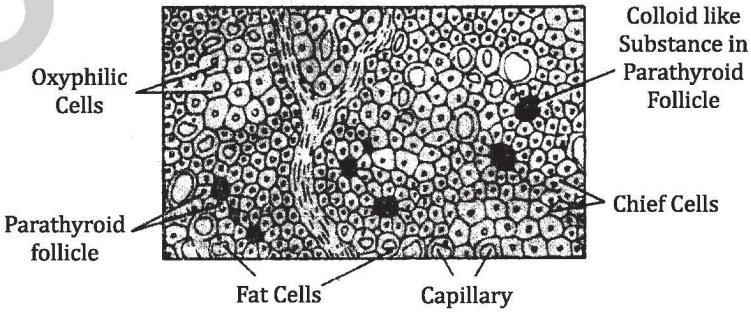


Fig. 2 : T.S. of parathyroid gland

2. **Oxyphil Cells or Eosinophils :** These are less in numbers and filled with granules which stain with acidic dyes.

Action of Parathormone : It controls the metabolism of calcium and perhaps phosphate. It favours deposition of these salts in the bone and increases the renal retention of Ca^{++} ions.

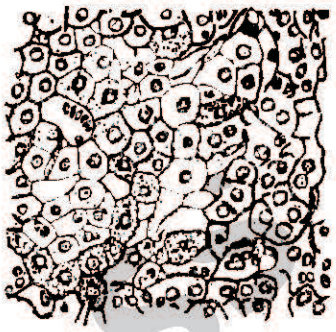


Fig. 3

It also promotes the absorption of Ca^{++} in intesstial tract. Thus it indirectly controls the blood calcium level.

Removal of parathyroids results in the fall in blood-calcium level and tetany occurs. Thus, it is essential for life. Under tetany spasms in the muscles of hands, feet and larynx and muscular convulsions take place.

Hypersecretion of parathormone brings about demineralization of the bones and the protein matrix may be absorbed, resulting in bone cysts and rise in blood calcium.

Calcification occurs kidneys, at arteries stomach and lungs. It causes :

1. Muscular weakness.
2. Dipress central nervous system.
3. Heart stops in systolic condition.

The excess calcium in blood is however, eliminated by kidneys and through intestine. High Concentration of calcium is blood induces the release of calcitonin of parafollicular cells of thyriod, thus, promoting deposition of calcium in bones.

Q.5. Write a short note on pineal gland.

Ans. **Pineal Gland**

The pineal gland is a minute white structure, an outgrowth from the roof of diencephaon, deeply embedded between the cerebral hemispheres. It secretes a hormone melatonin which is N-acetyl-5-methoxy-tryptamine synthesized from serotonin. Melatonin does not fit in the definition of hormones. It is not certain that metatonin reaches target cells via the blood which is an essential criterion for classification as a hormone. In fact, melotonin acts as a paracrine and autocrine. It is therefore called a candidate hormone. The function of pineal gland and melatonin is largely unknown in humans. The secretion of melatonin is stimulated by sympathetic postganglionic neurons and it undergoes a 24-hour cycle, being high at night and low during the day. The possible relationship of melatonin to "winter depression", its ability to reduce symptoms of jet-lag, and its possible role in the onset of puberty are conjectural and being currently probed. All these suspected functions ascribe the pineal acting as a "biological clock".

The main function of the pineal gland is to receive information about the state of the light-dark cycle from the environment and convey this information to produce and secrete the hormone melatonin.

Q.6. What do you mean by pheromones?

Ans. **Pheromones**

Pheromones are ecta hormones. These act as chemical messengers between the individuals of the same species. These also act as sex attractants between the two sexes of the same species. Thus pheromone denotes a chemical substance that is liberated by one animal and which causes a specific modification in the behaviour of the recipient animal of the same species.

Nature : Pheromones are aliphatic compounds, highly volatile and are transported by wind. These act through neuroendocrine mechanisms. They influence through olfactory stimulus.

Types : Pheromones are of two types :

1. **Signaller or releaser pheromones :** These bring about prompt behavioural reaction.
2. **Primer pheromones :** These cause lower effect, such as an alternation of the endocrine and reproductive systems.

Functions : Pheromones play an important role in insect reproduction and used in cradication of pesticide.

Q.7. Write about the factors controlling hormone secretion.

Ans. Factors Controlling Harmone Secretion

The various intrinsic factors that regulate secretion and concentration of hormones in the body are as follwos :

1. Feedback Control : The secretory activity of endocrine glands is modulated by feed back mechanism. In majority of cases it is controlled by negative feed-back but a few are of positive feedback type.

(i) **Negative Feedback or Feedback Inhibition :** In negative feedback, the concentration of hormone secreted by the target gland or a response to hormone by a target tissue has an inhibitory effect on the synthesis or secretion of hormone in question. In Fig. *A* stimulates *B* and *B* stimulates formation of *C*. The increased concentration of *C* inhibits functioning of *B*. This is also known as feedback inhibition.

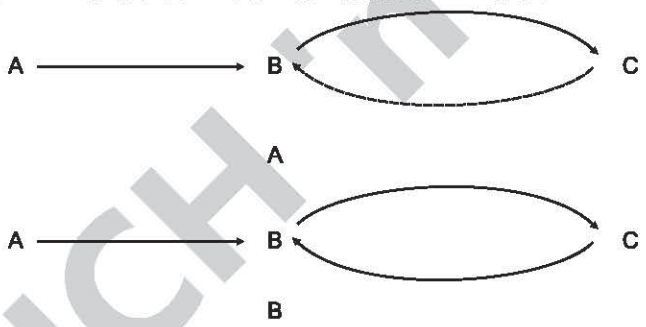


Fig. 1 : Diagrammatic representation of feedback control

Fig. 2 : Endocrine control showing action of hormone on specific cell

Examples :

1. Negative feedback control is common in physiological processes. For example, high blood concentration of thyrotropic hormone stimulates thyroid (the target gland) secretion. Increased level of thyroxin in turn inhibits synthesis and secretion of thyrotropic hormone.
2. ADH is secreted by adrenal medulla. On reaching kidneys it increases water reabsorption in the collecting duct from preurine to avoid loss of water. As a result plasma osmolarity is stabilized. This in turn inhibits secretion of ADH.

2. Positive feedback : In positive feedback, the end product or the hormone produced by target gland stimulates other gland to produce another hormone.

For example, in *A* stimulates *B* and *B* stimulates formation of *C*, whereas *C* also stimulates production of *B* to produce more *C*. For example, low level of estrogen stimulates secretion of

follicle stimulating hormone (FSH). This in turn stimulates secretion of estrogen. Thus, it is a positive feed back which increases level of estrogen and FSH in blood. This again is followed by negative feedback and high concentration of estrogen inhibits FSH production.

Low concentration of Estrogen
↓
Pituitary
↓
FSH ⟶ Secretion of Estrogen
Positive feedback

Q.8. What are prostaglandins? Also describe their functions.

Ans. **Prostaglandins**

Prostaglandins (PGs) are a unique group of biological compounds, secreted by the cells. These have hormone-like effects and help to regulate the action of other hormones by stimulating or inhibiting the formation of cyclin AMP. Chemically, prostaglandins are derivatives of polyunsaturated fatty acids, each with 5-carbon ring.

Prostaglandins are also called 'tissue hormones' because these are produced in a tissue and diffuse only a short distance and act on the cells within that tissue. There are three major classes of prostaglandins.

1. Prostaglandin-A (PGA), 2. Prostaglandin-E (PGE), 3. Prostaglandin-F (PGF).

Prostaglandins are released by different tissues including seminal vesicles, kidneys, lungs, liver digestive tract, iris, brain and thymus. The prostaglandins are rapidly inactivated and their half life is only a few minutes.

Functions : Prostaglandins have diverse physiological effects. These are intimately involved in overall endocrine regulation. These influence adenylcyclase and cyclic AMP activity. Prostaglandins dilate bronchial passage, inhibit gastric secretion, increase intestinal motility, stimulate contraction of uterus, raise or lower blood pressure, regulate metabolism and cause inflammation.

SECTION-C LONG ANSWER TYPE QUESTIONS

Q.1. What is nerve impulse? Describe the mechanism of transmission of nerve impulse through a nerve fibre.

Ans. **Nerve Impulse**

The structural and functional unit of nervous system is the nerve cell or neuron. Neurons are morphologically highly specialized for the conduction of nerve impulse. A typical neuron is composed of the cell body or perikaryon with a centrally situated nucleus cell body or perikaryon or soma possesses some characteristic organelles such as chromophyll substances or Nissl bodies, Rough endoplasmic reticulum, Golgi body, mitochondria and a reticulate network of neurofibrils. Perikaryon functions as the generator and susceptible to a variety of chemical electrical, thermal, mechanical and other stimuli to which it is exposed.

Basic function of neuron is to conduct nerve impulses and therefore, numerous branches are radiated from the perikaryon. These branches are dendrites, axons and collaterals. Collaterals are the sub-branches of the axon while dendrite are the peripheral arborizations of the perikaryon.

Structure of a Neuron : A neuron consists of a cell body of cyton with variable number of cytoplasmic processes. One of these processes is longest. It is known as axon. It may be as long as one metre. It terminates in fine processes, the axonal termination. The remaining smaller processes are termed as dendrons. These further ramify into dendrites, which form a spreading system of fine, naked protoplasmic strands. Through, these processes the neurons remain in contact (synapses) with the axonal termination from other neurons.

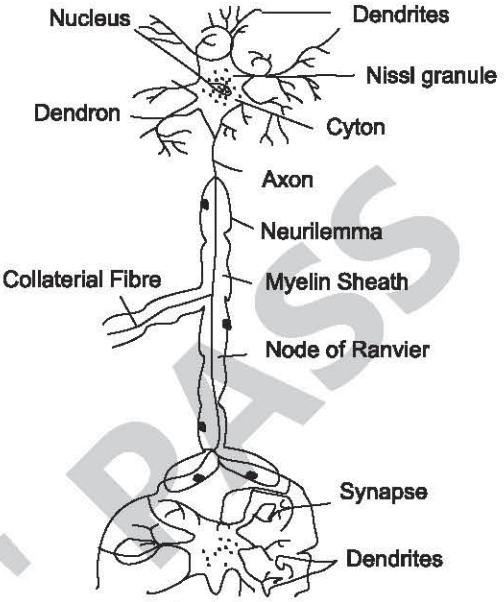


Fig. 1 : A neuron

The cyton or cell body is the site of all the cellular activities. The cytoplasm contains a nucleus, mitochondria. Golgi material and an intricate system of endoplasmic reticulum with many ribosomes. During certain stages in their activity, these membranous structures are recognized as nissl's granules visible with the ordinary optical methods. Nerve cells constantly synthesize new materials such as new axoplasm and neurosecretions. But the neurons cannot reproduce themselves.

Physiology of Nerve Impulse Conduction Nerve Impulse : A nerve impulse is an electro-chemical impulse, which brings about change in the resting potential of the nerve fibre and transmits the stimulus from the receptor to the central nervous system and from there to the end organ or effector.

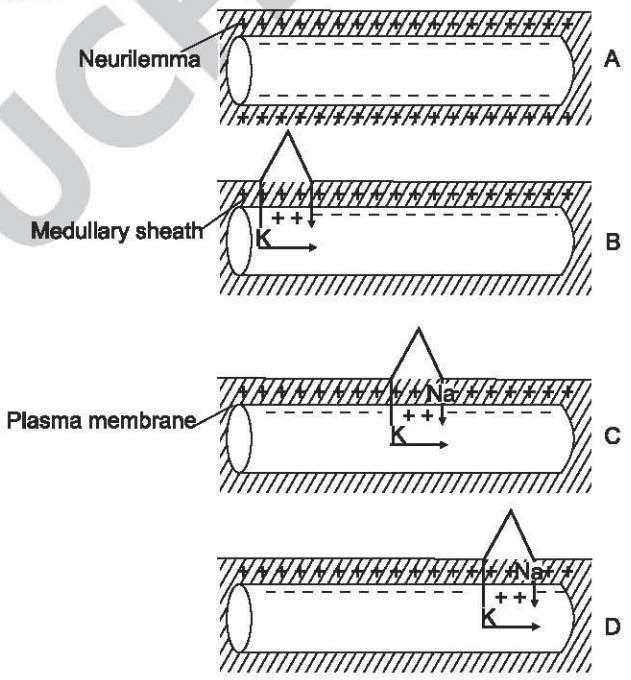


Fig. 2 : Depolarization and repolarization of nerve fibre

Transmission of Nerve Impulse

Conduction of Nerve Impulse : The conduction of nerve impulse is an electrochemical event, which involves the passage of measurable electric current along a nerve and a few metabolic activities within it and the synaptic ends.

