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First lectur

Carbohydrates

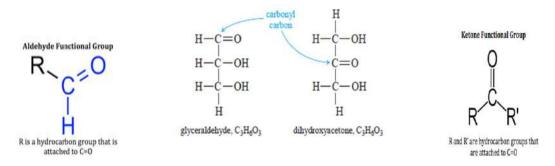
Introduction

The carbohydrates are widely distributed both in animal and plant tissues. Chemically, they contain the elements carbon, hydrogen and oxygen. The empirical formula of many simple carbohydrates is [CH2O]n. Hence, the name "carbohydrate", i.e. hydrated carbon. They are also called "saccharides". In Greek, saccharon means sugar.

Definition

Carbohydrates may be defined chemically as aldehyde or ketone derivatives of polyhydroxy (more than one hydroxy group) alcohols or as compounds that yield these derivatives on hydrolysis.

The simplest carbohydrates are glyceraldehyde and dihydroxyacetone:



These substances are "polyhydroxy" because each molecule has more than one hydroxylgroup. Glyceraldehyde contains a carbonyl carbon in a terminal position andis therefore an aldehyde. The internal carbonyl of dihydroxyacetone identifies it as aketone. Much of the chemistry and biochemistry of carbohydrates can be understoodfrom a basic knowledge of the chemistry of the hydroxyl and carbonyl functionalgroups.

Functions of Carbohydrates

Carbohydrates have a wide range of functions. The following are few of them:

- Source of energy for living beings, e.g. glucose
- Storage form of energy, e.g. glycogen in animal tissue and starch in plants
- Serve as structural component, e.g. glycosaminoglycans in humans, cellulose in plants and chitin in insects

- Non-digestable carbohydrates like cellulose, serve as dietary fibers
- Constituent of nucleic acids RNA and DNA, e.g. ribose and deoxyribose sugar
- Play a role in lubrication, cellular intercommunication and immunity
- Carbohydrates are also involved in detoxification, e.g. glucuronic acid.

Classification of Carbohydrates

Carbohydrates are classified into three groups:

- 1. Monosaccharides
- 2. Oligosaccharides
- 3. Polysaccharides.

Monosaccharides

Monosaccharides are also called simple sugars. The term sugar is applied to carbohydrates that are soluble in water and sweet to taste. They consist of a single polyhydroxy aldehyde or ketone unit, and thus cannot be hydrolyzed into a simpler form. They may be subdivided into two groups as follows:

- 1. Depending upon the number of carbon atoms they possess, e.g. Trioses Tetroses Pentoses Hexoses Heptoses.
- 2. Depending upon the functional aldehyde (CHO) or ketone (C=O) group present: Aldoses Ketoses. Classification of monosaccharides based on the number of carbon and the type of functional group present with examples is given in Table 2.1. The most abundant monosaccharide in nature is six carbon sugar -D-glucose. Biologically important monosaccharides are listed in Table 2.2.

Table 2.1: Classification of monosaccharides and their examples					
No.of Carbon	Empirical formula	Type of sugar	Aldoses	Ketoses	
3	C ₃ H ₆ O ₃	Trioses	Glyceraldehyde	Dihydroxyacetone	
4	C ₄ H ₈ O ₄	Tetroses	Erythrose	Erythrulose	
5	C ₅ H ₁₀ O ₅	Pentoses	Ribose, Xylose	Ribulose, Xylulose	
6	C ₆ H ₁₂ O ₆	Hexoses	Glucose, Galactose and Mannose	Fructose	
7	C ₇ H ₁₄ O ₇	Heptoses	Glucoheptose	Sedoheptulose	

Oligosaccharides

Oligosaccharides consist of a short chain of monosaccharide units (2 to 10 units), joined together by a characteristic bond called glycosidic bond which, on hydrolysis, gives two to ten molecules of simple sugar (monosaccharide) units. Oligosaccharides are subdivided into different groups based on the number of monosaccharide units present (Table 2.3). The disaccharides which have two monosaccharide units are the most abundant in nature. Oligosaccharides with more than three subunits are usually found in glycoproteins; such as blood group antigens.

Torrado de Maria de Caracia de Ca	Number of monosaccharide	Promoto	The same of the sa
Type of oligosaccharide	Number of monosacchande	Example	Type of monosaccharide present
Disaccharide	Two	Maltose	Glucose + Glucose
		Lactose	Glucose + Galactose
		Sucrose	Glucose + Fructose
Trisaccharide	Three	Raffinose	Glucose + Galactose + Fructose
Tetrasaccharide	Four	Stachyose	2 Molecules of Galactose + Glucose + Fructose
Pentasaccharide	Five	Verbascose	3 Molecules of Galactose + Glucose + Fructose

Polysaccharides

Polysaccharides are polymers consisting of hundreds or thousands of monosaccharide units. They are also called glycans or complex carbohydrates. They may be either linear, (e.g. cellulose) or branched, (e.g. glycogen) in structure. Polysaccharides have high molecular weight and are only sparingly soluble in water. They are not sweetish and do not exhibit any of the properties of aldehyde or ketone group. Polysaccharides are of two types (Table 2.4).

- 1-Homopolysaccharides (homoglycans)
- 2-Heteropolysaccharides (heteroglycans).

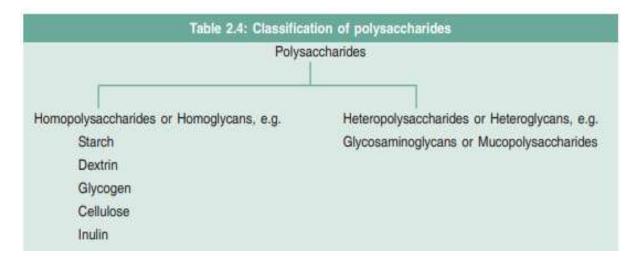
Homopolysaccharides (Homoglycans)

- When a polysaccharide is made up of several units of one and the same type of monosaccharide unit, it is called homopolysaccharide.
- The most common homoglycans are: Starch Dextrins Glycogen Inulin Cellulose.

• Some homopolysaccharides serve as a storage form of monosaccharides used as fuel, e.g. starch and glycogen, while others serve as structural elements in plants, e.g. cellulose.

Heteropolysaccharides (Heteroglycans)

- They contain two or more different types of monosaccharide units or their derivatives.
- Heteropolysaccharide present in human beings is glycosaminoglycans (mucopolysaccharides), e.g. Heparin Chondritin sulfate Hyaluronic acid Dermatan sulfate Keratan sulfate Blood group polysaccharides.



Structure of glucose

Physiologically and biomedically, glucose is the most important monosaccharide. The structure of glucose can be represented in the following ways (Figure 2.1)

- 1. The straight chain structural formula (Fisher projection).
- 2. Cyclic formula (Ring structure or Haworth projection.

Figure 2.1:- (Fisher projection & Haworth projection

Monosaccharide in solution is mainly present in ring form. In solution, aldehyde (CHO) or ketone (C=O) group of monosaccharide react with a hydroxy (OH) group of the same molecule forming a bond hemiacetal or hemiketal respectively.

- The aldehyde group of glucose at C-1 reacts with alcohol (OH) group of C-5 or C-4 to form either six membered ring called glucopyranose or five membered ring called glucofuranose, respectively. (Figure 2.1)
- However, in case of glucose, the six membered glucopyranose is much more stable than the glucofuranose ring. In the case of fructose, the more stable form is fructofuranose.

Isomerism

The compounds possessing identical molecular formula but different structures are referred to as isomers. The phenomenon of existence of isomers is called isomerism. (Greek 'isos' means equal, 'meros' means parts). The five types of isomerism exhibited by sugar are as follows:

- 1. Ketose-aldose isomerism
- 2. D and L isomerism
- 3. Optical isomerism
- 4. Epimerism
- 5. Anomerism.

Ketose-Aldose isomerism

Glucose and fructose are isomers of each other having the same chemical (molecular) formula $C_6H_{12}O_6$, but they differ in structural formula with respect to their functional groups. There is a keto group in position two of fructose and an aldehyde group in position one of glucose (Figure 2.2). This type of isomerism is known as ketose-aldose isomerism.

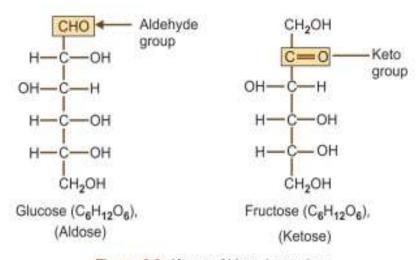
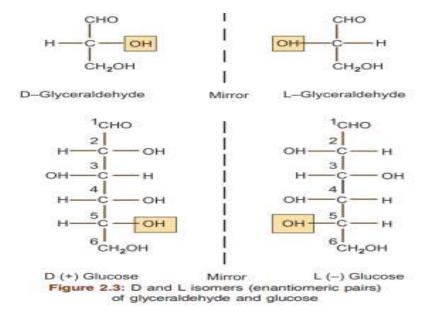


Figure 2.2: Ketose-Aldose isomerism

D and L isomerism

- D and L isomerism depends on the orientation of the H and OH groups around the asymmetric carbon atom adjacent to the terminal primary alcohol carbon, e.g. carbon atom number 5 in glucose determines whether the sugar belongs to D or L isomer.
- When OH group on this carbon atom is on the right, it belongs to D-series, when it is on the left, it is the member of the L-series. The structures of D and Lglucose based on the reference monosaccharide, D and L glyceraldehyde, a three carbon sugar (Figure 2.3).



- D and L isomers are mirror images of each other. These two forms are called enantiomers.
- Most of the monosaccharides in the living beings belong to the D-series.

Optical Isomerism

- The presence of asymmetric carbon atoms exhibits optical activity on the compound. Optical activity is the capacity of a substance to rotate the plane polarized light passing through it.
- When a beam of plane-polarized light is passed through a solution of an optical isomer, it will be rotated either to the right and is said to be dextrorotatary (D) or (+) or to the left and is said to be, levorotatory (L) or (-). When equal amount of D and L isomers are present, the resulting mixture has no optical activity. Since the activity of each isomer cancel one another, such a mixture is said to be a racemic or dl mixture.

Epimerism

When two monosaccharides differ from each other in their configuration around a single asymmetric carbon (other than anomeric carbon) atom, they are referred to as epimers of each other.

For example, galactose and mannose are two epimers of glucose (Figure 2.4). They differ from glucose in the configuration of groups (H and OH) around C-4 and C-2 respectively. Galactose and mannose are not epimers of each other as they differ in configuration at two asymmetric carbon atoms around C-2 and C-4.

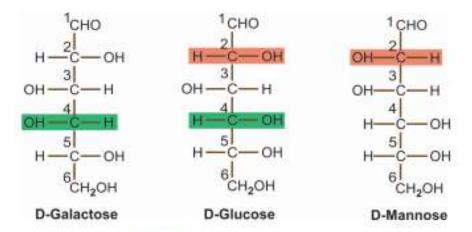


Figure 2.4: Epimers of glucose

Anomerism

 α and β Anomerism The predominant form of glucose and fructose in a solution are not an open chain. Rather, the open chain .

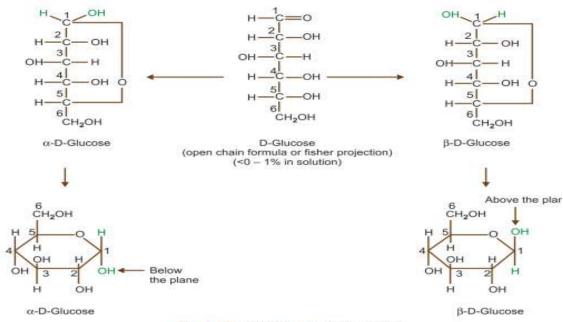


Figure 2.5: Formation of α and β anomers

form of these sugar in solution cyclize into rings. An additional asymmetric center is created when glucose cyclizes. Carbon-1 of glucose in the open chain form, becomes an asymmetric carbon in the ring form (Figure 2.5) and two ring structures can be formed. These are:

• α -D-glucose & β -D-glucose.

The designation α means that the hydroxyl group attached to C-1 is below the plane of the ring, β means that it is above the plane of the ring. The C-

1 carbon is called the anomeric carbon atom and so, α and β forms are anomers.

Second lecture

Carbohydrates

Oxidation of monosaccharides (Sugar Acid Formation)

When aldoses oxidize under proper conditions they may form: – Aldonic acid – Saccharic acids – Uronic acid.

• Oxidation of an aldose with hypobromous acid (HOBr), which acts as an oxidizing agent gives aldonic acid. Thus, glucose is oxidized to gluconic acid (Figure 2.8).

Oxidation of aldoses with nitric acid under proper conditions convert both aldehyde and terminal primary alcohol groups to carboxyl groups, forming saccharic acid.

• When an aldose is oxidized in such a way that the terminal primary alcohol group is converted to carboxyl without oxidation of the aldehyde group (usually by specific enzymes), a uronic acid is formed (Figure 2.8)

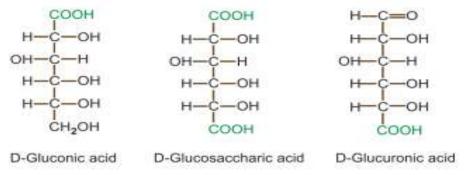


Figure 2.8: Sugar acids produced by oxidation of glucose

Reduction of monosaccharides (Sugar Alcohol formation)

Both aldoses and ketoses may be reduced by enzymes or non-enzymatically to the corresponding polyhydroxy alcohols. The alcohols formed from glucose, mannose, fructose and galactose are given in Figure 2.9. • Manitol, the sugar alcohol derived from mannose, is frequently used medically as an osmotic diuretic to reduce cerebral edema.

• Sorbitol, the sugar alcohol derived from glucose, often accumulates in the lenses of diabetics and produces cataracts.

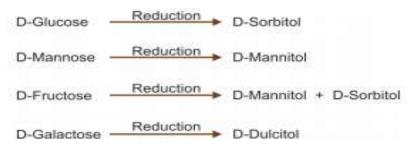


Figure 2.9: Reduction of sugar to form alcohol

Derivatives of Monosaccharides

Some important sugar derivatives of monosaccharides are:

- Phosphoric acid ester of monosaccharides
- Amino sugar
- Deoxy sugars
- Sugar acids
- Sugar alcohols

Phosphoric Acid Ester of Monosaccharides

These are formed from the reaction of phosphoric acid with hydroxyl group of the sugar, e.g. glucose-1- phosphate or glucose-6-phosphate (**Figure2:10**).

Importance

• Phosphorylation of sugar within cells is essential toprevent the diffusion of the sugar out of the cell.

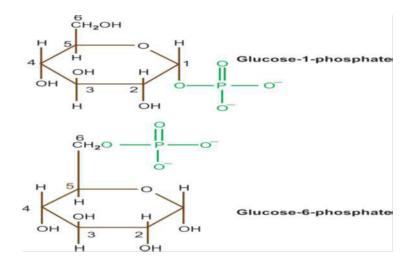


Figure 2.10: Phosphoric acid ester of glucose

• Nucleic acids (RNA and DNA) of cell nuclei also contain sugar phosphates of ribose and deoxyribose

Amino Sugar

Amino sugars have a hydroxyl group replaced by an amino or an acetylated amino (acetylamino) group. For example, glucosamine, N-acetyl glucosamine (**Figure2:11**), galactosamine and mannosamine.

Importance of amino sugar

- Amino sugars are components of glycolipid (ganglioside), glycoprotein and proteoglycans (glycosaminoglycans).
- Several antibiotics, e.g. erythromycin, carbomycin contain amino sugar.

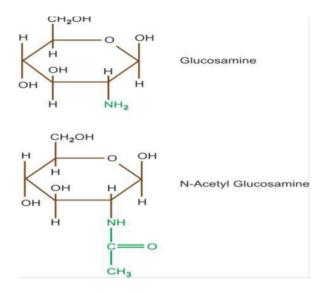


Figure 2.11: Structure of amino sugars

Deoxy Sugars

Deoxy sugars possess a hydrogen atom in place of one of their hydroxy groups (**Figure2:12**), e.g. 2-deoxyribose found in nucleic acid DNA.

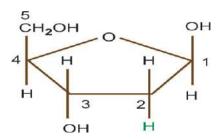


Figure 2.12: Structure of 2-deoxyribose sugar

Sugar Acids

Sugar acids are produced by oxidation of the monosaccharides, for example:

• Ascorbic acid or vitamin C (not synthesized by human beings) is required for the synthesis of collagen. It acts as water soluble antioxidant. Glucuronic acid (uronic acid) (See properties of monosaccharide-oxidation).

Sugar Alcohols

Discussed in properties of monosaccharide-reduction. They are not metabolically very active but have some medical importance in that they are used as non-glucose forming sweetners in food stuffs for diabetics, *sorbitol* and *xylitol* are the most commonly used.

Third lecture

Disaccharides

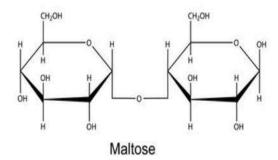
Disaccharides consist of two monosaccharide units. • They are crystalline, water soluble and sweet to taste. • They are subclassified on the basis of the presence or absence of free reducing (aldehyde or ketone) group (Table 2.5). 1. Reducing disaccharides with free aldehyde or keto group, e.g. maltose, lactose 2. Non-reducing disaccharides with no free aldehyde or keto group, e.g. sucrose.

	Table 2.5: Classification	on of disaccharides	
	Disacch	arides	
Reducing		Non	reducing
(with free aldehy	rde or ketone group)	(absence of free	e aldehyde or ketone group)
Example	Constituent	Example	Constituent
Maltose	Glucose + Glucose	Sucrose	Glucose + Fructose
Lactose	Galactose + Glucose	Trehalose	Glucose + Glucose
Isomaltose	Glucose + Glucose		

Maltose

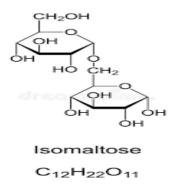
• Maltose contains two glucose residues, joined by glycosidic linkage between C-1 (the anomeric carbon) of one glucose residue and C-4 of the other, leaving one free anomeric carbon of the second glucose residue, which can act as a reducing agent. Thus, maltose is a reducing disaccharide.

- The numerical description like $(1 \rightarrow 4)$ of glycosidic bond represents the number of carbon atoms that connect the two sugars. The sugar contributing anomeric carbon is written first.
- Maltose is produced as an intermediate product in the digestion of starch and glycogen by the action of the enzyme α -amylase.



Isomaltose

- It consists of two glucose molecules linked by an $(\alpha-1 \rightarrow 6)$ glycosidic bond.
- Isomaltose is a disaccharide derived from the digestion of starch or glycogen. It is hydrolyzed to glucose in the intestinal tract by an enzyme called isomaltase.



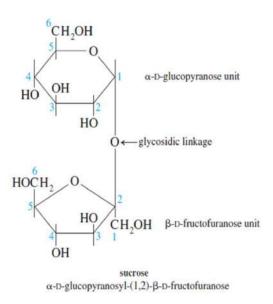
Lactose (Milk sugar)

- It is present in milk. Lactose contains one unit of β -galactose and one unit of β -glucose that are linked by a β (1 \rightarrow 4) glycosidic linkage
- The anomeric carbon of the glucose unit is available for oxidation and thus lactose is a reducing disaccharide.
- Lactose is hydrolyzed to glucose and galactose by lactase enzyme in human beings.

LACTOSE (a - form)

Sucrose (Common Table Sugar)

- Sucrose is a disaccharide of glucose and fructose. It is formed by plant but not by human beings. Sucrose is an intermediate product of photosynthesis. Sucrose is the commonly used table sugar.
- In contrast to maltose and lactose, sucrose contains no free anomeric carbon atom. The anomeric carbon of both glucose and fructose are involved in the glycosidic bond . Sucrose is therefore, a non-reducing sugar.
- Sucrose is hydrolyzed to fructose and glucose by an enzyme sucrase which is also called invertase.



Polysaccharides (Glycans)

Carbohydrates composed of ten or more monosaccharide units or their derivatives (such as amino sugars and uronic acids) are generally classified as polysaccharides. Polysaccharides are colloidal in size. In polysaccharides, monosaccharide units are joined together by glycosidic linkages. Another term for polysaccharides is a "glycans". Polysaccharides are subclassified in two groups (Table 2.4).

- 1. Homopolysaccharides (Homoglycans): When a polysaccharide is made up of several units of one and the same type of monosaccharide unit only, it is called homopolysaccharide.
- 2. Heteropolysaccharides (Heteroglycans): They contain two or more different types of monosaccharide units or their derivatives.

Homopolysaccharides or Homoglycans

Starch

It is the storage form of glucose in plants, e.g. in potato, in grains and seeds and in many fruits. Starch is composed of two constituents viz. amylose and amylopectin.

1-Amylose

Amylose is a linear polymer of D-glucose units joined by α -1 \rightarrow 4 glycosidic linkages (Figure 2.17).