Like all other cells, the nerve cells exist in a fluid environment in which salts and ions are dissolved. The medium is known as interstitial fluid. The neurilemma is impermeable to most of these ions, permitting only potassium (K^+) ions to diffuse freely and keeping sodium (Na^+) and chloride (Cl^-) ions outside.

(i) **Resting Potential :** Under resting condition sodium ions are actively transported from inside to the outside of the nerve fibre. This is known as sodium pump. As a result, they are in high concentration outside the membrane in the interstitial fluid and in low concentration in the axoplasm. As a result, the outer surface of the membrane is electrically positive and the inner surface is negatively charged. The charge on neurilemma is described as resting potential. It is about 70-80 mv. (millivolt).

(ii) **Depolarization :** When a stimulus of any kind, mechanical, electrical or chemical impinges upon the nerve fibre, momentarily, a local increase occurs in the membrane permeability at the site of stimulus, which permits more sodium ions to rush into the cell. This is just the opposite of the resting state and is called reverse potential. It results in depolarization of the membrane and a local negatively charged area.

(iii) **Action Potential :** This changed electric potential of the neurilemma is known as action potential. The initial change produces an ionic imbalance in the membrane on either side of the point of stimulus producing local electric current. These areas of negative depolarization, in turn initiate changes in the membrane adjacent to them. A wave of electric change or depolarization along the length of nerve fibre or axon is known as nerve impulse.

The propagation of nerve impulse can be compared to the pushing over of a row of dominoes. Energy is required for the initial disturbance, but after that the displacement of domino works to displace the next and once the stimulus has set off a nerve the impulse passes without any change down the length of the fibre.

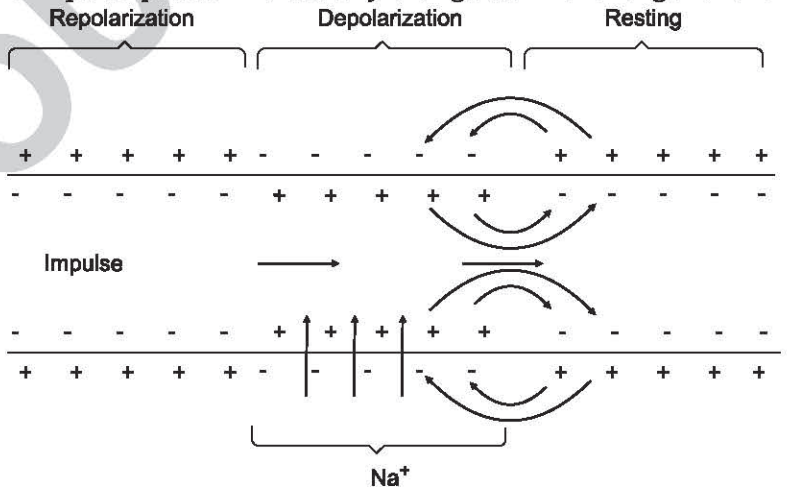


Fig. 3 : Transmission of nerve impulse through nerve fibre

(iv) **Repolarization :** With the increase of positive charge inside, further entry of Na^+ is prevented and permeability of membrane decreases and Na^+ ions are pushed out. With the establishment or sodium pump the inside of the membrane becomes negative and outside becomes positive and the membrane restores the original resting potential. This is known as repolarization. The repolarization starts exactly on the same spot where depolarization had started and then continues to advance in both directions.

The entire process of repolarization requires some time during, which the nerve cannot be stimulated again. This period is known as refractory period.

Threshold Stimulus : A very weak stimulus is unable to propagate a nerve impulse. Intensity of stimulus which is just adequate to cause an impulse is called the threshold stimulus. Stimulus below threshold causes a small membrane depolarization but no action potential.

Q.2. Describe the resting and action potentials with the suitable diagrams.

Ans. Neurones communicate with each other via brief electrical signals known as action potentials. They are brief changes in the voltage across the membrane due to the flow of certain ions into and out of the neurone. In this article, we will discuss how an action potential (AP) is generated and how the conduction of an action potential occurs.

Resting Membrane Potential : The resting membrane potential of cells varies depending on the cell type. For neurones, it typically sits between –50 and –75 mV. This value depends on the types of ion channels that are open and the concentrations of different ions in the intracellular and extracellular fluids during the resting state. In neurones, K^+ and organic anions are typically found at a higher concentration within the cell than outside, whereas Na^+ and Cl^- are typically found in higher concentrations outside the cell.

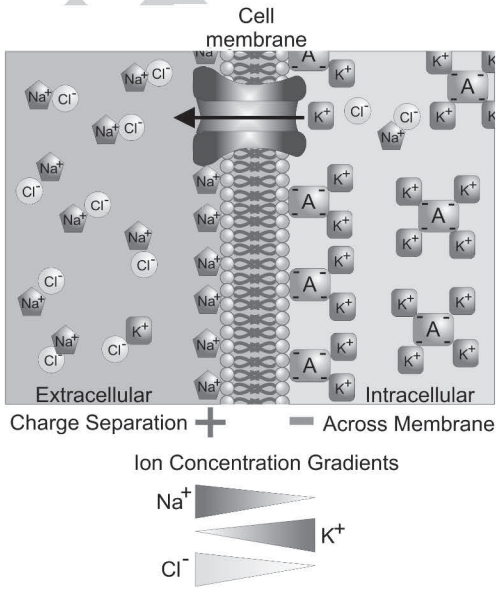


Fig. 1 : Diagram demonstrating the ions involved in setting the resting membrane potential, as well as the direction of the ion concentration gradients ing the ions involved in setting the resting membrane

This difference in concentrations provides a concentration gradient for ions to flow down when their respective channels are open. Hence, K^+ ions would be moving out of the cells,

while Na^+ and Cl^- ions would be moving into the cell. At the resting state, the cell is mostly permeable to K^+, as such this exerts the greatest influence on the resting membrane potential out of the three ions.

These concentration gradients are maintained by the action of the Na^+/K^+ ATPase *via* active transport, which in turn allows the membrane potential to be maintained.

Generation of Action Potentials : During the resting state, the membrane potential arises because the membrane is predominantly permeable to K^+. An action potential begins at the axon hillock as a result of depolarisation. During depolarisation voltage-gated sodium ion channels open due to an electrical stimulus. As the sodium ions rush back into the cell, their positive charge changes potential inside the cell from negative to more positive.

If a threshold potential is reached, then an action potential is produced. Action potentials will only occur if a threshold is reached. Additionally, if the threshold is reached, then the response of the same magnitude is always elicited, irrespective of the strength of the stimulus. Hence, action potentials are described as "all-or-nothing".

Once the cell has been depolarised the voltage-gated sodium ion channels begin to close. The positive potential inside the cell causes voltage-gated potassium channels to open and K^+ ions now move down their electrochemical gradient out of the cell. As the K^+ moves out of the cell, the membrane potential becomes more negative and starts to approach the resting potential.

Typically, repolarisation overshoots the resting membrane potential, making the membrane potential more negative. This is known as hyperpolarisation. It is important to note that the Na^+/K^+ ATPase is not involved in the repolarisation process following an action potential.

Every action potential is followed by a refractory period. This period can be further divided into :

- The absolute refractory period which occurs once the sodium channels close after an AP. Sodium channels then enter an inactive state during which they cannot be reopened, regardless of the membrane potential and
- The relative refractory period which occurs when sodium channels slowly come out of the inactivation. During this period the neurone can be excited with stimuli stronger than the one normally needed to initiate an AP. Early on in the relative refractory period, the strength of the stimulus required is very high. Gradually, it becomes smaller throughout the relative refractory period as more sodium channels recover from the inactivation stage.

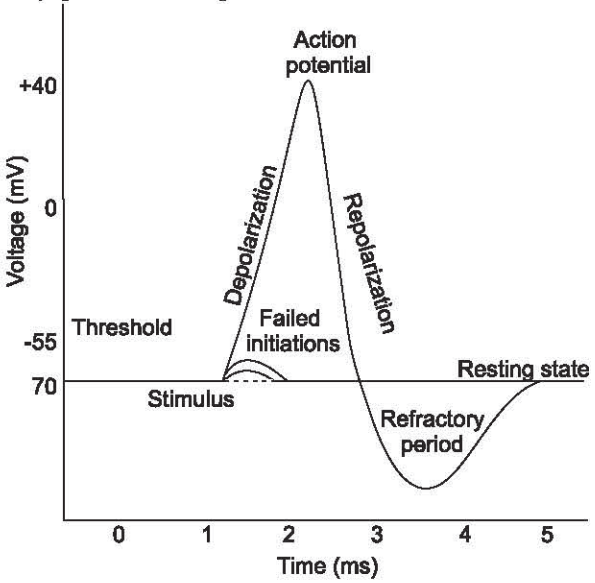


Fig. 2 : Diagram showing the phases of an action potential in relation to the membrane voltage over time.

Propagation of Action Potentials : Action potentials are propagated along the axons of neurones *via* local currents. Local currents

induce depolarisation of the adjacent axonal membrane and where this reaches a threshold, further action potentials are generated. The areas of the membrane that have recently depolarised will not depolarise again due to the refractory period - meaning that the action potential will only travel in one direction.

These local currents would eventually decrease in charge until a threshold is no longer reached. The distance that this would take depends on the membrane capacitance and resistance :

- **Membrane capacitance :** The ability to store charge. The lower capacitance results in a greater distance before the threshold is no longer reached.
- **Membrane resistance :** Depends on the number of ion channels open. The lower the number of channels open, the greater membrane resistance is. A higher membrane resistance results in a greater distance before the threshold is no longer reached.

Myelinated Axons : In order to allow rapid conduction of electrical signals through a neurone and make them more energy-efficient certain neuronal axons are covered by a myelin sheath. The myelin sheath surrounds the axon to form an insulating layer.

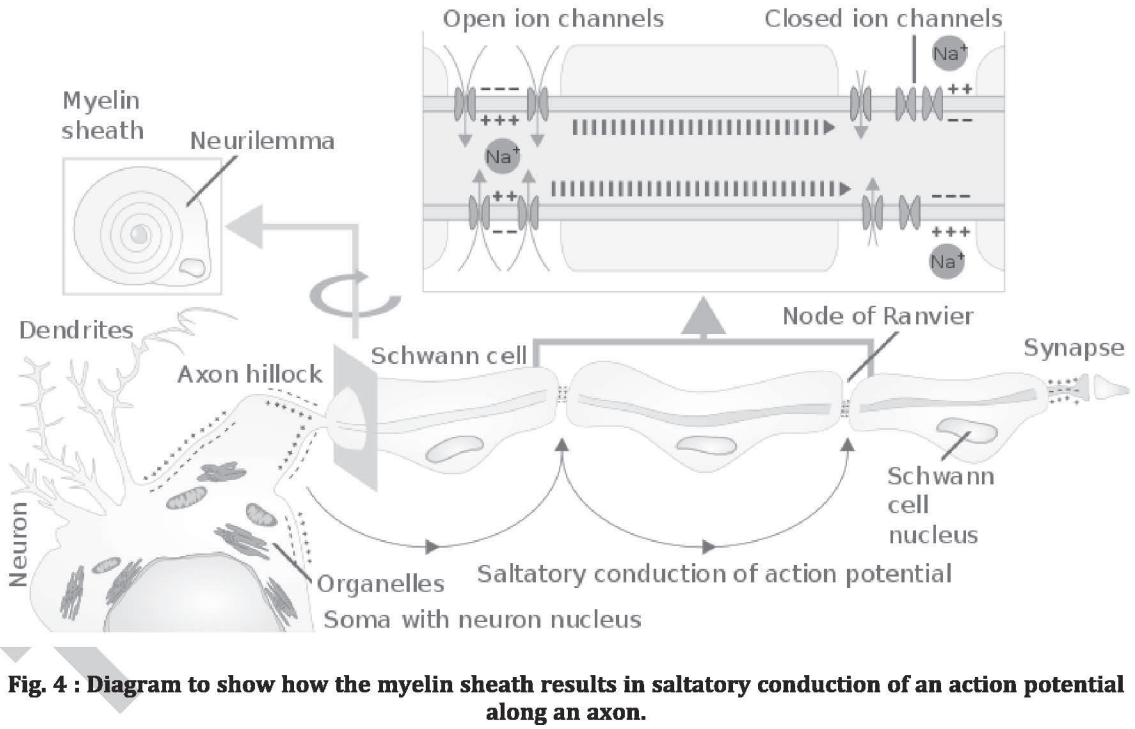


Fig. 4 : Diagram to show how the myelin sheath results in saltatory conduction of an action potential along an axon.