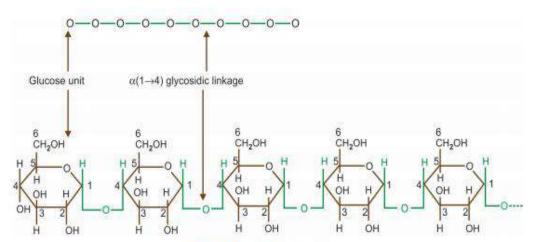


Figure 2.17: Structure of amylose

2-Amylopectin

Amylopectin is structurally identical to those of amylose $(\alpha-1 \rightarrow 4 \text{ glycosidic linkages})$ but with side chains joining them by $\alpha-1 \rightarrow 6 \text{ linkages}$ (Figure 2.18). Thus, amylopectin is a branched polymer having both $\alpha-(1 \rightarrow 4)$ and $\alpha-(1 \rightarrow 6)$ linkages. The branch points in amylopectin are created by $\alpha-1 \rightarrow 6$ bonds and occur at an interval of 20 to 30 units of

glucose. Figures 2.17 and 2.18 represent diagrammatically the difference in the amylose and amylopectin molecules.

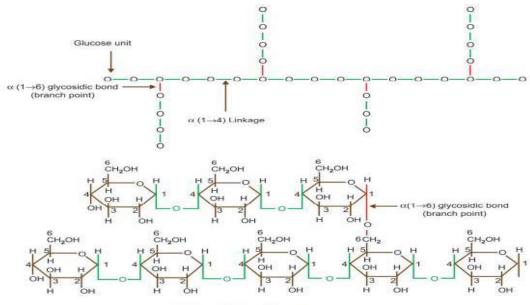


Figure 2.18: Structure of amylopectin

Dextrin

Partial hydrolysis of starch by acids or α -amylase (enzyme) produces substances known as dextrins. These also occur in honey. All dextrins have few free aldehyde groups and can show mild reducing property. They are not fermented by yeast.

Glycogen

Glycogen is the major storage form of carbohydrate (glucose) in animals, found mostly in liver and muscle. It is often called animal starch. The structure of glycogen is similar to that of amylopectin, except that it is more highly branched, (Figure 2.19) having α -(1 \rightarrow 6) linkages at intervals of about 8 to 10 glucose units.

Function

- The function of muscle glycogen is to act as a readily available source of glucose for energy within muscle itself.
- Liver glycogen is concerned with storage and maintenance of the blood glucose.



Figure 2.19: Diagrammatic representation of glycogen molecule

Cellulose

Cellulose is the chief constituent of cell wall of plants. It is an unbranched polymer of glucose and consists of long straight chains which are linked by β -(1 \rightarrow 4) glycosidic linkages and not α -(1 \rightarrow 4) as in amylose (Figure 2.20). Since humans lack an enzyme cellulase that can hydrolyze the β -(1 \rightarrow 4) glycosidic linkages, cellulose cannot be digested and absorbed and has no food value unlike starch. However, the ruminants can utilize cellulose because they have in their digestive tract microorganisms whose enzymes hydrolyze cellulose.

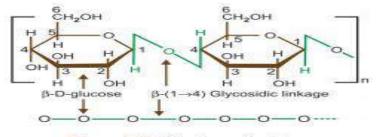


Figure 2.20: Structure of cellulose

Importance of Cellulose

For human cellulose has nutritional significance. • Cellulose is a component of fiber in the diet.

- Although there is no known metabolic requirement for fiber, yet high fiber diet is associated with reduced incidence of a number of diseases like: Cardiovascular disease Colon cancer Diabetes Diverticulosis.
- Cellulose is present in unrefined cereals. It increases bulk of stool, aids intestinal motility, acts as a stool softener and prevents constipation.

Inulin

Inulin is a polymer of D-Fructose (Fructosans) linked together by β -(1 \rightarrow 2) glycosidic linkage. It occurs in the tubers of some plants, e.g. chicory,

bulb of onion and garlic. Inulin is not hydrolyzed by α -amylase but is hydrolyzed by inulinase, which is not present in the humans and so it is not utilized as food.

Heteropolysaccharides or Heteroglycans Glycosaminoglycans (GAGs) or Mucopolysaccharides

Structure of GAG

GAG is a polymer of [uronic acid-amino sugar]n • This polymer is attached covalently to extracellular proteins called core protein (except hyaluronic acid) to form proteoglycans.

The amount of carbohydrates in proteoglycans is usually much greater than is found in a glycoprotein and may comprise upto 95 percent of its weight.

Glycoproteins

Glycoproteins are proteins to which oligosaccharides are covalently attached to their polypeptide chain.

- Glycoproteins contain much shorter carbohydrate chain than proteoglycans.
- The distinction between glycoproteins and proteoglycans may be based on the amount of carbohydrate. Glycoproteins contain less than 4 percent carbohydrate in the molecule. Proteoglycans contain more than 4 percent carbohydrate.

Functions of Glycoproteins

- Almost all the plasma proteins of humans are glycoproteins, except albumin.
- Many integral membrane proteins are glycoproteins.
- Most proteins that are secreted, such as antibodies, hormones and coagulation factors are glycoproteins.

Glycoproteins serve as lubricant and protective agent, e.g. mucin of gastrointestinal and urogenital tracts.

• Glycoproteins also serve as transport molecules, such as transferrin and ceruloplasmin.

Fourth lecture

Lipids

Introduction

Lipids are a major source of energy for the body besides their various other biochemical function and their role in cellular structure. Lipids are a heterogenous group of water insoluble (hydrophobic) organic molecules. Lipids include fats, oils, steroids, waxes and related compounds. This chapter introduces the chemistry and functions of lipids.

Definition of Lipids

Lipids may be defined as organic substances insoluble in water but soluble in organic solvents like chloroform, ether and benzene. They are esters of fatty acids with alcohol esters and are utilizable by the living organism.

Fatty acid o	Number of C atom:		Solubility 100 g water)	Melting point (°C
Saturated acids				
Butyric acid	4	CH3CH2CH2COOH	00	-7.9
Caproic acid	6	CH ₃ (CH ₂) ₄ COOH	1.08	-3.4
Caprylic acid	8	CH ₃ (CH ₂) ₆ COOH	0.07	17
Capric acid		CH ₃ (CH ₂) ₈ COOH	0.015	31
Lauric acid		CH ₃ (CH ₂) ₁₀ COOH	insoluble	44
Myristic acid	14	CH ₃ (CH ₂) ₁₂ COOH	insoluble	59
Palmitic acid		CH ₃ (CH ₂) ₁₄ COOH	insoluble	63
Stearic acid	18	CH ₃ (CH ₂) ₁₆ COOH	insoluble	70
Arachidic acid		CH ₃ (CH ₂) ₁₈ COOH	insoluble	76
Unsaturated acids	k.			
Palmitoleic acid	16	$CH_3(CH_2)_5CH = CH(CH_2)_7COOH$	_	0.5
Oleic acid	18	$CH_3(CH_2)_7CH = CH(CH_2)_7COOH$	_	14
Linoleic acid	18	$CH_3(CH_2)_4CH = CHCH_2CH = CH(CH_2)_7COOH$	_	-12
Linolenic acid	18	$CH_3CH_2CH = CHCH_2CH = CHCH_2CH = CH(CH_2)_7COO!$	Н —	-11
Arachidonic acid		$CH_3(CH_2)_4(CH=CHCH_2)_4CH_2CH_3COOH$	_	-50
Eicosapentaenoic a		$CH_3CH_2(CH=CHCH_2)_5CH_2CH_2COOH$	_	-60
Docosahexaenoic a		$CH_3CH_2(CH=CHCH_2)_6CH_2COOH$	_	-45

^{*}Omega (ω) is the last letter in the Greek alphabet. Correspondingly, the last carbon atom in a carbon chain of a compound is often referred to as the omega carbon. In reference to unsaturated carboxylic acids, omega plus a number (e.g., ω-3) indicates the location of the first carbon-carbon double bond, counting from the omega carbon.

Consider fatty acids, which are common components of lipids. as the fatty acids get larger, the water solubility of the fatty acid decreases dramatically. The four-carbon compound butyric acid is infinitely soluble in water, while fatty acids with more than about ten carbons long are insoluble in water. The fatty acids become increasingly "unlike" water as they become larger and more nonpolar. The hydrophobic nature of lipids

The omega designations of these acids are palmitoleic (ω-7); oleic (ω-9); linoleic (ω-6); linolenic (ω-3); arachidonic (ω-6); eicosapentaenoic (ω-3); docosahexaenoic (ω-3).

contributes significantly to the biological functions of these molecules. Their water insolubility allows lipids to serve as barriers to aqueous solutions.

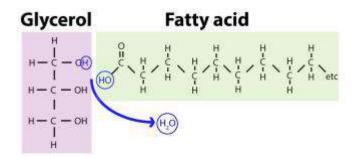
Classification of Lipids

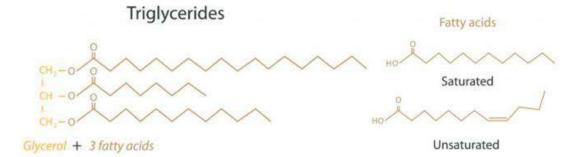
1-Simple Lipids

These are esters of fatty acids with various alcohols. Depending on the type of alcohols, these are subclassified as:

1-Neutral fats or triacylglycerol or triglycerides

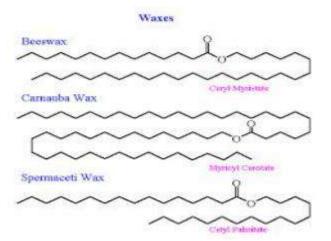
These are esters of fatty acids with alcohol glycerol, e.g. tripalmitin. Because they are uncharged, they are termed as neutral fat. The fat we eat are mostly triglycerides. A fat in liquid state is called an oil, e.g. vegetable oils like groundnut oil, mustard oil, corn oil, etc.





2- Waxes

These are esters of fatty acids with higher molecular weight monohydric long chain alcohols. These compounds have no importance as far as human metabolism is concerned.



2. Compound lipids

- (a) **Phospholipids**: substances that yield glycerol, phosphoric acid, fatty acids, and a nitrogen-containing base upon hydrolysis.
- **(b) Sphingolipids**: substances that yield an unsaturated amino alcohol (sphingosine), a long-chain fatty acid, and either a carbohydrate or phosphate and a nitrogen base upon hydrolysis.
- (c) Glycolipids: substances that yield sphingosine, a fatty acid, and a carbohydrate upon hydrolysis.

3. Steroids

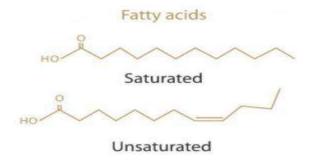
Substances that possess the steroid nucleus, which is a 17-carbon structure consisting of four fused carbocyclic rings. Cholesterol and several hormones are in this class.

4. Miscellaneous lipids

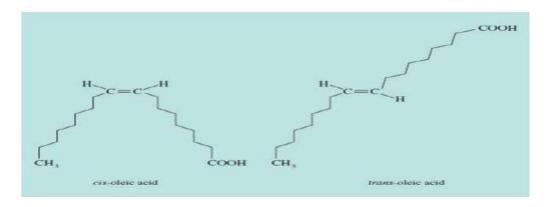
Substances that do not fit into the preceding classifications; these include the fat-soluble vitamins A, D, E, and K, and lipoproteins. The most abundant lipids are the fats and oils. These substances constitute one of the three important classes of foods.

Simple Lipids

Fatty Acids Fatty acids, which form part of most lipids, are carboxylic acids with long, hydrophobic carbon chains. A common fatty acids are straight-chain compounds with an even number of carbon atoms. Seven of the fatty acids in the table—palmitoleic, oleic, linoleic, linolenic, arachidonic eicosapentaenoic acid and docosahexaenoic acid—are unsaturated, having carbon—carbon double bonds in their structures. Animal and higher plant cells produce lipids in which palmitic, oleic, linoleic, and stearic acids predominate.



Over one-half of plant and animal fatty acids are unsaturated plant lipids, which tend to be more unsaturated than their animal counterparts. Double bonds impart some special characteristics to the unsaturated fatty acids. Remember that the presence of double bonds raises the possibility of geometric isomerism. Unsaturated fatty acids may be either cis or trans isomers.



trans isomer is almost a linear molecule, while the double bond in the cis isomer introduces a kink into the fatty acid structure. Unsaturated fatty acids found in nature are almost always cis isomers. These kinked fatty acids cannot stack closely together and hence do not solidify easily. Unsaturated fatty acids have lower melting points than saturated fatty acids of a similar size. Cooking oils are liquids at room temperature because a high percentage of their fatty acids are unsaturated. In like manner, biological membranes are very fluid because of the presence of fatty acid cis isomers.

Recently it has become clear that trans unsaturated fatty acids are harmful. Consumption of these isomers can cause cardiovascular problems, and the food industry has moved to eliminate trans fats from all prepared foods.

Palmitic acid

Essential fatty acids

Fatty acids, that are required for optimal health and cannot be synthesized by the body and should be supplied in the diet are called essential fatty acids. They are polyunsaturated fatty acids, namely linoleic acid and linolenic acid. Arachidonic acid can be synthesized from linoleic acid. Therefore, in deficiency of linoleic acid, arachidonic acid also becomes essential fatty acids. Humans lack the enzymes to introduce double bonds at carbon atoms beyond C9 in the fatty acid chain. Hence, humans cannot synthesize linoleic acid and linolenic acid having double bonds beyond C9. And thus, linoleic and linolenic are the essential fatty acids.

Fifth lecture

Eicosanoids

Certain fatty acids, as well as other lipids, are biochemical precursors of several classes of hormones. The omega-6 and omega-3 fatty acids are also used to make hormones, the most common of which are the eicosanoids. These hormones are derived from fatty acids with 20 carbon atoms, either the omega-6 (arachidonic acid) or the omega-3 (eicosapentaenoic acid).

Fats and Oils

Chemically, fats and oils are esters of glycerol and the higher-molar-mass fatty acids. They have the following general formula: The R's can be either long-chain saturated or unsaturated hydrocarbon groups. The R's can be either long-chain saturated or unsaturated hydrocarbon groups. Most of the fatty acids in these esters have 14–18 carbons. Because there are three ester groups per glycerol, the molecules are called triacylglycerols or triglycerides (an older name that is still commonly used). The three R groups are usually different. They are large molecules, averaging more than 50 carbon atoms per molecule and have many nonpolar, uncharged groups. Triacylglycerols are insoluble in water.

Waxes

Waxes are esters of high-molar-mass fatty acids and high-molar-mass alcohols. They have the general formula in which the alcohol (ROH) contributes up to about 30 carbons, and the fatty acid (R COOH) also provides an equivalent number of carbons. Waxes are very large molecules with almost no polar groups. They represent one of the most hydrophobic classes of lipids. Their extreme water insolubility allows waxes to serve a protective function. Leaves, feathers, fruit, and fur are often naturally coated with a wax. Hardwood floors, automobile paint, and leather goods are just a few of the many products that can be protected by a wax. Waxes tend to be the hardest of the lipids because

their carbon chains are long and have very few double bonds. As with fats and oils, the size of the wax molecule and the number of double bonds contained in its carbon chains determine whether the wax will be a liquid or a solid.

Compound Lipids

Phospholipids

A group of compounds that yield one or more fatty acid molecules, a phosphate group, and usually a nitrogenous base upon hydrolysis. Often have negative and positive charges. Consequently, in contrast to the triacylglycerols, phospholipids have a hydrophilic end that interacts with water

$$\begin{array}{c} CH_{\overline{2}}O - \overline{Fatty\ acid} \\ CH - O - \overline{Fatty\ acid} \\ CH_{\overline{2}}O - \overline{Fatty\ acid} \\ \end{array} \right\} \begin{array}{c} CH_{\overline{2}}O - \overline{Fatty\ acid} \\ CH_{\overline{2}}O - \overline{Fatty\ acid} \\ \end{array} \right\} \begin{array}{c} hydrophobic \\ CH_{\overline{2}}O - \overline{Fatty\ acid} \\ \end{array} \\ \begin{array}{c} hydrophobic \\ CH_{\overline{2}}O - \overline{Fatty\ acid} \\ \end{array} \right\} \begin{array}{c} hydrophobic \\ hydrophilic \\ a\ phospholipid \end{array}$$

phospholipids are one of the most important membrane components, because this lipid with both hydrophobic and hydrophilic character. Phospholipids are also involved in the metabolism of other lipids and nonlipids. Although they are produced to some extent by almost all cells, most of the phospholipids that enter the bloodstream are formed in the liver.

Phosphatidic Acids

glyceryl esters of fatty acids and phosphoric acid. The phosphatidic acids are important intermediates in the synthesis of triacylglycerols and other phospholipids.

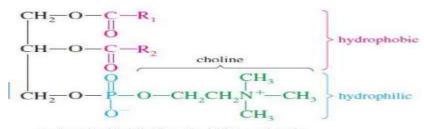
$$\begin{array}{c}
CH_{2}-O-C-R_{1} \\
O \\
CH-O-C-R_{2}
\end{array}$$
hydrophobic
$$CH_{2}-O-P-O$$
hydrophilic

a phosphatidic acid

As with all common phospholipids, the fatty acid chains are large relative to the rest of this molecule. Other phospholipids are formed from a phosphatidic acid when specific nitrogen-containing compounds are linked to the phosphate group by an ester bond. Three commonly used nitrogen compounds are choline, ethanolamine, and L-serine.

Phosphatidylcholines

Glyceryl esters of fatty acids, phosphoric acid, and choline. Phosphatidylcholines are synthesized in the liver and are present in considerable amounts in nerve tissue and brain substance, used extensively in the food industry and pharmaceutical preparations as emulsifying agent. The single most important biological function for phosphatidylcholine is as a membrane component. This phospholipid makes up between 10 and 20% of many membranes.



a phosphatidylcholine (lecithin) molecule

Phosphatidylethanolamines

Another important constituent of biological membranes. These lipids are glyceryl esters of fatty acids, phosphoric acid, and ethanolamine (HOCH2CH2NH2). They are found in essentially all living organisms.

$$\begin{array}{c|c} CH_2-O-C-R_1 \\ \hline O \\ CH-O-C-R_2 \\ \hline O \\ CH_2-O-P-OCH_2CH_2NH_3^+ \end{array}$$
 hydrophobic

a phosphatidylethanolamine (cephalin) molecule

Phosphatidylserine

It contains the amino acid serine rather than ethanolamine and is found in most tissues

Sphingolipids

They hydrolyzed, yield a hydrophilic group (either phosphate and choline or a carbohydrate), a long-chain fatty acid (18–26 carbons), and sphingosine (an unsaturated amino alcohol). When drawn as follows, the similarities between sphingosine and glycerol esterified to one fatty acid become recognizable. The starred atoms on sphingosine react further to make sphingolipids, just as the starred atoms on the glycerol compound react further to give triacylglycerols or phospholipids. Sphingolipids are common membrane components because they have both hydrophobic and hydrophilic character. For example, sphingomyelins are found in the myelin sheath membranes that surround nerves. Sphingomyelins can also be classified as phospholipids.

OH
$$CH-CH=CH(CH_2)_{12}CH_3$$

$$CH-NH_2$$

$$CH-NH_2$$

$$CH_2-NH$$

$$CH_2-NH$$

$$CH_2-NH$$

$$CH_2-NH$$

$$CH_3-NH$$

$$CH_3-$$

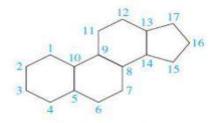
Glycolipids

Sphingolipids that contain a carbohydrate group are also known as glycolipids. The two most important classes of glycolipids are cerebrosides and gangliosides. These substances are found mainly in cell membranes of nerve and brain tissue. A cerebroside may contain either D-galactose or D-glucose. Gangliosides resemble cerebrosides in structure, but they contain complex oligosaccharides instead of simple monosaccharides.

Sixth lecture

Steroids

Consists of four fused carbocyclic rings. This nucleus contains 17 carbon atoms. Examples of steroids and steroid-containing materials is cholesterol.



steroid ring nucleus

Cholesterol

Cholesterol is the major sterol in animal tissues. Sterols are a class of steroids containing hydroxyl group. • It consists of steroid nucleus namely phenanthrene containing 19-carbon atoms (Figure 3.11). • It consists of methyl side chains at position C10 and C13 which are shown as single bonds. • Cholesterol, a 27-carbon compound, has an 8-carbon side chain attached to the D ring at C17 and a hydroxyl group attached to C3 of the A ring, with one double bond between carbon atoms 5 and 6

Cholesterol is amphipathic, with a polar head the hydroxyl group at C3 and a nonpolar, the steroid nucleus and hydrocarbon side chain at C17. • Most of the cholesterol in the body exists as a cholesterol ester, with a fatty acid attached to the hydroxyl group at C3. • Cholesterol is widely distributed in all the cells of the body but particularly in nervous tissue. • It occurs in animal fats but not in the plant fats.