Along a myelinated axon, there are periodic gaps where there is no myelin and the axonal membrane is exposed. These gaps are called nodes of Ranvier. In contrast to myelinated sections of the axon that lack voltage-gated ion channels, nodes of Ranvier harbour a high density of ion channels. For this reason, an action potential can only occur at the nodes. The myelin sheath speeds up the conduction by increasing the membrane resistance and reducing the membrane capacitance. Hence, the action potential is able to propagate along the neurone at a higher speed than would be possible in unmyelinated neurons. The electrical signals are rapidly conducted from one node to the next, where is causes depolarisation of the

membrane. If the depolarisation exceeds the threshold, it initiates another action potential which is conducted to the next node. In this manner, an action potential is rapidly conducted down a neuron. This is known as saltatory conduction.

Q.3. Describe the morphology and histology of thyroid gland. Also explain their hormones function.

Ans.

Thyroid Gland

Thyroid gland is located on the anterior part of the trochea on the sides of thyroid and cricoid cartilages of larynx. Thyroid gland is H. shaped, bilobed soft mass of pink colour. Its two lobes are connected by a connective tissue called isthmus :

Histology : Thyroid gland is composed of a mass of numerous small rounded follicles. These are held together by connective tissue, called stroma. Stroma contains blood capillaries and groups of parafollicular cells or C-cells. The follicles are lined with a single layer of cuboidal epithelium. Their cavity is filled with transparent, jelly like colloidal fluid, called iodothyroglobulin. It is the iodine containing protein and represents the storage form of thyroid hormone.

Cuboidal epithelium has three types of cells :

1. **Typical Follicular Cells or Chief Thyrocytes :** These form bulk of follicular epithelium. These produce tetraiodothyronin (T_4) and tri-iodothyronin (T_3) which collectively form thyroid hormone.

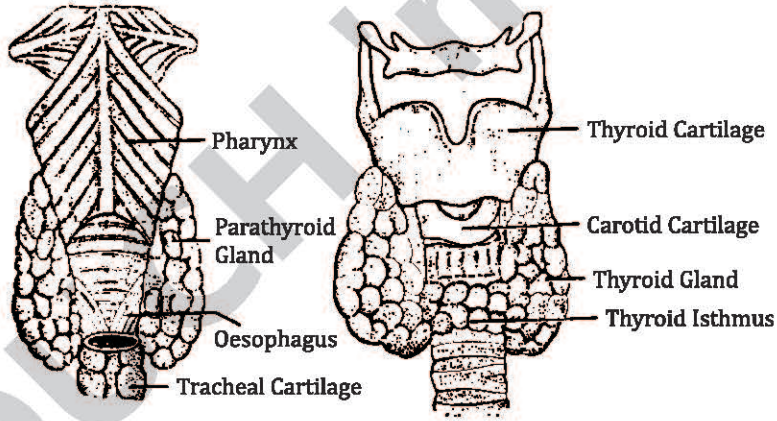


Fig. : Diagram to show position and structure of thyroid gland.

2. **Parafollicular Cells or Clear Cells (C-cells) :** These are present both in follicular epithelium and in connective tissue as well. These have clear cytoplasm and secrete the hormone thyrocalcitonin.
3. **Colloid Cells :** These are regenerating cells and are very few in number.

Hormones Secreted by Thyroid Gland : Thyroid gland secretes following three hormones :

1. **Thyroxin or Tetraiodothyronin (T_4) :** It forms 65-90% of thyroid secretion. It is secreted by follicular cells of thyroid. It is formed of two molecules of di-iodothyrosine.
2. **Tri-iodothyronin (T_3) :** It forms 10-35% of thyroid secretion. It is more effective than thyroxin but in unstable. It is formed of 3 molecules of iodothyrosine.
3. Thyrocalcitonin (TCT) : It is a hypocalcemic hypophosphatemic hormone. It is secreted by parafollicular cells present in the stroma. It is proteinaceous in nature and ia formed of 32 amino acids.

Functions or Biological Action of Thyroid Hormone : Tri-iodothyronin (T_3) and tetra-iodothyronin (T_4) have the same functions. (T_3) is more effective than thyroxin (T_4) but thyroxin constitutes the major part of thyroid secretion. Thyroid hormones directly affect growth, development, reproduction, behaviour and metabolism. They exert effects on almost every tissue of the body throughout life. The effects are produced by stimulation of cellular protein synthesis. These regulator effects are on the following systems :

1. **General Metabolism :** Thyroxin controls general rate of metabolism activities. It influences rate of energy production by enhancing energy releasing oxidative activities. This effect is known as calorigenic effect. Each one milligram of thyroxin raises BMR to about 1000 calories of heat.
2. **Carbohydrate Metabolism :** Thyroxin stimulates : Absorption of glucose by intestinal wall, Consumption of glucose inside the cells, Glycogenolysis in liver and muscles, Gluconeogenesis *i.e.,* synthesis of glucose from noncarbohydrate sources.
3. **Lipid Metabolism :** Thyroxin increases synthesis as well as catabolism of lipids by enhancing lipolytic response of adipose tissue.
4. **Protein Metabolism :** Thyroid hormone is anabolic. Within physiological limits it increases synthesis of proteins and RNA which precedes increased metabolism.
5. **Body Weight :** Thyroxin controls body weight. Its increased production leads to weight loss and decreased amount leads to obesity.
6. **Body Temperature :** It is raised due to increased metabolism.
7. **Heart Rate :** Thyroxin accelerates rate of heart beat, systolic arterial pressure, pulse rate and local blood flow.
8. **Growth and Differentiation :** Thyroxin is essential for growth. Growth hormone secreted by pituitary can exert its full effect on target cells only in the presence of thyroxin. It also controls the functioning of adrenal cortex and gonads. Growing children with hyper-thyroidism show extraordinary growth of skeleton producing very tall persons. The hypothyroidism results in dwarfs.
9. **Respiration :** By influencing metabolism, thyroxin increases rate of utilization of oxygen and release of CO_2.
10. **Metamorphosis :** Thyroxin is essential for metamorphosis in amphibian tadpoles. In the absence of thyroxin metamorphosis does not occur. In case of hypothyroidism in larva, metamorphosis is delayed. Tadpole larvae of Ambystoma fail to metamorphose when placed in water without iodine or if living in areas with iodine deficiency. They remain permanently in larval stage, but develop gonads and start reproduction. These sexually mature larvae are called Axolotl larvae and this phenomenon is known as paedogenesis or neoteny.
11. **Mineral Metabolism :** Hormone thyrocalcitonin (TCT) secreted by parafollicular cells (C-cells) controls amount of calcium and phosphorus ions in the body fluid. It lowers blood calcium but increases calcification of bones. Its hypersecretion causes excretion of these ions in urine. It may lead to diuresis with the loss of potassium in urine.
12. **Osmoregulation and Moulting :** In cold blooded vertebrates, thyroid controls osmoregulation and moulting or sloughing of integument.

Q.4. What are hormones? Describe chemical nature and mechanism of hormone action.

Ans.

Hormone

Term hormone was coined by starling and Bayliss (1905)—Hormones are chemical messengers produced by endocrine glands and transported by blood to other tissue or organs where these stimulate a change in metabolic activity. The tissue or organ which are stimulated by a specific hormone is called target tissue or target organ.

Physical Nature of Hormones

1. Hormones are secreted by endocrine cells.
2. Hormones are chemical messengers.
3. The hormones regulate the behaviour of the target cells.

Chemical Nature of Hormones

Hormones include diverse chemical substances (hence called chemical messengers). These may be :

1. **Amino Acid Derivatives :** The hormone secreted by thyroid gland-thyroxin (tri iodothyronin and tetra-iodothyronin) is a simple iodine derivative of amino acid tyrosine.
2. **Amines of Catecholamines :** *e.g.* epinephrine and norepinephrine, secreted by adrenal medulla.
3. **Peptide Hormones :** Some hormones are formed of polypeptides or of small proteins. The polypeptide hormones such as oxytocin, vasopressin, prolactin, etc., are water soluble. These protein hormones are insulin, glucagon, secretin, relaxin, adrenocorticotropin and somatotropin. The protein hormones are the largest and most complex hormones.
4. **Glycoproteins :** The thyrotropin (TSH), follicular stimulating hormone (FSH) and luteinizing hormones (LH) or ICSH secreted by adenohypophysis of pituitary gland are glycoproteins.
5. **Steroids :** Sex hormones and hormones secreted by adrenal cortex are steroids. These are fat soluble. These are closely related to Vitamin-D, cholesterol and bile salts. Examples : Cortisone, aldosterone, testosterone, estrogen and progesterone. Embryonic inductors are also steroids.
6. **Fatty Acids Derivatives :** Prostaglandins secreted by individual cells for intercellular communication are derivations of unsaturated fatty acids. These are 20-carbon fatty acids.

Mechanism of Hormone Action

Three different theories have been put forward to explain mechanism of hormone action. These are :

1. **By Changing Permeability of Cell Membranes :** Certain hormones change permeability of cell membrane for ions or substrates like glucose and amino acids. Growth hormone, glucagon, glucocorticosteroids, testosterone, oestrogen and vasopressin can change membrane permeability. This changes metabolism of the cell, accelerating or blocking the entrance of certain substrates into the cell.
2. **Activation of Genes (Action of Steroid Hormones) :** Steroid hormones are small molecules. Being highly soluble in lipids, these easily pass through the cell membrane of a target cell into its cytoplasm. Here steroid hormones combine with specific intracellular receptor molecules.

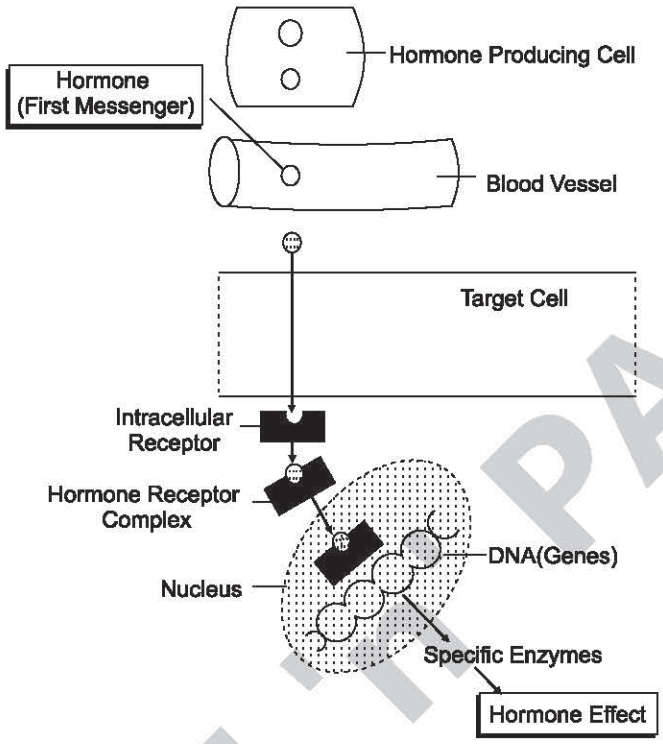


Fig. 1 : Mechanism of action of steroid hormones by the activation of genes

The hormone-receptor complex moves into the nucleus and combines with another receptor, a protein associated with specific sites on the chromatin of chromosome. This combination activates certain gene or genes inducing synthesis of a specific mRNA molecules which in turn initiate synthesis of specific protein. Examples are corticosteroids. Thyroid hormones (not steroid) are small hydrophobic molecules that pass through the cell membrane and bind to protein receptors within the nucleus.