Reactions of Lipids

Saponification

Hydrolysis of a fat by *alkali* is called *saponification*. The products are glycerol and the alkali salts of the fattyacids, which are called **soaps** (**Figure 3.4**). Acid hydrolysis of a fat yields the free fatty acids and glycerol

Figure 3.4: Saponification of fat

Hydrogenation

Hydrogenation of unsaturated fats in the presence of a catalyst (nickel) is known as "hardening". It is commercially valuable as a method of converting these liquid fats, usually of plant origin into solid fats as margarines, vegetable ghee, etc.

Peroxidation

Peroxidation (auto-oxidation) of lipids exposed to oxygen is responsible not only for deterioration of foods (rancidity) but also for damage to tissues *in vivo*, where it may be a cause of **cancer.** Lipid peroxidation is a chain reaction generating free radicals that initiate further peroxidation.

To control and reduce peroxidation, humans make use of *antioxidants*. Naturally occurring antioxidant sinclude vitamin E (tocopherol) and β -carotene (provitaminA), which are lipid soluble and vitamin C, which is water soluble.

Rancidity

The unpleasant odor and taste, developed by natural fats upon aging, is referred to as "rancidity". Rancidity may be due to hydrolysis or oxidation of fat.

- Rancidity due to hydrolysis: Naturally occurring fats, particularly those from animal sources, are contaminated with enzyme lipase. The action of lipase brings about partial hydrolysis of glycerides of fat.
- Rancidity may also be caused by various oxidative processes.

For example, oxidation at the double bonds of unsaturated fatty acids of glycerides may form peroxides, which then decompose to form aldehydes of unpleasant odor and taste, this process is increased by exposure to light or heat. Many natural vegetable fats and oils may contain antioxidants like vitamin E which prevent onset of rancidity. Therefore, vegetable fats can be preserved for a longer time than animal fats.

CHARACTERIZATION OF FAT (TESTS FOR PURITY OF FAT)

Fats are characterized and their purity assayed by the following tests:

Saponification Number

It is defined as, number of mgs of KOH required to saponify one gm of fat. It is inversely proportional to the molecular weight of fat. This value is high in fats containing a short chain fatty acids. For example, the saponification number of:

- Butter = 220
- Coconut oil = 260

Iodine Number

The number of gms of iodine required to saturate 100 gms of a given fat is known as iodine number. Since iodine is taken up by the double bonds, a high iodine number indicates a high degree of unsaturation of the fatty acids in fat, e.g.

- Butter fat = 27
- Coconut oil = 8
- Linseed oil = 200.

Iodine number is important in the identification of the fat or oil as well as is used for identification of adulteration of oils.

Acid Number

Number of mg of KOH required to neutralize the free fatty acids present in one gm of fat is known as acid number. The acid number indicates the degree of rancidity of the given fat. Acid number is directly proportional to the rancidity. The edibility of a fat is inversely proportional to the acid number. Refined oil should not contain free fatty acids. The presence of free fatty acids in any oil indicates that it is not pure.

Reichert Meissl Number

The number of ml of 0.1 N alkali, required to neutralize the volatile fatty acids distilled from 5 gm of fat, e.g. the Reichert Meissl value for:

- Butter = 26
- Coconut oil = 7.

It is less than one for other edible oils. The admixture of certain fats may be used to prepare synthetic butter which may simulate butter in most of the constants except RM value and hence, can be detected.

Atherosclerosis

Atherosclerosis is a metabolic disease that leads to deposits of cholesterol and other lipids on the inner walls of the arteries (called plaque). The arterial passages become progressively narrower. The walls of the arteries also lose their elasticity and their ability to expand to accommodate the volume of blood pumped by the heart. Blood pressure increases as the heart works harder to pump sufficient blood through the narrowed passages, which may eventually lead to a heart attack. The accumulation of plaque also causes the inner walls to have a rough rather than a normal smooth surface, which is a condition that may lead to coronary thrombosis (heart attack due to blood clots). Atherosclerosis can cause as a result of

- 1-Lipid
- 2-White cell (macrophage)
- 3-foam cell

Seventh lecture

Amino Acids

General Nature of Amino Acids

There are approximately 300 amino acids present in various animal, plant and microbial systems, but only **20 amino acids are involved in the formation of proteins.**

- All the 20 amino acids found in proteins (**Table 4.1**) have a carboxyl group (-COOH) and an amino acid group (-NH2) bound to the same carbon atom called the α -carbon (**Figure 4.1**).
- Amino acids differ from each other in their **side chains** or **R-groups**, attached to the α -carbon.
- The 20 amino acids of proteins are often referred to as the **standard** or **primary** or **normal amino acids.**

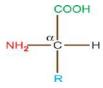


Figure 4.1: General structure of α -amino acid found in protein

- The standard amino acids have been assigned three letters abbreviations and one letter symbol, e.g. amino acid **glycine** has abbreviated name **Gly** and symbol letter **G**.
- All the amino acids found in proteins are exclusively of the **L-configuration.**

Name	Symbol	Structural formula
Aliphatic side chain		
Glycine	Gly (G)	H—CH—COO" NH ₃ *
Alanine	Ala (A)	CH ₃ -CH-COO ⁻
Valine	Val (V)	CH ₃ CH-CH-C00 ⁻
Leucine	Leu (L)	H ₃ C CH— CH ₂ —CH—COO ⁻ NH ₃ *
Isoleucine	lle (I)	CH ₂ CH—CH—COO ⁻ CH ₃ NH ₃ *
Hydroxylic (OH) group containing sid	de chains	
Serine	Ser (S)	CH ₂ —CH-COO ⁻ OH NH ₃ *
Threonine	Thr (T)	CH ₃ -CH-CH-COO OH NH ₃ *
Tyrosine	Tyr (Y)	See aromatic group containing side chain amino acids
Sulfur containing side chains		
Cysteine	Cys (C)	CH2-CH-COOT SH NH3*
Methionine	Met (M)	CH2-CH2-CH-COO* S-CH3 NH3*
Side chains containing acidic groups	(-COOH) and their amides	
Aspartic acid	Asp (D)	COO ⁻ —CH ₂ —CH—COO ⁻ NH ₃ *
Aspargine	Asn (N)	H ₂ N-C-CH ₂ -CH-C00 ⁻
Glutamic acid	Glu (E)	00С—СН ₂ —СН ₂ —СН—СОО ⁻
Glutamine	Gln (Q)	NH ₂ —C—CH ₂ —CH ₂ —CH—COC

Table 4:1 (contd)			
Name	Symbol	Structural formula	
Basic groups containing side chains			
Arginine	Arg (R)	H—N—CH ₂ —CH ₂ —CH ₂ —CH—COO ⁻ C=NH ₂ + NH ₃ + NH ₃	
Lysine	Lys (K)	CH2—CH2—CH2—CH2—CH—COOT	
Histidine	His (H)	CH ₂ —CH—COO"	
Aromatic group containing side chains			
Histidine	His (H)	See above	
Phenylalanine	Phe (F)	CH2—CH—C00	
Tyrosine	Tyr (Y)	OH————————————————————————————————————	
Tryptophan	Trp (W)	CH ₂ —CH—C00°	
lmino acids			
Proline	Pro (P)	CH2 CH COO"	

Classification of Amino Acids

There are five ways of classifying amino acids depending on the:

- 1. Chemical nature of the amino acid in the solution
- 2. Structure of the side chain of the amino acids
- 3. Nutritional requirement of amino acids
- 4. Metabolic product of amino acids
- 5. Nature or polarity of the side chain of the amino acids.

Classification Based on Chemical Nature of the Amino Acid in Solution

According to this type of classification, amino acids are classified as follows:

- i. Neutral amino acids
- ii. Acidic amino acids
- iii. Basic amino acids.

Neutral amino acids

The amino acids which are neutral in solution and are monoaminomonocarboxylic acids (i.e. having one amino group and one carboxylic group), e.g. Glycine Serine Phenylalanin

Alanine Threonine Tyrosine
Valine Cysteine Tryptophan
Leucine Methionine Aspargine
Isoleucine Proline Glutamine

Acidic amino acid

These are acidic in solution and are monoamino dicarboxylic acids, e.g.

• Aspartic acid

• Glutamic acid.

Basic amino acid

These are basic in solution and are diamino-monocarboxylic acids, e.g.

• Lysine

• Arginine

• Histidine.

Classification Based on Chemical Structure of Side Chain of the Amino Acid

According to this type of classification, amino acids are classified as:

- 1. Aliphatic amino acids
- 2. Hydroxy amino acids
- 3. Sulfur containing amino acids
- 4. Dicarboxylic acid and their amides
- 5. Diamino acids
- 6. Aromatic amino acids
- 7. Imino acids or heterocyclic amino acids.

Aliphatic amino acids

Amino acids having aliphatic side chain, e.g.

- Glycine
- Alanine
- Valine Leucine
- Isoleucine.

Hydroxy amino acids

Amino acids having hydroxy group in the side chain, e.g.

• Threonine • Serine • Tyrosine.

Sulfur containing amino acids

Amino acids having sulfur in the side chain, e.g.

• Cysteine • Methionine.

Dicarboxylic acid and their amides

Amino acids having carboxylic group in their side chain, e.g.

- Glutamic acid
- Glutamine (amide of glutamic acid)
- Aspartic acid
- Aspargine (amide of aspartic acid).

Diamino acids

Amino acids having amino group (-NH2) in the side chain, e.g.

- Lysine
- Arginine
- Histidine.

Aromatic amino acids

Amino acids containing aromatic ring in the side chain, e.g.

• Phenylalanine • Tyrosine • Tryptophan.

Imino acids or heterocyclic amino acids

• One of the 20 amino acids, **proline** is an **imino** (-NH) acid not an amino (-NH2) acid as are other 19. The side chains of proline and its α -amino group form a ring structure and thus proline differs from other amino acids, in that it contains an imino group, rather than an amino group.

Imino group
$$\longrightarrow$$
 NH $\xrightarrow{\alpha}$ C \xrightarrow{C} COOH $\xrightarrow{CH_2}$ CH₂

Structure of proline

Nutritional Classification of Amino Acids

On the basis of nutritional requirement, amino acids are classified into two groups:

i. Essential or indispensable amino acids

ii. Nonessential or dispensable amino acids.

Essential amino acids

Essential amino acids cannot be synthesized by the body and must, therefore, be essentially supplied through the diet. Ten amino acids, essential for humans include:

• Phenylalanine • Methionine

Histidine

• Threonine • Arginine

Tryptophan

Isoleucine

• Leucine

Lysine

• Valine.

Among the ten essential amino acids; **arginine** and **histidine** are known as **semi-essential** amino acids since these amino acids are synthesized partially in human body. Arginine and histidine become essential in diet durin periods of rapid growth as in childhood and pregnancy.

A deficiency of an essential amino acid impairs protein synthesis and leads to a negative nitrogen balance (nitrogen excretion exceeds nitrogen intake).

Nonessential amino acids

Nonessential amino acids can be synthesized in human body and are not required in diet, e.g.

• Glycine

- Alanine
- Proline

- Tyrosine
- Serine

Cysteine

- Glutamic acid
- Aspartic acid
- Glutamine

• Aspargine.

Metabolic Classification of Amino Acids

On the basis of their catabolic end products, the twenty standard amino acids are divided in three groups.

- i. Glucogenic amino acids: Those which can be converted into glucose. Fourteen out of the twenty standard amino acids are glucogenic amino acids. Glycine, alanine, serine ,cysteine, aspartic acid, aspargine, glutamic acid, glutamine, proline, histidine, arginine, methionine, threonine, valine.
- ii. **Ketogenic amino acids:** Those which can be converted to ketone bodies. Two amino acids **leucine** and **lysine** are exclusively ketogenic.
- iii. Both glucogenic and ketogenic: Those which can be converted to both glucose and ketone bodies. Four amino acids isoleucine, phenylalanine, tryptophan and tyrosine are glucogenic and ketogenic.

Classification Based on Nature or Polarity of Side Chain of Amino Acid

According to this type of classification, amino acids are classified into two major classes (**Figure 4.2**):

- i. Hydrophilic or polar amino acids.
- ii. Hydrophobic or nonpolar amino acids.

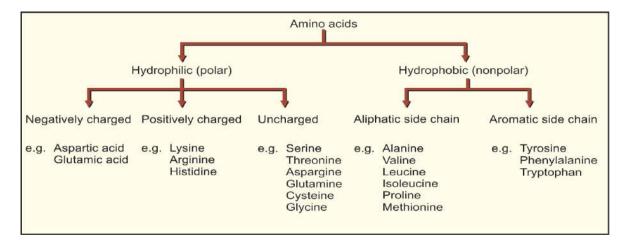


Figure 4.2: Classification of amino acids based on polarity

• Biologically important of Amino Acids:

Specific amino acids can give rise to specific biologically important compounds in the body (**Table 4.3**).

Table 4.3: Biologically important compounds formed by amino acids		
Amino acid	Biologically important compound	
Tyrosine	Hormone, e.g. adrenaline and thyroxine, skin pigment, e.g. melanin	
Tryptophan	Vitamin, e.g. niacin	
Glycine, arginine and methionine	Creatine	
Glycine and cysteine	Bile salts	
Glycine	Heme	
Aspartic acid and glutamic acid	Pyrimidine bases	
Glycine, aspartic acid and glutamine	Purine bases	
β-alanine	Coenzyme-A	

Properties of Amino Acids

Physical Properties

They are colorless, crystalline substances generally soluble in water.

Optical Properties

All naturally occurring amino acids are optically active except **glycine** which is optically inactive. At pH 7.0, all amino acids have the same L-configuration and hence L- α -amino acid (**Figure 4.4**).

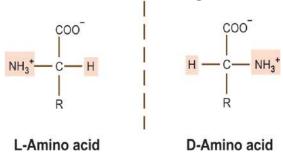


Figure 4.4: D and L forms of amino acids

Ionization of Amino Acids

Due to ionizing property of amino acids, amino acids exert:

- Acid base behavior
- Amphoteric properties (zwitter ion formation)

Acid/base behavior of amino acids

- The acid base properties of amino acids depend on the **amino** and **carboxyl** groups attached to the α -carbon.
- The **carboxyl** (-COOH) group of an amino acid can donate proton (H+) and behave as an acid, forming a negatively charged **anion**.

• Amino group (-NH2) of an amino acid can accept the proton (H+) which behave as a base, forming positively charged **cation**.

Thus, amino acids in aqueous solution are ionized and act as acids and bases (Figure 4.5).

Figure 4.5: Ionization of amino acid

Amphoteric properties of amino acids and formation of zwitter ion at isoelectric pH

Substances having a two-way property are called **amphoteric**. As amino acids have both acidic and basic groups, they can donate a proton or accept a proton, hence amino acids are regarded as ampholytes.

Zwitter ion (Dipolar molecule)

- Monoamino monocarboxylic acids exist in aqueous solution as **dipolar molecule** or **zwitter ions**, which means that they have both positive and negative charges on the same amino acids.
- The α -COOH group is ionized and becomes negatively charged anion (COO⁻) and
- The α -NH2 group is protonated to form a positively charged cation (NH3⁺).
- Thus, the overall molecule is electrically neutral. Thus, the molecular species which contain an equal number of ionizable group of opposite charge and as a result bear no net charge, are called **zwitter ions**.
- The net charge of an amino acid depends upon the pH of the medium.
- At acidic pH, amino acid is positively charged because ionized COO–group accepts a proton and becomes uncharged (COOH), so that the overall charge on the molecule is positive.
- While at alkaline pH it is negatively charged as the NH3 ⁺ group loses its proton and becomes uncharged; thus the overall charge on the molecule is negative (**Figure 4.6**).

Isoelectric pH (PI)

The pH at which amino acid bears no net charge (zwitter ion) and therefore does not move in an electric field is called **isoelectric pH (PI)**.

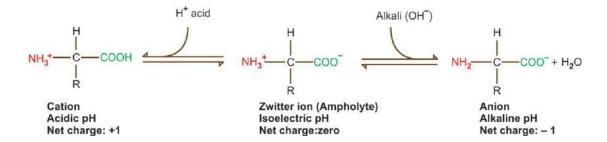


Figure 4.6: Ionic forms of amino acid in acidic, basic and isoelectric PH

Eighth Lecture

Biologically Important Peptides

- Peptides are chains (polymer) of amino acids. Two amino acid molecules can be covalently joined through a **peptide bond**, to yield **dipeptide**. Peptide linkage is formed by the removal of a molecule of water from the α -carboxyl group of one amino acid and the α -amino group of another (**Figure 4.7**).
- When many amino acids are joined, the product is called **polypeptide**. Proteins are polypeptides with thousands of amino acids.
- There are many naturally occurring small polypeptides some of which have important biological activities and are called **biologically important peptides**. Suach as Glutathione(GSH) is a tripeptide containing **glutamate**, **cysteine** and **glycine**.

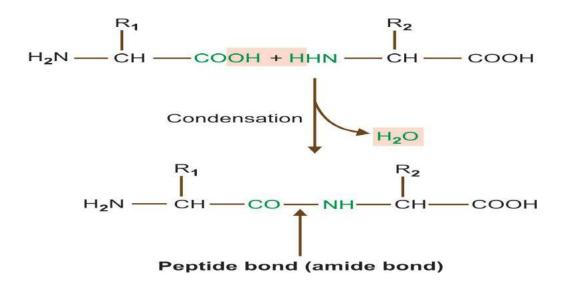


Figure 4.7: Formation of peptide bond

Glutathione (GSH)

- GSH is a tripeptide (γ glutamyl cysteinyl glycine) containing glutamate, cysteine and glycine.
- Glutathione is found in all mammalian cells *except* the neurons.
- Glutathione may exist as the reduced (GSH) or oxidized (G-S-S-G) form (**Figure 4.8**) and can thus play a role in some oxidation—reduction reactions.
- In oxidized form, two molecules of glutathione are linked by disulfide bond.
- The sulfhydryl (-SH-) is the functional group primarily responsible for the properties of glutathione.

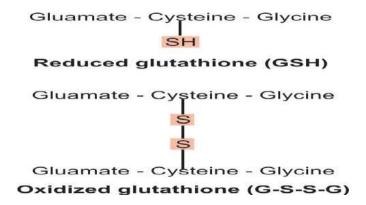


Figure 4.8: Reduced and oxidized glutathione

Functions of glutathione

- The reduced form of glutathione with a free sulfhydryl (-SH-) group serves as a **redox buffer** regulating the redox state of the cell.
- It helps in keeping the enzymes in an active state by preventing the oxidation of sulfhydryl (-SH-) group of enzyme to disulfide (-S-S-) group.
- Reduced glutathione is essential for maintaining the normal structure of red blood cells and for keeping hemoglobin in the ferrous state. Cells with lowered level of reduced glutathione are more susceptible to hemolysis.
- Glutathione plays a key role in detoxification by reducing H2O2—the harmful byproduct of metabolism.

• Glutathione is involved in transport of aminoacids across the cell membrane of the kidney and intestine.

Proteins

Definition

Proteins are linear chains of amino acids that are linked together by covalent, **peptide bonds.** Each protein has specific and unique sequence of amino acids that defines both its three-dimensional structure and its biologic function.

Classification of Proteins

Proteins have been classified in several ways. They are most conveniently classified on the basis of their:

1. Function 2. Physical and chemical properties.

Classification of Proteins Based on Functions

In a functional classification, they are grouped according to their biological role. Some functions that proteins serve and examples of specific functional proteins are as follows:

Catalytic Proteins or Enzymes

These proteins act as enzymes, e.g.

- Glucokinase
 - Dehydrogenases
- Transaminases
- Hydrolytic enzymes, pepsin, trypsin, etc.

Transport Proteins

These proteins are involved in the process of transportation, e.g.

- Hemoglobin transports oxygen
- Transferrin transports iron
- Albumin carries fatty acids and bilirubin.

Storage Proteins

Many proteins serve as storage form, e.g.

- Apoferritin stores iron in the form of ferritin
- Myoglobin stores oxygen in muscles.

Structural Proteins

Many proteins serve as supporting framework of cells to give biological structure, strength or protection, e.g.

- Collagen in bone • Cartilage, elastin of ligaments
- Keratin of hair, nail.

Defence Proteins

Many proteins involved in defence mechanism against invasion of foreign substances such as viruses, bacteria and cells. Examples of defence proteins are:

- Immunoglobulins or antibodies
- Fibrinogen and thrombin are blood clotting proteins.

Regulatory Proteins

Some proteins regulate cellular or physiological activity, e.g.

- Many hormones, e.g. **insulin**, regulate sugarm etabolism; **growth hormone** of pituitary gland regulates growth of the cells.
 - Classification of Proteins Based on Physical and Chemical Properties of Protein

According to the joint committee of the American Society of Biological Chemists and American Physiological Society, proteins are classified into three main groups as follows:

- 1. Simple proteins
- 2. Conjugated proteins
- 3. Derived proteins.