The Gene Activation Theory orginated in Germany based on the working of insect hormones ecdysone. Ecdysone activates certain gene loci on the salivary gland chromosomes of *Diptera*. This activation has been observed under the microscope in the form of puffing of specific regions.

3. **Second Messenger Hypothesis (Stimulation of Membrane Receptors) :** Second messenger hypothesis or role of cyclic AMP in hormone action was proposed by Sutherland for which he got Nobel Prize in 1971. According to this concept, many of protein, polypeptide and amide type of hormones do not enter the cell because plasma membrane is not permeable to them. They act as first messenger and deliver the chemical message from the endocrine gland to the membrane receptor on the surface of target cell.

   The membrane receptor is a mobile protein molecule having a specific recognition site for a specific hormone. It extends outward from the surface of plasma membrane. On reaching the target cell, each protein-like hormone combines with the membrane receptor. This combination promotes association of receptor moiety with regulatory

protein (GDP). It permits GTP to bind to regulatory unit. The activated regulatory protein (N-GTP) dissociates from the receptor and interacts with the enzyme adenylate cyclase present on the inner surface of cell membrane. Activated adenylate cyclase catalyzes conversion of ATP to cyclic AMP in the cell cytoplasm.

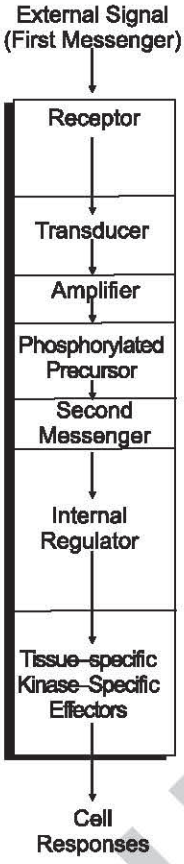


Fig. 2 : Diagram showing second messenger hypothesis.

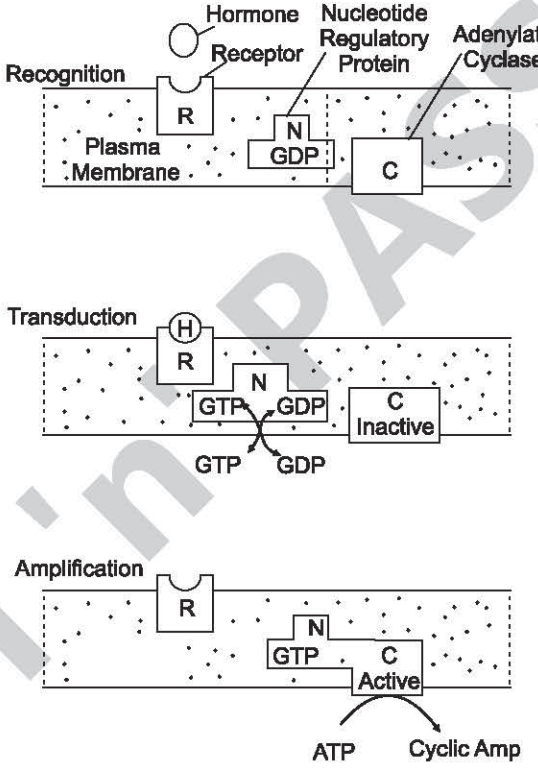


Fig. 3 : Role of membrane receptor and GDP in peptide hormone action on the surface of cell

Each cAMP dependent protein kinase is composed of two components :

1. a regulatory subunit
2. a catalytic subunit

Q.5. What is adrenal gland? Also explain the structure and function of stress combating hormones.

Ans. **Adrenal Gland**

Location : Adrenal glands are a pair of cap-like structures, roughly triangular in shape and browinsh in colour lying on the dorsal side of kidneys. These are also called as supra renal glands.

Structure : It weighs about 4-6 g and measures 1-2 inch in length. If is enclosed in a fibrous capsule of connective tissue containing fibroblasts, Collagen and elastic fibres. Its matter is differentiated into two parts :

1. **Adrenal Cortex :** It is yellowish peripheral part, derived from embryonic mesodermal. coelomic epithelium covering the anterior part of mesonephrons. It is distinguished into three regions :
   (i) **Zona Glomerulosa :** It is the outer most zone which produces new cells. It is formed of groups of small, aviod to collumnar cells, thickly arranged into spherical masses with their long axis parallel to the surface. It secretes mineralocortisone or mineralocorticoid or aldosterone which regulates salt and water balance.
   (ii) **Zona Fasciculata :** It is the middle zone. It is widest and is formed of large, polyhedral cells, arranged in radiating columns of two cells thick cords. The columns the vertical to the surface, the cells are rich in lepid. These secrets glucocorticoids which controls carbohydrate metabolism.
   (iii) **Zona Reticularis :** It is the inner layer. It is formed of irregular anastomosing network of rows of cells. The meshes of network are filled with blood spaces or sinusoids. The cells are degenerating with pycnotic nuclei. These synthesis sex-hormones.

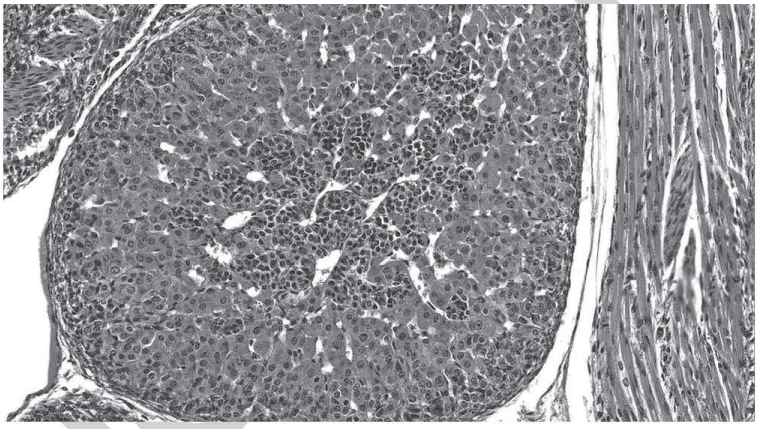


Fig. : Diagram to show histological structure of adrenal gland.

2. **Adenal Medulla :** It occupies the central part of adernal gland. It is brownish in colour. It is neuroectodermal in origin. It is derived from the tissue from which sympathetic ganglia originate.

   The cells of medulla wave neuro-secretory. These are stained brown with chromic acid, hence called as Chromaffin cells. These are stimulated by preganglionic sympathetic fibres and produce hormones adrenalin (epinephrine) and noradrenaline (norepinephrine).

Functions of Adrenal Hormones

1. **Mineralocorticoids :** Their major effect is on the metabolishm of sodium ions and indirectly potassium ions. The major minereto corticoid is aldosterone. It promotes the resorption of Na^+ ions from the renal glomerular filtrate. It causes retention of Na^+ acid Cl^- ions and water.

   It causes increased excretion of K^+ leading to decreased intracellular K^+ ions (Hypokalemisa). It controls water balance and capillary permeability; kidney functions and blood pressure are also controlled.

2. **Glucocorticoids :** These are autoagonistic to insulin. These carry out following functions :

   It promotes conversion of glycogen into glucose in liver and raises sugar level (Hyperglycemia). During stress, promotes synthesis of glucose from proteins and fats (gluconeogensis).

   These are antiinfammatory and antiallergic. These control distribution of water and electrolytes, thus helping in osmoregulation. These are immunosuppressors. Thus used in the treatment of allergic reactions. Raise blood pressure.

3. **Sex Hormones :** Adrenal cortex secretes hormones. Androgens in males and Oestrogens in females.

Functions of Medullary Hormones

1. **Adrenalin or Epinephrine :** Adrenalin is a sympathomimetic hormone. It controls all those activities that are under autonomic control and are influenced by sympathetic stimulation. It influences α-and β-receptors of effector organs like glands and unstriped muscles causing the constriction of blood vessels and blood capillaries (vasoconstriction).

   Thus, increases heart beat and blood pressure, dilates trachea to provide more oxygen, increases BMR, decreases secretion of insulin, preventing removal of glucose from blood for storage. Adrenal prepares the body for "fight or flight situation" *i.e.,* emergency functions such as fear, shock, excitement and fatigue.

2. **Nor-adrenalin or Nor-epinephrine :** Except for a few, it carries out of same functions as adrenalin. However, it influences only α-receptors. It helps in bringing body back to normal after the effect of adrenalin or excitement.

Abnormalities : Hypofunctioning of adrenal cortex produces hypoaldosterone which causes Addison's disease. It is characterized by :

Dehydration, loss of Na^+ and Cl^- ions in urine; Retention of K^+ ions in the body (hyperkalemia); lowered B.P., body temperature and blood pressure. Loss of appetite, nausia, vomiting & gastro-intestinal disorders. Disturbed carbohydrate metabolism (Hypoglycemia) isomnia, giddiness; Depressed sex functions. Hyper functioning of Adrenal Cortex causes cushing syndrome; Hyperaldosteronism and Adrenogenital syndrome.

Causes

Hyper functioning of Adrenal medulla casuses permanent hypertension; high blood pressure; rapid palpitation; emotional disturbances; weight loss, anorexia and increased Basal Metabolic Rate (BMR).

❑❑❑

UNIT-VIII

Muscular System in Humans

SECTION-A VERY SHORT ANSWER TYPE QUESTIONS

Q.1. Where do muscle contractions derive their energy from?

Ans. From ATP, Every myosin molecule contains myosin ATPase, an enzyme at its head. In the presence of this enzyme along with Ca^{2+}, Mg^{2+} ions the inorganic phosphate and ADP it is desintegrated by ATP to release energy from the myosin head. This energy causes myosin to cross bridges to bind to actin. These cross bridges that are energized move, resulting in the sliding of thin myofilaments with the thick myofilaments, thereby causing muscle contraction.

Q.2. Write the difference between actin and myosin.

Ans. Differences between Actin and Myosin are as follows :

S.No.	Actin	Myosin
1.	Actin is a thin contractile protein.	Myosin is a thick contractile protein.
2.	It is present in light bands and is called an isotropic band.	It is present in dark bands and is called an anisotropic band.

Q.3. How is the structure of a sarcomere suitable for the contractility of the muscle? And also write its function according to sliding filament theory.

Ans. Each sarcomere contains two types of myofilaments-thick filament composed primarily of the contractile protein myosin and the filaments composed primarily of the contractile protein actin.

According to the sliding filament model, the interaction between the actin and myosin filaments in the A-band of the sarcomere is responsible for the muscle contraction.

Q.4. Red muscle fibres can continue contracting for prolonged durations without fatigue. Why?

Ans. The contractions of red muscle fibres mainly depend on metabolism without accumulating much lactic acid. So these fibres can go on contracting for prolonged durations without fatigue.

Q.5. What is sliding filament theory?

Ans. This theory explains the process of muscle contraction during which the thin filaments slide over the thick filaments that shortens the myofibril.

Q.6. What is the role of ATP in the sliding filament theory?

Ans. ATP releases myosin from the actin filaments. During contraction, myosin attaches to the actin filaments. ATP attaches to the myosin head and releases it from the actin molecule, thereby causing relaxation.

Q.7. Does calcium ion concentration in blood cause tetany in some cases? Compare fluctuation in blood calcium with tetany.