Simple Proteins

Simple proteins are defined as those proteins that upon hydrolysis, yield only amino acids or their derivatives. They are subclassified according to their solubility and heat coagulability as follows:

Albumins

The albumins are **soluble in water, coagulated by heat.** It is deficient in glycine, e.g.

- Egg albumin
- Serum albumin
- Lactalbumin of milk.

Globulins

The globulins are insoluble in water, but they are soluble in dilute neutral salt solution and are heat coagulable, e.g.

- Ovaglobulin of egg yolk
- Serum globulin
- Myosin of muscle.

Prolamins or alcohol soluble proteins

The prolamins are soluble in **70 to 80% alcohol,** but they are **insoluble in water, neutral solvent** or **absolute alcohol.** The prolamins are rich in proline but are **deficient in lysine.** They are plant proteins, e.g.

Zein of corn

• Gliadin of wheat.

Histones

The histones are **soluble in water, but are not coagulated by heat.** Histones are basic proteins as they are rich in basic amino acids. The histones, being basic, usually occur in tissues in salt combinations with acidic substances, such as nucleic acids (RNA and DNA), e.g. Nucleoprotein.

Protamines

They are strongly basic and rich in basic amino acid arginine. The protamines are **soluble in water but are not heat coagulable.** Like histones, they occur in tissues with nuleic acids, e.g. nucleoproteins.

Scleroproteins (fibrous proteins)

Fibrous proteins are also called **sclero proteins.** They are insoluble, (in all common solvents like water, neutral salt solution, organic solvents, dilute acid and alkali) high molecular weight fibers. Examples of sclero proteins are:

- Collagen found in cartilage and tendons
- Elastin found in tendon and arteries
- Keratin of hair, skin and nail.

Conjugated Proteins

Conjugated proteins are composed of simple protein combined with some non-protein substance. The nonprotein group is referred to as the **prosthetic** (additional) group. Following are the examples of conjugated proteins:

Nucleoproteins

The nucleoproteins are composed of simple basic proteins (histones or protamines) with **nucleic acids**

(RNA and DNA) as the prosthetic groups. They are proteins of cell nuclei, e.g.

Nucleohistone

• Nucleoprotamine.

Glycoproteins and proteoglycans or mucoproteins

These consist of simple protein and carbohydrate as a prosthetic group.

- When carbohydrate content is less than 4% of protein it is called **glycoprotein**, e.g.
- Mucin of saliva
- Immunoglobulins
- When carbohydrate content is more than 4%, it is called **proteoglycans**, e.g. glycosaminoglycans.

Chromoproteins

Chromoproteins are composed of simple proteins with a **colored prosthetic group**, e.g.

- Hemoglobin
- Cytochromes
- Catalase
- Peroxidase

In all these chromo proteins, prosthetic group is heme.

Phosphoproteins

The phosphoproteins are formed by a combination of protein with **prosthetic group phosphoric acid,** e.g. Casein of milk

Lipoproteins

The lipoproteins are formed by a combination of protein with a **prosthetic group lipid**, e.g.

- Serum lipoproteins like:
- Chylomicrons
- Very low density lipoprotein (VLDL)
- Low density lipoprotein (LDL) and
- High density lipoproteins (HDL).

Metaloproteins

The prosthetic group is metallic elements such as: Fe, Co, Mn, Zn, Cu, Mg, etc., for example;

- Ceruloplasmin is a copper containing protein
- Carbonic anhydrase, carboxypeptidase and DNA polymerase are zinc containing proteins.

Derived Proteins

This class of proteins as the name implies, includes those substances formed from simple and conjugated proteins. Derived proteins are subdivided into:

- Primary derived proteins (denatured proteins)
- Secondary derived proteins.

Primary derived proteins (denatured proteins)

These protein derivatives are formed by agents, such as heat, acids, alkalies, etc. which cause only slight changes in the protein molecule and its properties without hydrolytic cleavage of peptide bond. These are synonymous with denatured proteins (**Figure 4.9**), e.g.

- Proteans
- Metaproteins.

Secondary derived proteins

These substances are formed in the progressive hydrolytic cleavage of the peptide bonds of metaproteins (coagulated proteins) into progressive smaller molecules, e.g.

- Proteoses
- Peptones
- Peptides (Figure 4.9).

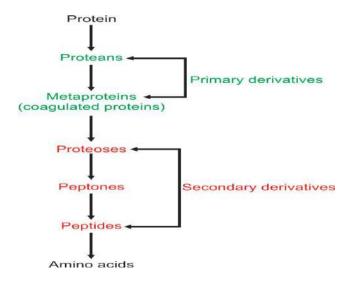


Figure 4.9: Formation of primary and secondary derived proteins

Ninth Lecture

Structure of Proteins

Every protein in its native state has a unique threedimensional structure which is referred to as its **conformation** and made up of only 20 different amino acids. The number and sequence of these amino acids are different in different proteins. Protein structure can be classified into four levels of organization:

Primary structure.
 Secondary structure
 Operations structure

3. Tertiary structure. 4. Quaternary structure.

Primary Structure of Proteins

- The sequence of amino acids forming the backbone of proteins and location of any disulfide bond in a protein is called, the primary structure of the protein (**Figures 4.10**).
- In proteins, amino acids are joined covalently by **peptide bonds**, which are formed between α -carboxyl group of one amino acid and α -amino group of another with the elimination of a water molecule (**Figure 4.7**).

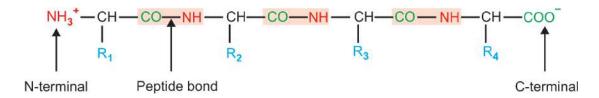


Figure 4.10: Polypeptide chain showing N-terminal and C-terminal

- Linkage of many amino acids through peptide bonds results in an unbranched chain called a **polypeptide** (**Figure 4.10**). Each amino acid in a polypeptide is called a **residue** or **moiety.** Each polypeptide chain is having free amino group at one end called *Nterminal* and free carboxyl group at another end, called *C-terminal*.
- Proteins have unique amino acid sequences that are specified by genes. This amino acid sequence of a protein is referred to as its primary structure.

Clinical Importance of Primary Structure

Understanding of primary structure of a protein is important because many genetic diseases result due to an abnormal amino acid sequences. If the primary structure of the normal and mutated proteins are known, this information may be used to diagnose or study the disease.

Secondary Structure of Proteins

- For stability of primary structure, **hydrogen bonding** between the hydrogen of NH and oxygen of C=O groups of the polypeptide chain occurs, which gives rise to folding or twisting of the primary structure.
- Thus, regular folding and twisting of the polypeptide chain brought about by hydrogen bonding is called secondary structure of protein. The most important kinds of secondary structure are:
- $-\alpha$ -Helix (helicoidal structure)
- $-\beta$ -Pleated sheet (stretched structure).

α-Helix

It is called α because it was the first structure elucidated by Pauling and Corey. If a backbone of polypeptide chain is twisted by an equal amounts about each α -carbon, it forms a coil or helix. The helix is a rod-like structure.

- The helix is stabilized by hydrogen bonds beween the NH and CO groups of the same chain.
- These hydrogen bonds have an essentially optimal nitrogen to oxygen (N-O). Thus, CO group of each amino acid is hydrogen bonded to the -NH of the amino acid that is situated four residues ahead in the linear sequence (**Figure 4.12**).

Helix destabilizing amino acids

Glycine and proline are the helix-destabilizing amino acids.



Figure 4.12: Formation of hydrogen bond in α -helix

B-Pleated Sheet Structure or Stretched State Structure

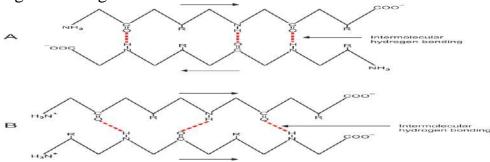
Pauling and Corey discovered another type of structure which they named β -pleated sheet (β because it was the second structure they elucidated). The surfaces of β -sheet appear "pleated" and these structures are therefore often called " β -pleated sheet'.

- A polypeptide chain in the β -pleated sheet is almost fully extended rather than being tightly coiled as in the α -helix.
- Unlike α -helix, β -pleated sheets are composed of two or more polypeptide chains.
- β -pleated sheet is stabilized by hydrogen bonds between NH and C=O groups in a different polypeptide chain whereas in α -helix, the hydrogen bonds are between NH and CO groups in the same polypeptide chain.
- In β -sheet, the hydrogen bonds are perpendicular to the polypeptide backbone rather than parallel as in the α -helixes.

The arrangement of polypeptide chains in β -pleated sheet conformation can occur in two ways:

- **1. Parallel pleated sheet:** The polypeptide chains lie side-by-side and in the same direction (with respect to N- and C-terminal), so that their N-terminal residues are at the same end (N-terminal faces to N-terminal) and stabilized by hydrogen bonding. Here the hydrogen bonds are (interchain) formed between NH of a polypeptide in one chain and carbonyl (C=O) of a neighboring chain (**Figure 4.14 B**).
- **2. Anti-parallel pleated sheet:** The polypeptide chains lie in opposite directions, i.e.

N-terminal end of one is next to the C-terminal of the other. (N-terminal faces to C-terminal) (**Figure 4.14A**). It is stabilized by interchain hydrogen bonding.



Figures 4.14 A and B: β-pleated sheet structure. (A) Anti-parallel; (B) Parallel

Tertiary Structure

The peptide chain, with its secondary structure, maybe further folded and twisted about itself forming three-dimensional arrangement of the polypeptide chain (**Figure 4.15**). Amino acid residues which are very distant from oneanother in the sequence can be brought very neardue to the folding and thus form regions essential for the functioning of the protein, like **active site** or catalytic site of enzymes. Thus, the three-dimensional folded compact and biologically active conformation of a protein isreferred to as its tertiary structure, e.g. myoglobin. The three-dimensional tertiary structure of a protein is stabilized by:

• Hydrogen bonds ,• Hydrophobic interactions ,• Van der Waals forces ,• Disulfide bond ,• Ionic (electrostatic) bonds or salt bridges



Figure 4.15: Tertiary structure of protein

Quaternary Structure of Protein

Only those proteins that have **more than one polypeptide chain** (**polymeric**) have a quaternary structure. Not all proteins are polymeric. Many proteins consist of a **single polypeptide chain and are called monomeric** proteins, e.g. myoglobin. The arrangement of these polymeric polypeptidesubunits in three-dimensional complexes is called the quaternary structure of the protein (**Figure 4.16**). Examples of proteins having quaternary structure are:— **Lactatedehydrogenase**—**Pyruvatedehydrogenase**—**Hemoglobin.** The subunits of polymeric protein are held together by noncovalent interactions or forces such as:

• Hydrophobic interactions ,• Hydrogen bond ,• Ionic bonds.