Ans. In the regulation of muscle contraction, calcium plays a significant role. The parathyroid hormone (PTH) that is secreted by the parathyroid gland increases the calcium level in the blood. In hypoporathyroidism (PTH defficiency), the level of calcium in blood dips which causes an increase in the excitability of muscles and nerves resulting in convulsions and cramps. It also produces sustained contractions of the muscles of face, hands, feet and larynx. This disorder is referred to as parathyroid tetany.

Q.8. What is muscle insertion?

Ans. Muscle insertion refers to a muscle's distal attachment the end of the muscle furthest away from the torso. For example, the bicep insertion occurs at the elbow.

Q.9. Does calcium bind to troponin?

Ans. Troponin is red (subunits not distinguished) upon binding calcium, troponin moves tropomyosin away from the myosin binding sites an actin (bottom) effectively unblocking it.

Q.10. What are the three cardiac enzymes?

Ans. Cardiac enzymes also known as cardiac biomarkers which include myoglobin, troponin and creative kinase.

Q.11. Where is troponin located?

Ans. Troponins are proteins found in cardiac muscle. Their presence in the blood is widely used in determining the extent of cardiac damage in diseases such as mycocardial infarction, however they can also be released in right heart failure and plasma troponin levels have also been utilized in predicting the prognosis.

Q.12. What is cross bridge cycling?

Ans. It is essentially acting like a bridge when the head is covalently bonded to actin and this bridge is continuously being formed and broken during muscle contraction the cross bridges are being cycled and it is this action which is allowing for the filaments to slide the way they do.

Q.13. Where is the sarcolemma?

Ans. The sarcolemma is the plasma membrane of the muscle cell and is surrounded by basement membrane and endomysial connective tissue. The sarcolemma is an excitable membrane and shares many properties with the neuronal cell membrane.

SECTION-B SHORT ANSWER TYPE QUESTIONS

Q.1. What is motor unit?

Ans. **Motor Unit**

Motor nerves that initiates the contraction of muscles may supply any number of muscle cells. One motor nerve fibre, with all the muscle fibres it supplies constitute a motor unit. The number of muscle fibres in a motor unit may vary from as low as 3 to as high as 3000. In most fast muscles like those of hand (finger) and those concerned with eye motion (eye muscles) the muscle fibres are 3-6 per motor unit. On the other hand about 120-162 fibres per unit are known in cat leg muscles and even more upto 3000 fibres per motor unit are found in the leg and back (postural) muscles of man.

Infact the strength of a muscular contraction depends on the number of motor units activated at one time. If a stimulus is weak, muscle fibre of lesser motor units will contract resulting in a weak response. However, if the stimulus strength is increased, more motor units are stimulated resulting in a stronger contraction until all the motor units excited. After such a stage any further increase in stimulus strength will not increase further the strength of contraction.

Q.2. Write a short note on functions of muscles.

Ans. **Functions of Muscles**

Muscles convert chemical energy into mechanical energy and perform work. The nerve impulses initiate the above process by depolarizing the membrane of the muscle fibre. Under activation, the fibre structure in the muscles is changed and their length diminishes. The energy for this purpose is derived from exothermic, energy-yielding reactions. The complete work done by the contractile elements of the muscles is not applied on the load. Part of it is spent on pulling and stretching the non-contractile parts of the muscles, namely, the sarcoplasm, sarcolemma and the connective tissue. The shortening of the contractile elements is known as the contraction of muscles. For this reversible process the energy is derived from the metabolism of lipids and carbohydrates. After contraction, the muscle filaments return to their normal position, known as the relaxation state. However, the relaxation state is not a passive state, as energy is consumed from the starting of the contraction to until nearly the end of relaxation. This period is referred to as an active state. According to Hill (1950), the active state is defined as "the load that a muscle can just bear without lengthening or as the tension exerted when the contractile elements neither lengthen nor shorten, or as the tension of the contractile elements if this could be measured directly without the series of elastic elements intervening."

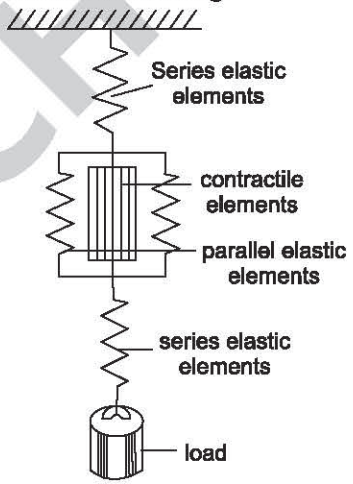


Fig. Mechanical model of a muscle fibre showing the relationship between elastic and contractile components

Q.3. Write about the tetanus and summation.

Ans. **Tetanus**

If a muscle fibre is stimulated before it relaxes for a second time, it can contract again. Therefore, a muscle can be maintained in a continuously contracted phase, if stimulated frequently within a given time, A continuous contraction of this type is known as "tetanus".

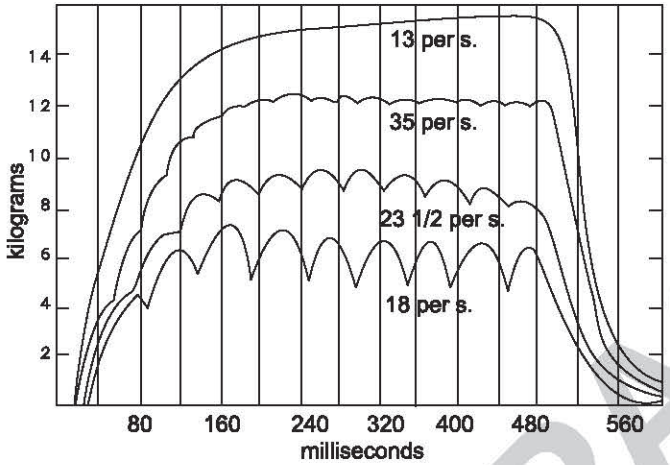


Fig. 1 : Complete and incomplete tetanus due to stimuli on the gastrocnemius muscle

Summation

When the pre-synaptic portion of a nerve is stimulated more than two times, it tends to have an additive effect on the post synaptic portion. In the case of muscles, the effects may either be mechanical or electrical; accordingly summation or addition takes place in the electric behaviour of the membrane of the muscle fibre and in the contractile elements.

However, as the electric membrane responses are of short duration, it is essential that the stimulations should be at short intervals. In muscles a series of stimuli causes contraction, which gradually increase and the resulting final contraction is greater than a simple contraction, excited by a stimulus of greater intensity and excites all the fibres of a muscle. The additive effect of repeated contractions is known as summation.

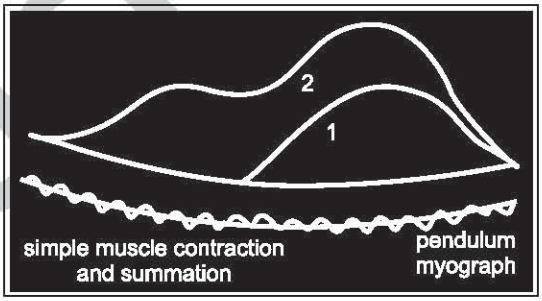


Fig. 2 : Showing summation.

Q.4. Write a short note on physical and electrical changes during muscle contraction.

Ans. Physical changes during Muscle Contraction

During the contraction of muscle a number of changes take place. Important physical changes are given below :

1. **Shortening :** During isotonic contraction of the muscles cells get shortened and the shortening (degree of response) is proportional to the number of motor units involved and therefore, the strength of stimulus.
2. **Viscosity :** Muscle contraction causes densening of the sarcoplasm. In other words the viscosity of the cytoplasm is increased during, muscle contraction.

3. **Tone :** Isometric contraction of the muscles is subjected to a considerable increase of tonicity. However, it does not change during isotonic contraction.
4. **Production of heat :** During muscle contraction heat is produced. In fact the high energy bonds of phosphagenes and ATP release energy which is used up in work done by the muscle. Considerable amount of this energy is converted into heat energy which is also helpful in maintaining body heat in homeotherms. That is why we feel hot after excercise and the body temperature shoots up after shivering in malaria.

Electrical changes during muscle contraction : As recorded by two electrodes connected to an oscilloscope the following sequence wise electrical events occur during muscle contraction.

1. Resting potential (–70 mv) is disturbed.
2. The potential difference along two surfaces of sarcolemma comes to 0.0 mv (depolarization).
3. The potential difference reaches to +35 mv which suggests that the inner surface of sarcolemma is positive by 35 mv (reverse polarization). A potential difference of – 70 mv (resting potential) is set in repolarization.

As described already the functional unit of the muscle is sarcomere. On excitation of the muscle, depolarization followed by repolarization occurs. These changes liberate Ca^{++} into the sarcoplasm from T-sarcotubular system to L-sarcotubular system. These ions bring about the sliding (interdigitation) of actin filaments into myosin. During this process energy is supplied by ATP. The degree of interdigitation of actin and myosin is dependent on the amount of Ca^{++}. The amount of Ca^{++} liberated is dependent on electrical events and finally on the intensity of stimulus to a certain extent. Thus the strength of such contraction is dependent on the stimulus intensity to certain extent.

Q.5. Write about the myosin.

Ans. **Myosin**

Biochemical and physiological studies have shown the fibrous protein myosin to be the main constituent of the thick filaments. Myosin reacts with itself, other proteins, ATP and with divalent cations. Part of its biochemical properties are dependent on the strength of the ionic medium. Myosin possesses the properties of the enzyme Adenosine Triphosphotase and can combine with actin to form the complex protein actomyosin.

The molecular weight of myosin is 490,000. It can be hydrolyzed into a variety of subfragments whose characteristics are dependent upon the agents and conditions used to break bonds in the molecule. On digestion with trypsin myosin yields two major subfragments, the light meromyosin (LMM) and heavy meromyosin (HMM). Light meromyosin on treatment with alcohol leads to the formation of a soluble fraction LMM-I. Thus, LMM contains LMM-1 and other proteins. These subfragments are formed due to the breakage of peptide bonds and are not subunits of LMM from which a polymeric myosin is built up. Subunits of myosin are produced on treatment with urea due to breakage of hydrogen bonds. HMM molecule possesses a globular head and a tail region.

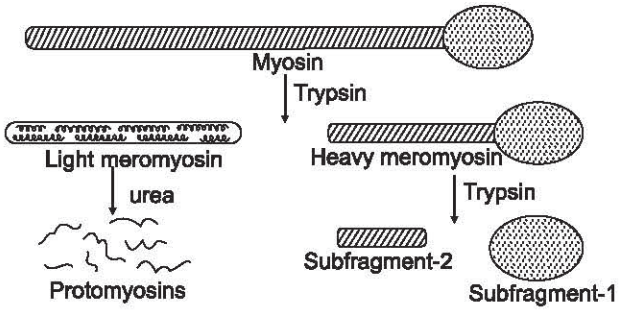


Fig. Various subunits of the myosin molecule

The shape of the myosin molecule is the result of the arrangement of the meromyosin molecules. There is one HMM molecule to one LMM in myosin. As HMM combines with actin, the bridges on the myosin molecule are the polypeptides of HMM subfragment. These bridges are used to combine actin and myosin during muscle contraction.

Q.6. Write difference between red and white muscle fibre.

Ans. Differences between Red and White Muscles

S.No.	Red Muscle Fibre	White Muscle Fibre
1.	Red muscle fibres are thin and smaller in size.	White muscle fibres are thick and larger in size.
2.	They are red in colour as they contain large amounts of myoglobin.	They are white in colour as they contain small amounts of myoglobin.
3.	They contain numerous mitochondria.	They contain less number of mitochondria.
4.	They carry out slow and sustained contractions for a long period.	They carry out fast work for short duration.
5.	They provide energy by aerobic respiration.	They provide energy by anaerobic respiration.

Q.7. Write about the important steps in muscle contraction.

Ans. Muscle Contraction

During skeletal muscle contraction, the thick filament slides over the thin filament by a repeated binding and releases myosin along the filament. This whole process occurs in a sequential manner :

Step 1 : Muscle contraction is initiated by signals that travel along the axon and reach the neuromuscular junction or motor end plate. Neuromuscular junction is a junction between a neuron and the sarcolemma of the muscle fibre. As a result, Acetylcholine (a neurotransmitter) is released into the synaptic cleft by generating an action potential in sarcolemma.

Step 2 : The generation of this action potential releases calcium ions from the sarcoplasmic reticulum in the sarcoplasm.

Step 3 : The increased calcium ions in the sarcoplasm leads to the activation of actin sites. Calcium ions bind to the troponin on actin filaments and remove the tropomyosin, wrapped around actin filaments. Hence, active actin sites are exposed and this allows myosin heads to attach to this site.

Step 4 : In this stage, the myosin head attaches to the exposed site of actin and forms cross bridges by utilizing energy from ATP hydrolysis. The actin filaments are pulled. As a result, the H-zone reduces. It is at this stage that the contraction of the muscle occurs.

Step 5 : After muscle contraction, the myosin head pulls the actin filament and releases ADP along with inorganic phosphate. ATP molecules bind and detach myosin and the cross bridges are broken.

Stage 6 : This process of formation and breaking down of cross bridges continues until there is a drop in the stimulus, which causes an increase in calcium. As a result, the concentration of calcium ions decreases, thereby masking the actin filaments and leading to muscle relaxation.

SECTION-C LONG ANSWER TYPE QUESTIONS

Q.1. Write a detailed note on muscle twitch.

Ans. Simple Contraction or Muscle Twitch

The response of a muscle to a single brief stimulus, such as an electric shock, is known as twitch. A twitch can be divided into three portions or phases.

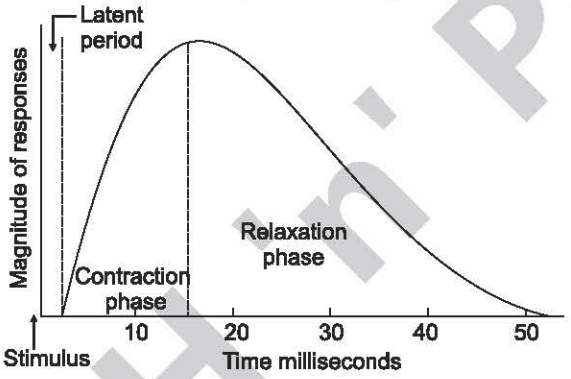


Fig. Single contraction of skeletal muscle showing different components

1. A latent period in which the length of the muscle remains constant.
2. A contraction period during which the muscle shortens, and
3. A relaxation period in which the length of the muscle and its tension reach the normal level.

Latent period : By very sensitive recording methods, Roos (1932) found that the true latent period is of the order of 0.4 milliseconds. The duration of the latent period varies with the species, type of muscle, temperature and internal conditions of muscle.

The latent period covers the time between the stimulation and the activation of the lever. This period covers two conditions over the muscle namely, the excitation wave due to the electrical disturbances, and the development of tension, which, according to Roos, spreads simultaneously with the electrical disturbance. Sandow (1944) has devised a method to convert the mechanical energy into electric potential and this is recorded by cathode ray oscillograph. It has been shown by this method that the isometric contraction of the frog sartorius muscle not only has a true latent period, but the muscle actually relaxes a little (latency relaxation) before developing tension. If the total latent period is 3.5 m. sec., the quiescent period is about 1.5 m sec. after direct excitation of the muscle during which no tension develops. This is followed by the latency relaxation period of about 1.5 m. sec. If the muscle is excited indirectly through nerves, the latent period increases. Thus, if the latent

period is about 3.5 m. sec. for direct excitation of the muscle, it is 6.0 m. sec. for indirect excitation.

Contraction period : During this phase, in isotonic contraction shortening of the muscle filament takes place. The dark bands of the fibrils become shorter and wider. The light bands also decrease in length in isotonic contraction and may slightly increase in length during isometric contraction. During the phase of shortening of the muscle fibres, external work is done. The work done by a muscle is dependent on the size of the muscle, the type of muscle, its nutritive condition, and upon external conditions such as temperature. The working power of a muscle can be estimated by finding the weight or load the muscle fails to lift and dividing this weight by the area of its cross section. The glycogen content of a muscle is directly proportional to the work done by it. The height to which the muscle lifts a given weight under maximal excitation usually increases for the first 5-15 contractions and after that a long resting period follows. This phenomenon of a muscle is called as treppe or staircase.

The amount of external work done by a muscle is also dependent on the amount of load which it lifts. With load on a muscle external work is done. The work done by a muscle is expressed in grammillimeters. A frog gastrocnemius muscle can lift 20 gms of load to a height of 5mm by performing 100 g. mm of work. With increased amounts of load, if a single muscle is made to give a series of single contractions, the work done shows an optimum at a certain weight above and below this point the work done decreases gradually.

Relaxation period : Relaxation phase is the reversal of the contraction phase and involves activity which is dependent upon certain physicochemical changes within the muscle cells. Relaxation phase consumes more time than the contraction process. It is dependent upon certain conditions in the muscle. Cold prolongs the relaxation process and during fatigue also this phase is prolonged very much. The failure of a muscle to relax is known as contracture.

Q.2. What are muscles? Also explain their types with suitable diagrams.

Ans. Muscles are specialized for contractile ability. Muscle cells can change their shapes very rapidly and reversibly, exerting a mechanical force on neighbouring cells or environment. This change is regulated by the central nervous system and is initiated by the synaptic transmission. However, in certain types of muscles contraction can be produced by the excitation of the motor nerve action.

Although all muscles function on the same molecular basis, they differ considerably in rate of shortening, amount of force produced and so on. There is a wide variety of muscle types because there is a wide variety of functions to be served by muscles including movement of an animal through environment, maintainance of body posture and orientation, circulatory movements, gastrointestinal tract movements, etc. For survival in environment, different animals require different muscular outputs, and the basic contractile machinery has been adapted to various needs.

Muscle cells, in general contain special organelles, called myofibrils or myofilaments, composed of strands of protein molecules, the actin and myosin which can be differentiated into many kinds. A muscle cell is elongated, and the myofibrils are arranged through the horizontal axis.

Muscle cells are capable of changing their shapes very rapidly and reversibly, exerting on the neighbouring cells or environment, a mechanical force. This change is usually controlled by

the central nervous system and is initiated by the synaptic transmission. However, in certain types of muscles contraction can be produced by the excitation of the motor nerve action. Muscle cells organized in the form of muscles are very important for the functioning of many systems and occur in varied shapes such as flat sheets, cylinders, thin strands, hollow tubes or a loose network. Movement of the different organs, and the organism as a whole, posture of the animal, shape, functioning of the heart, blood vessels, acquisition of food by the movement of the mouth parts, swallowing, movement of the alimentary canal, expulsion of the secretory products of the glands, and functioning of the sense organs are all controlled by the activity of the muscles. Even in protozoans, contractile elements in the form of myonemes occur, while sponges have contractile epithelial cells or myocytes for the closing of osculum. The functional unit of a muscle is the muscle fibre of which many fuse and constitute a whole muscle. The size of the muscle fibres has no direct relationship with the muscle they constitute. Some of the muscle fibres are small and short, while other muscles consist of large muscle cells running the whole length of the muscle.

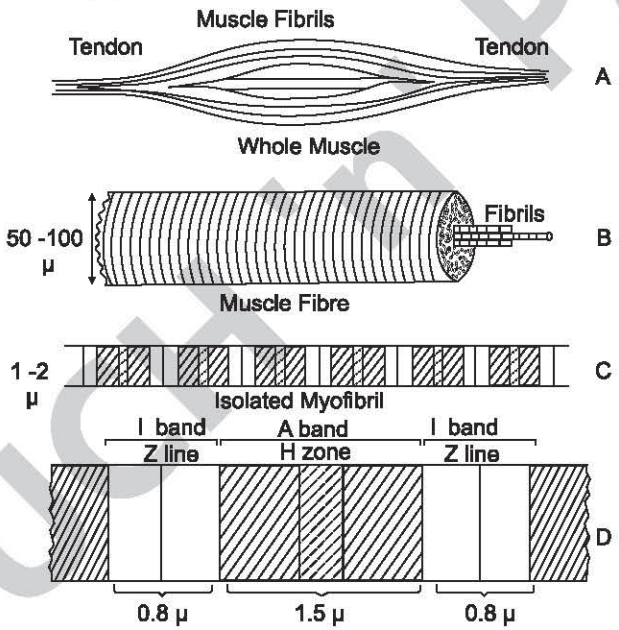


Fig. 1 : Diagrams showing the arrangement of the contractile filaments in striated (skeletal) muscle : A. Whole muscle. B. Whole muscle consists of muscle fibres. C. Each muscle fibre is made up of striated myofibrils. D. The appearance of myofibril under polarized light.

Generally muscle fibres are covered over by a layer of collagen fibres and connective tissue. Near the ends, they form tendons by means of which they are attached to the bones. In the absence of bones, muscles are directly attached to the epidermis or septa through connective tissue fibres.

According to Bowman (1940), muscle fibres are covered by a membrane; sarcolemma; consisting of a typical plasma membrane with trilaminate structure and an outer basement membrane. The fluid portion in muscle fibre is called as sarcoplasm (Rollet, 1891) contractile elements, myofibrils and myofilaments, made up of proteins are embedded in the sarcoplasm. The sarcosomes are the mitochondria accompanying the myofibrils. The myofibrils are

composed of myofilaments made up of a strands of protein. The myofilaments constitute the contractile elements of the muscles. A sarcoplasmic reticulum (Bennett and Porter, 1953) or sarcotubules (Sjostrand and Andersson-Cedergren, 1957), arranged in a definite fashion in relation to the myofibrils, is present in the muscles.

Muscles may be differentiated into smooth and striated types, though in strict sense these terms are very narrow to accommodate all the different varieties of muscles that exist. The smooth muscles include visceral muscles of vertebrates and a few varieties of invertebrates. Striated muscles denote all muscles whose fibres contain fibrils showing a periodic structure of repetitive parallel arrays of myofilaments. In this category are the skeletal muscles of frog, tail muscles of ascidian larvae, muscles of the crayfish gut, the muscle bundles of coelenterates etc.

1. **Striped or Striated muscles :** The striated muscles exhibit an alternating arrangement of dark and light bands crossed by thin dark lines. Under the polarizing microscope, the dark bands are found to be doubly refracting; and the light bands are singly refracting (Weismann, 1913). Under the high power of a light microscope the striated pattern is seen as a regular alternation of isotropic 'I'-bands or light bands, through which light passes equally in all directions and anisotropic 'A'-bands or dark bands, possessing different refractive indices in different directions. The length of a A-band of a vertebrate fibril is usually about 1.5 microns and that of an I-band is 0.8 micron. In the I-band is a dark line known as the 'Z'-line, derived from the term zwischenscheibe which bisects the I-band.

   In the middle of the A-band is another zone which takes a light stain known as the H'-band or 'H'-zone, derived from the German name "Hensen's" line. The portion of the muscle fibre from one Z-line to that of adjacent I-band is termed as the sarcomere.

   Examination under electron microscope reveals that the myofibril is made up of two kinds of small filaments, one twice as thick as the other. The dense A-band consists of the overlapping thick and thin filaments; the lighter I-band consists of thin filaments, while the H-band consists of the thick filaments only. The thin filaments about in the middle of their length pass through a narrow zone of dense material, the Z-line. The thicker filaments are about 100 Å in diameter and 1.5 microns long and the thinner ones are 50 Å in diameter and 2 microns long. Each thin filament lies in between three thick ones. A myofibril of 1 micron diameter contains about 5,000 filaments in each cross section of an A-band.

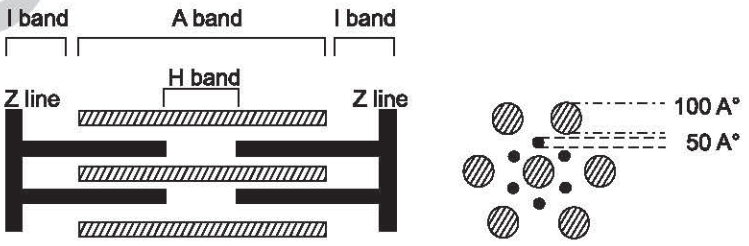


Fig. 2 : Arrangement of thick and thin filaments : Left-Longitudinal view. Right-Cross section through A-band.