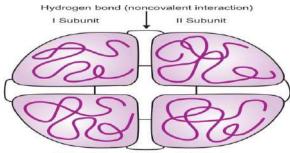


Figure 4.16: Schematic representation of quaternary structure of polymeric protein

Bonds Responsible for Protein Structure

Protein structure is stabilized by two types of bonds

- 1. Covalent bond, e.g.
 - Peptide bonds
 - Disulfide bond
- 2. Noncovalent bond, e.g.
 - Hydrogen bond
 - Hydrophobic bond or interaction
 - Electrostatic or ionic bond or salt bond or saltbridge
 - Van der Waals interactions.

Denaturation of Proteins

The three-dimensional conformation, the **primary**, **secondary**, **tertiary** and even in some cases **quaternary** structure is characteristic of a native protein. **Hydrogen bond**, **ionic bond** and **hydrophobic bond** stabilize the structure to maintain its conformation in space. This conformation can upset and disorganized **without breakage of any peptide linkage**, only by the rupture of ionic bond, hydrogen bonds and hydrophobic bond which stabilize the structure. This is called **denaturation** (**Figure 4.17**). Denaturation of proteins leads to:

- Unfolding of natural coils of native protein.
- Decrease in solubility and increase in precipitability.
- Loss of biological activities, (e.g. enzyme activity) and antigenic properties
- Increased digestibility

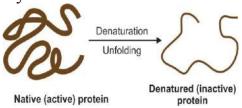


Figure 4.17: Denaturation of protein

Denaturing Agents

- Denaturation is brought about by certain:
- **Physical agents :** Heat, Ultraviolet rays and ionizing radiations can denature proteins.
- Chemical agents: Acids, alkalies and certain acid solutions of heavy metals, e.g. mercury, lead, detergents; organic solvents like alcohol, acetone, etc. denature proteins.
- **Mechanical means**: Vigorous shaking or grinding leads to denaturation of the protein.

Examples of Denatured Protein

Cooked meat or boiled egg, milk paneer, etc

Significance of Denaturation

• Digestibility of native protein is increased on denaturation by gastric HCI or by heat on cooking. Denaturation causes unfolding of native polypeptide coil so that hidden peptide bonds are exposed to the action of proteolytic enzyme in the gut. It also increases reactivity of certain groups. • Denaturation property of a protein is used in blood analysis to eliminate the proteins of the blood (deproteinization of blood).

Coagulation

Denaturation may, in rare cases be reversible, in which case the protein refolds into its original native structure, when the denaturing agent is removed. However, most proteins, once denatured, remain permanently disordered and are called **irreversible denaturations** or **coagulation**, e.g. coagulated egg white of boiled egg.

Tenth Lecture

Nucleic Acids

Nucleic Acids

Nucleic acids are polymers of nucleotides, linked by phosphodiester bond, they are therefore called polynucleotides.

- The nucleic acids are of two main types: Deoxyribonucleic acid or DNA Ribonucleic acid or RNA.
- DNA is present in nuclei and small amounts are also present in mitochondria, whereas 90% of the RNA is present in cell cytoplasm and 10% in the nucleolus.

Nucleotide

Each nucleotide consists of three components: 1. A nitrogenous base 2. A pentose sugar 3. A phosphate group.

Nitrogenous Bases of RNA and DNA

Two classes of nitrogenous bases namely purines and pyrimidines are present in RNA and DNA.

Purine Bases

• Two principal purine bases found in DNAs, as well as RNAs (Figure 9.1) are: i. Adenine (A) ii. Guanine (G).

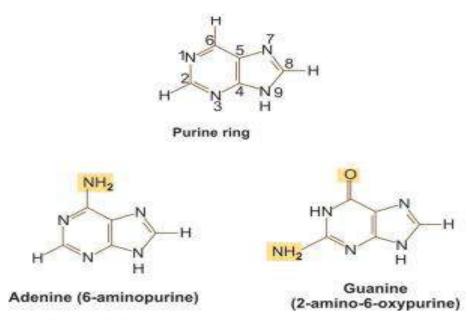


Figure 9.1: Structure of purine ring and purine bases

Pyrimidine Bases

• Three major pyrimidine bases (Figure 9.2) are: i. Cytosine (C) ii. Uracil (U) iii. Thymine (T). • Cytosine and uracil are found in RNAs and cytosine and thymine in DNA. • Both DNA and RNA contain the pyrimidine cytosine but they differ in their second pyrimidine base. DNA contains thymine whereas RNA contains uracil.

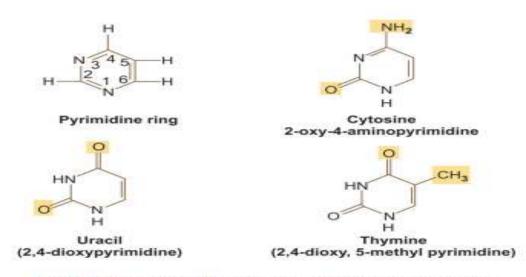


Figure 9.2: Structure of pyrimidine ring and pyrimidine bases

Pentose Sugars Present in RNA and DNA

• The pentose sugar is either D-ribose or D-2-deoxyribose (Figure 9.3). DNA and RNA are distinguished on the basis of the pentose sugar present. DNA contains D-2-deoxyribose and RNA contains D-ribose. • A pentose sugar (D-ribose or D-2-deoxyribose) is linked to a base (purine or pyrimidine) via covalent N-glycosidic bond (Figure 9.4). The term nucleoside is used for structures containing only sugar and nitrogen base. • This linkage joins nitrogen-9 of the purine base or nitrogen 1 of the pyrimidine base with carbon 1 of pentose sugar (Figure 9.4). • The atoms of the base in nucleosides are given cardinal numbers, whereas the carbon atoms of the sugars are given primed numbers as shown in Figure 9.4 to distinguish sugar atoms from those of the nitrogen base.

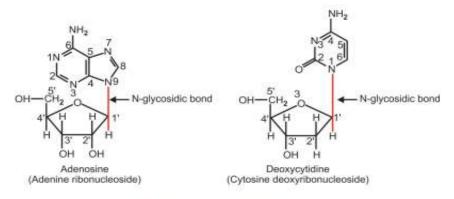


Figure 9.4: Structures of nucleoside

Table 9.1: Different major bases with their corresponding nucleosides and nucleotides		
Base	Ribonucleoside	Ribonucleotide
Adenine (A)	Adenosine	Adenosine monophosphate (AMP)
Guanine (G)	Guanosine	Guanosine monophosphate (GMP)
Uracil (U)	Uridine	Uridine monophosphate (UMP)
Cytosine (C)	Cytidine	Cytidine monophosphate (CMP)
Base	Deoxyribonucleoside	Deoxyribonucleotide
Adenine	Deoxyadenosine	Deoxyadenosine monophosphate (dAMP)
Guanine	Deoxyguanosine	Deoxyguanosine monophosphate (dGMP)
Uracil	Deoxyuridine	Deoxyuridine monophosphate (dUMP)
Cytosine	Deoxycytidine	Deoxycytidine monophosphate (dCMP)
Thymine	Deoxythymidine	Deoxythymidine monophosphate (dTMP)

Structure of nucleotides

Nucleotides are phosphorylated nucleosides. Nucleosides are nitrogen bases containing pentose sugar. The phosphate group is attached to the nucleoside by an ester linkage to the hydroxyl group of the pentose sugar. The nucleotides are of two types depending on the kind of pentose sugar present.

- 1. **Deoxyribonucleotides:** These nucleotides contain pentose sugar, deoxyribose and are monomeric units of DNA (Figure 9.5).
- 2. Ribonucleotides: These nucleotides contain pentose sugar, D-ribose and are monomeric units of RNA (Figure 9.5). Mononuleotides are nucleosides in which single phosphate group is attached to hydroxyl group of the pentose sugar. For example, AMP (adenosine monophosphate) is adenine + ribose + phosphate. If an additional phosphate group is attached to the pre-existing phosphate of mononucleotide A nucleoside diphosphate, e.g. ADP A nucleoside triphosphate, e.g. ATP results (Figure 9.6). The principle bases, their respective nucleosides and nucleotides found in the structure of nucleic acids are given in Table 9.1.

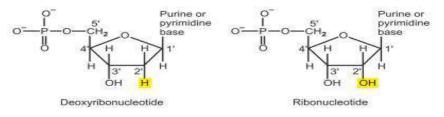


Figure 9.5: Structure of nucleotide

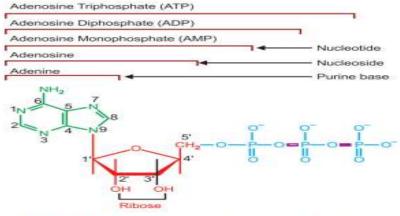


Figure 9.6: Structure of ATP and its components

Structure of DNA

• DNA is a very long, thread like macromolecule made up of a large number of deoxyribonucleotides. Deoxyribonucleotide is composed of a nitrogenous base, a sugar and phosphate group. • The bases of DNA molecule carry genetic information, whereas their sugar and phosphate groups perform a structural role. • The sugar in a deoxyribonucleotide is deoxyribose. • The purine bases in DNA are adenine (A), and guanine (G). • Pyrimidine bases are thymine (T) and cytosine (C). • DNA is a polymer of many deoxyribonucleotides linked covalently by 3', 5' phosphodiester bonds. The 3'-hydroxyl group of the sugar moiety of one deoxyribonucleotide is joined to the 5'-hydroxyl group of the adjacent sugar moiety of deoxyribonucleotide by a phosphodiester linkage (Figure 9.7).

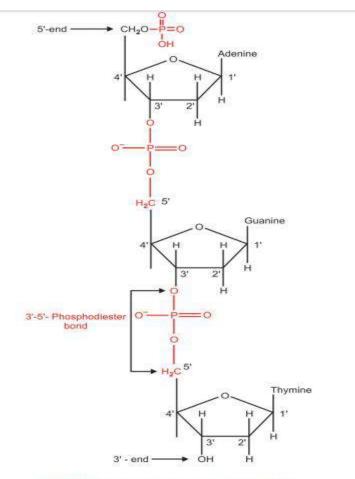


Figure 9.7: Structure of polynucleotide chain of DNA