2. **Unstriated or Smooth muscles : Classic or Visceral smooth muscle :** The smooth muscles of the stomach, gut, urinary bladder, uterus, the retractor muscles of the

extrovert of the sipunculid worms, penis muscles of molluscs and the pharynx are composed of small muscle fibres (20-40 μm in length) with usually only one nucleus. In longitudinally arranged parallel filaments, as they do not form regular arrays, no optical pattern of dense and light bands are visible.

Helical smooth muscle : In this type, the myofibrils are helically arranged, and though the filaments are arranged longitudinally, do not show a periodic structure. A majority of the cephalopod molluscs and the somatic muscles of annelids are examples of this type of muscle.

Paramyosin muscle : Due to the presence of paramyosin or tropomyosin (Bailey, 1957; Kominz, et al., 1957) in addition to actin and myosin, the tonic muscles of molluscs are termed as paramyosin muscles. Paramyosin in these muscles is in the form or ribbons of diameters ranging from 15-150 μm. The paramyosin crystallizes during the contracted phase of the muscle and under this condition the ribbons show an axial periodicity of 15 μm.

3. **Cardiac muscles :** The cardiac muscle fibres are short, cylindrical cells with a single nucleus. They are striated both longitudinally and transversely and are enclosed in it. These muscle fibres are branched and interdigitate. The two adjacent fibres unite with each other through the extensive series of their membrane folds. The junctions, which always occur at 2-lines, are called intercalated discs. The cardiac muscles are not structural syncytium, but the impulse spreads, quickly in the muscle meshwork suggesting that it is a functional syncytium, even though there are no protoplasmic bridges between the cells. Cardiac muscles are also composed of myofibrils having large number of mitochondria in contact. They are supplied by both sympathetic and parasympathetic nerves.

Q.3. Describe the ultrastructure of skeletal muscle with the suitable diagrams.

Ans.

Skeletal Muscles

Each skeletal muscle is an organ that consists of various integrated tissues. These tissues include the skeletal muscle fibres, blood vessels, nerve fibres, and connective tissue. Each skeletal muscle has three layers of connective tissue that enclose it, provide structure to the muscle, and compartmentalize the muscle fibres within the muscle. Each muscle is wrapped in a sheath of dense, irregular connective tissue called the epimysium, which allows a muscle to contract and move powerfully while maintaining its structural integrity. The epimysium also separates muscle from other tissues and organs in the area, allowing the muscle to move independently.

Inside each skeletal muscle, muscle fibres are organized into bundles, called fascicles, surrounded by a middle layer of connective tissue called the perimysium. This fascicular organization is common in muscles of the limbs; it allows the nervous system to trigger a specific movement of a muscle by activating a subset of muscle fibres within a fascicle of the muscle. Inside each fascicle, each muscle fibre is encased in a thin connective tissue layer of collagen and reticular fibres called the endomysium. The endomysium surrounds the extracellular matrix of the cells and plays a role in transferring force produced by the muscle fibres to the tendons.

In skeletal muscles that work with tendons to pull on bones, the collagen in the three connective tissue layers intertwines with the collagen of a tendon. At the other end of the

tendon, it fuses with the periosteum coating the bone. The tension created by contraction of the muscle fibres is then transferred though the connective tissue layers, to the tendon, and then to the periosteum to pull on the bone for movement of the skeleton. In other places, the mysia may fuse with a broad, tendon-like sheet called an aponeurosis, or to fascia, the connective tissue between skin and bones. The broad sheet of connective tissue in the lower back that the latissimus dorsi muscles (the "lats") fuse into is an example of an aponeurosis.

Every skeletal muscle is also richly supplied by blood vessels for nourishment, oxygen delivery, and waste removal. In addition, every muscle fibre in a skeletal muscle is supplied by the axon branch of a somatic motor neuron, which signals the fibre to contract. Unlike cardiac and smooth muscle, the only way to functionally contract a skeletal muscle is through signaling from the nervous system.

Skeletal Muscle Fibres : Because skeletal muscle cells are long and cylindrical, they are commonly referred to as muscle fibres (or myofibres). Skeletal muscle fibres can be quite large compared to other cells, with diameters up to 100 μm and lengths up to 30 cm (11.8 in) in the Sartorius of the upper leg. Having many nuclei allows for production of the large amounts of proteins and enzymes needed for maintaining normal function of these large protein dense cells. In addition to nuclei, skeletal muscle fibres also contain cellular organelles found in other cells, such as mitochondria and endoplasmic reticulum. However, some of these structures are specialized in muscle fibres. The specialized smooth endoplasmic reticulum, called the sarcoplasmic reticulum (SR), stores, releases, and retrieves calcium ions (Ca^{++}).

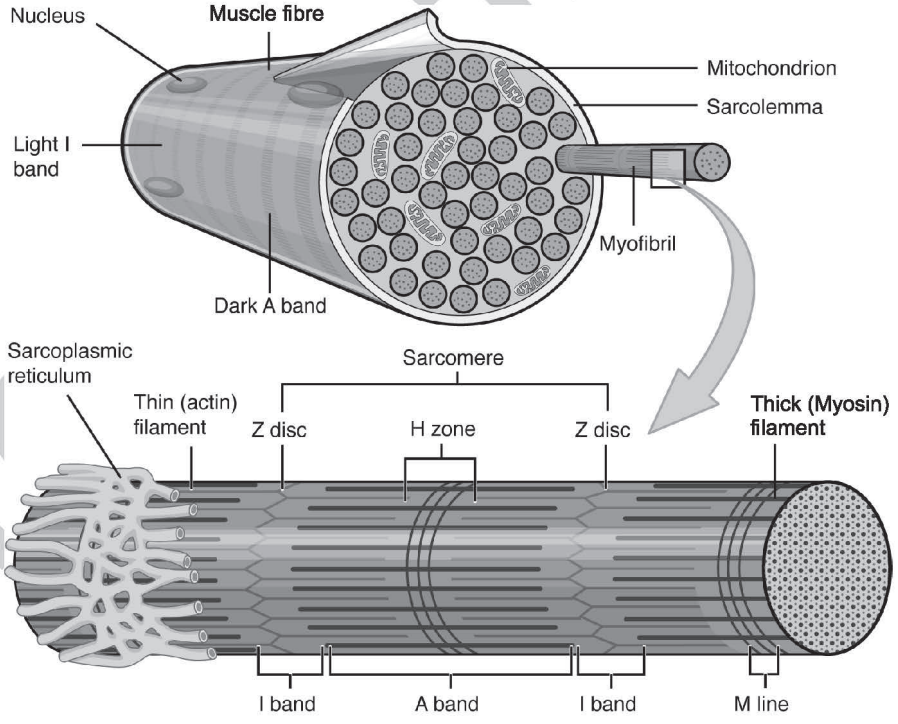


Fig. 1 : Muscle Fibre : A skeletal muscle fibre is surrounded by a plasma membrane called the sarcolemma, which contains sarcoplasm, the cytoplasm of muscle cells. A muscle fibre is composed of many myofibrils, which contain sarcomeres with light and dark regions that give the cell its striated appearance.

The plasma membrane of muscle fibres is called the sarcolemma and the cytoplasm is referred to as sarcoplasm. Within a muscle fibre, proteins are organized into structures called myofibrils that run the length of the cell and contain sarcomeres connected in series. Because myofibrils are only approximately 1.2 μm in diameter, hundreds to thousands (each with thousands of sarcomeres) can be found inside one muscle fibre. The sarcomere is the smallest functional unit of a skeletal muscle fibre and is a highly organized arrangement of contractile, regulatory, and structural proteins. It is the shortening of these individual sarcomeres that lead to the contraction of individual skeletal muscle fibres (and ultimately the whole muscle).

Sarcomere : A sarcomere is defined as the region of a myofibril contained between two cytoskeletal structures called Z-discs (also called Z-lines), and the striated appearance of skeletal muscle fibres is due to the arrangement of the thick and thin myofilaments within each sarcomere. The dark striated A band is composed of the thick filaments containing myosin, which span the center of the sarcomere extending toward the Z-dics. The thick filaments are anchored at the middle of the sarcomere (the M-line) by a protein called myomesin. The lighter I band regions contain thin actin filaments anchored at the Z-discs by a protein called α-actinin. The thin filaments extend into the A band toward the M-line and overlap with regions of the thick filament. The A band is dark because of the thicker myosin filaments as well as overlap with the actin filaments. The H zone in the middle of the A band is a little lighter in colour, because the thin filaments do not extend into this region.

Because a sarcomere is defined by Z-discs, a single sarcomere contains one dark A band with half of the lighter I band on each end. During contraction the myofilaments themselves do not change length, but actually slide across each other so the distance between the Z-discs shortens. The length of the A band does not change (the thick myosin filament remains a constant length), but the H zone and I band regions shrink. These regions represent areas where the filaments do not overlap, and as filament overlap increases during contraction these regions of no overlap decrease.

Myofilament Components : The thin filaments are composed of two filamentous actin chains (F-actin) comprised of individual actin proteins. These thin filaments are anchored at the Z-disc and extend toward the center of the sarcomere. Within the filament, each globular actin monomer (G-actin) contains a myosin binding site and is also associated with the regulatory proteins, troponin and tropomyosin. The troponin protein complex consists of three polypeptides. Troponin I (Tnl) binds to actin, troponin T (TnT) binds to tropomyosin, and troponin C (TnC) binds to calcium ions. Troponin and tropomyosin run along the actin filaments and control when the actin binding sites will be exposed for binding to myosin.

Thick myofilaments are composed of myosin protein complexes, which are composed of six proteins : two myosin heavy chains and four light chain molecules. The heavy chains consist of a tail region, flexible hinge region, and globular head which contains an Actin-binding site and a binding site for the high energy molecule ATP. The light chains play a regulatory role at the hinge region, but the heavy chain head region interacts with actin and is the most important factor for generating force. Hundreds of myosin proteins are arranged into each thick filament with tails toward the M-line and heads extending toward the Z-discs.

Other structural proteins are associated with the sarcomere but do not play a direct role in active force production.

Titin, which is the largest known protein, helps align the thick filament and adds an elastic element to the sarcomere. Titin is anchored at the M-Line, runs the length of myosin, and

extends to the Z disc. The thin filaments also have a stabilizing protein, called nebulin, which spans the length of the thick filaments.

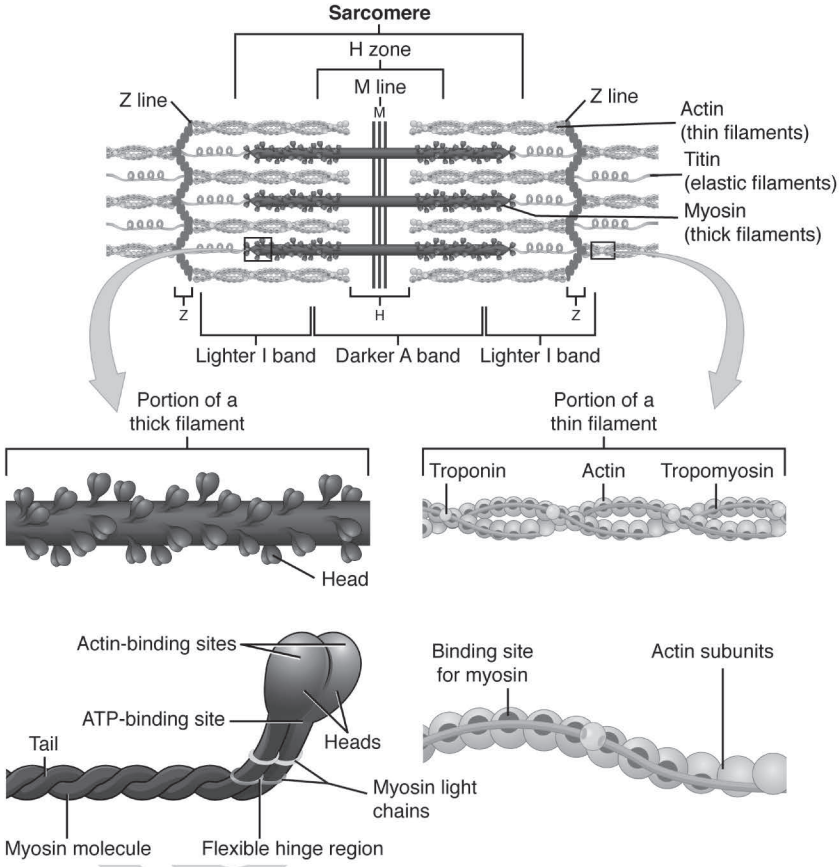


Fig. 2 : The Sarcomere : The sarcomere, the region from one Z-line to the next Z-line, is the functional unit of a skeletal muscle fibre.

Sliding Filament Model of Contraction

The arrangement and interactions between thin and thick filaments allows for the shortening of the sarcomeres which generates force. When signaled by a motor neuron, a skeletal muscle fibre contracts as the thin filaments are pulled and slide past the thick filaments within the fibre's sarcomeres. It is important to note that while the sarcomere shortens, the individual proteins and filaments do not change length but simply slide next to each other. This process is known as the sliding filament model of muscle contraction.

The filament sliding process of contraction can only occur when myosin-binding sites on the actin filaments are exposed by a series of steps that begins with Ca^{++} entry into the sarcoplasm. Tropomyosin winds around the chains of the actin filament and covers the myosin-binding sites to prevent actin from binding to myosin. The troponin-tropomyosin complex uses calcium ion binding to TnC to regulate when the myosin heads form cross-bridges to the actin filaments. Cross-bridge formation and filament sliding will occur when

calcium is present, and the signaling process leading to calcium release and muscle contraction is known as Excitation-Contraction Coupling.

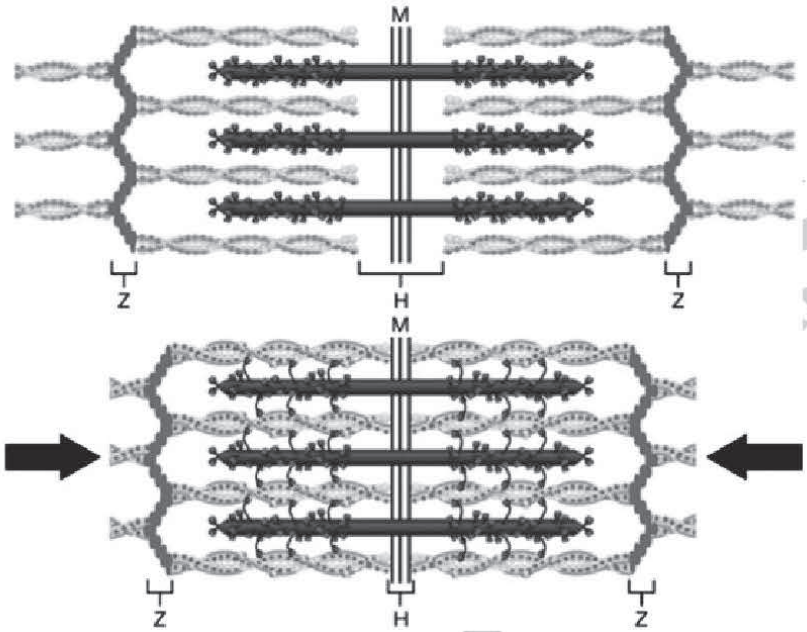


Fig. 3 : The Sliding Filament Model of Muscle Contraction : When a sarcomere contracts, the Z lines move closer together, and the I band becomes smaller. The A band stays the same width. At full contraction, the thin and thick filaments overlap.

Q.4. Describe the chemical composition of muscle and mechanism of muscle contraction.

Ans.

Chemical Composition of Muscle

In order to have the property of contractility muscle cells are provided with a special class of proteins called contractile proteins. The proteins make up about 25% of the bulk of muscles.

The contractile proteins are of three types—myosin, actin and tropomyosin. Besides these some other types of non-contractile proteins are also present in the muscles *e.g.,* globulins, albumins and all other enzymes necessary for cell metabolism. Lipids are present in traces, and carbohydrates mostly in the form of glycogen in amounts between 0.5 to 1%. ATP is also present in appreciable quantities. These together constitute about 5% of the muscle, the remaining 75% in water.

Myosin : The molecular weight of myosin ranges from 350,000 to 450,000, length 1500 Å and diameter about 20 Å to 50 Å. Because of its anisotropic properties it splits light waves into two mutually perpendicular vibrations (double refraction) hence it shows beautiful streaming birefringence. Myosin also acts as an ATPase, it hydrolyses ATP into ADP and inorganic phosphate and releases energy stored in ATP. On hydrolysis with trypsin, myosin splits into two fragments of unequal size. These are called meromyosins. The lighter fragment in called L-meromyosin and heavier fragment H-meromyosin. The ATPase property of myosin is present in the H-meromyosin fragment.

Actin : Actin has the form of a double helix and a molecular weight of 70,000. It constitutes about 20 to 25% of the protein of mammalian skeletal muscle.

Actomyosin : When solutions of actin and myosin are mixed in the presence of salts (especially KT) a complex of high viscosity, called actomyosin, is formed. The viscosity of actomyosin is higher than the combined viscosities of actin and myosin. Electron microscope studies have shown that a network is formed by the electrostatic association of the two proteins. When actomyosin is mixed with ATP in the presence of 0.6 MKCl then the thread of actomyosin contracts. The composition and particle weight of actomyosin depend upon the pH, KCl and MgCl, concentrations. Electron microscopy has shown that only the head of a myosin molecule binds with an actin molecule and ATP is hydrolysed.

Tropomyosin : Tropomyosin forms only 2.5% of the muscle protein. Its molecular weight is 60,000. It forms a complex with troponin and is part of the thin filament. This complex mediates the interaction of actin and myosin and thus regulates contraction.

Mechanism of Muscle Contraction

The architecture of the muscle fibres is designed for contraction. Two theories have been advanced to explain the mechanism of contraction :

Folding theory : This theory envisages that the contractile protein molecules fold and unfold. Their folding reduces the length of the myofilaments and their unfolding increases the length of the filaments. The folding is caused by the presence of equal number of positive and negative charges on the protein molecules which attract each other and the unfolding is caused by the presence of similar changes on the molecules which repel each other.

Sliding filament theory : The most widely accepted theory, advanced by Huxley and Hanson links the structure of the fibres with their movement. According to this, the myosin filaments send out cross-bridges which form chemical couplings with special receptors on the actin filaments. The bridges are permanent parts of the myosin molecule jutting out towards the actin filaments. Each molecule of myosin has one such cross bridge. During contraction a chemical reaction takes place between actin and myosin, which causes the myosin cross bridges to pull the actin filaments in a ratchet like action for a short distance postulated to be about 10 nm. The cross bridge then fits the next receptor on actin filament and son till the actin filaments on the two ends of the sacromere come to meet in the centre of the H band. Further contraction crumples the actin and myosin filaments. The actin filaments as they slide towards each other shorten the length of the myofibrils so that the muscle contracts. During the process of contraction hydrolysis of ATP takes place which provides the energy for contraction. It is believed that a single pull of a cross bridge causes the hydrolysis of one ATP molecule. When the hydrolysis of ATP stops as a result of inactivation of ATPase activity of actomyosin by the removal of Ca^{++} the myosin and actin dissociate and the muscle returns to its original relaxed state.

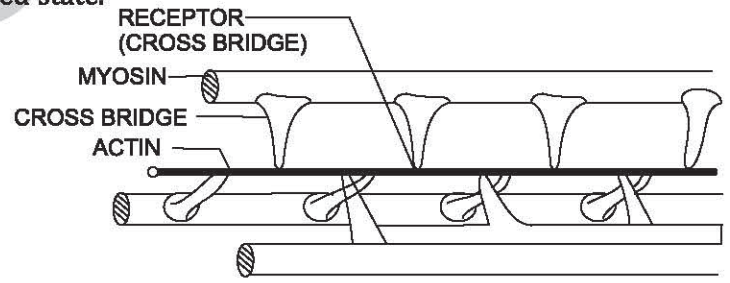


Fig. 1 : Diagram showing cross-bridges arising out of a myosin filament which fit into actin filaments and pull the latter in a ratchet-like action during contraction. One cross-bridge fits into a receptor and the actin filament pulls it for a short distance then fits into the next and so on.

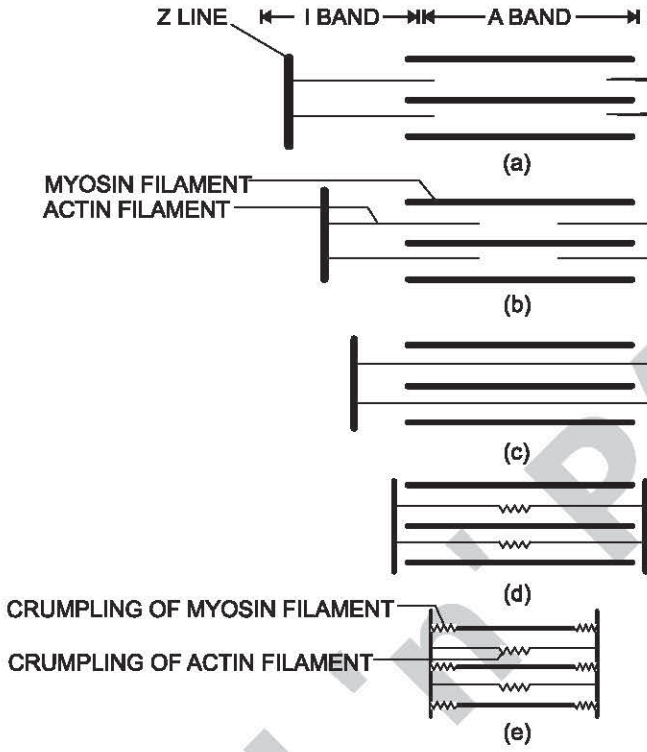


Fig. 2 : Diagrammatic representation of muscle contraction according to the sliding filament theory; (a) relaxed muscle; b, c, d, e, progressive contraction of muscle in which the Z lines are pulled towards each other. In (c) the actin filaments have met in the centre (d) the actin filaments crumple in the middle due to further contraction (e) still more contraction produces crumpling of myosin filaments also.

MODEL PAPER

Biochemistry and Physiology

B.Sc.-I (SEM-II) [M.M. : 75

Note : Attempt all the sections as per instructions.

Section-A : Very Short Answer Type Questions

Instruction : Attempt all **FIVE** questions. Each question carries **3 Marks**. Very Short Answer is required, not exceeding 75 words.

1. Which carbohydrate is used in animals?
2. What is enzyme action called?
3. What is the site for gluconeogenesis?
4. Which glands are associated with the alimentary canal?
5. What happens if the blood does not coagulate?

Section-B : Short Answer Type Questions

Instruction : Attempt all **TWO** questions out of the following 3 questions. Each question carries **7.5 Marks**. Short Answer is required not exceeding 200 words.

6. Write a short note on structure and properties of maltose.

Or What are isoenzymes?

7. Write about the calciferol.

Or What is synaps? How does an impulse transmitted across the synapse?

8. Write about the structure and functions of islets of Langerhans.

Or Write about the myosin.

Section-C : Long Answer Type Questions

Instruction : Attempt all **THREE** questions out of the following 5 questions. Each question carries **15 Marks**. Answer is required in detail, between 500-800 words.

9. What are carbohydrates? Also describe classification and biological role of carbohydrates.

Or What are proteins? Also write their classification.

10. Describe the nomenclature and classification of enzyme.

Or Describe the regulation of enzyme activity in the living system.

11. Describe the glycolysis pathway with the suitable structure.

Or Describe the urea cycle.

12. Describe the organisation of gastrointestinal tract with suitable diagrams.

Or What is cardiac cycle? Describe different phases of the cardiac cycle.

13. What are hormones? Describe chemical nature and mechanism of hormone action.

Or What are muscles? Also explain their types with suitable diagrams.

❑