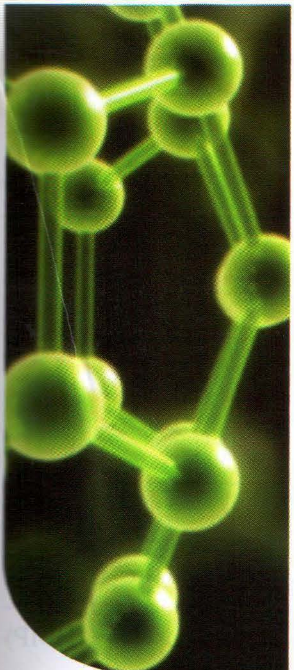

1

Carbohydrates

Carbohydrates, also called **saccharides** (Greek *Sakcharon* – sugar), are the **aldehyde or ketone derivatives of higher polyhydroxyalcohols or their anhydrides**. These are most abundant biological molecules which contain C, H and O, in the ratio of 2:1, i.e. as $(CH_2O)_n$ where *n* is 3 or more.

CLASSIFICATION OF CARBOHYDRATES

Depending upon the number of monomeric units present in the molecule, carbohydrates are classified as **monosaccharides**, **disaccharides**, **oligosaccharides** and **polysaccharides** (Fig. 1.1).

MONOSACCHARIDES

Monosaccharides are the **simple sugars**, which join in several ways to form di-, oligo- and polysaccharides.

Classification of monosaccharides

Monosaccharides are further sub-divided into different groups, according to:

- **Chemical nature** of the carbonyl group, or
- **Number of carbon atoms** in the chain (Table 1.1).

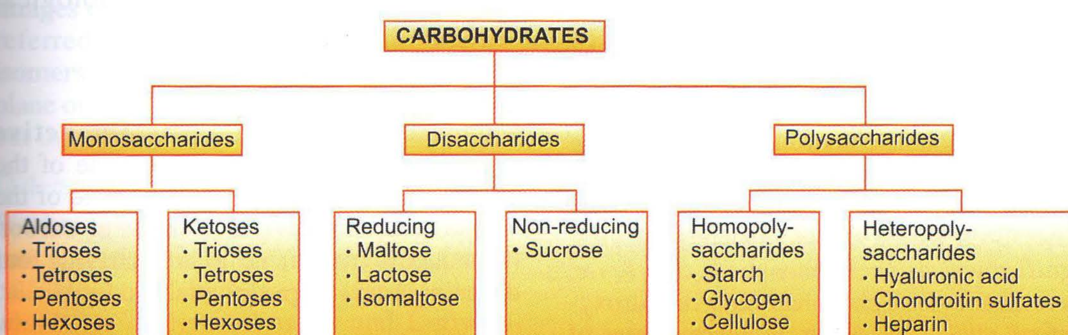

Fig. 1.1. Classification of carbohydrates.

Table 1.1. Classification of monosaccharides

Monosaccharides	Number of carbons	Aldoses	Ketoses
Trioses	3	Glyceraldehyde	Dihydroxyacetone
Tetroses	4	Erythrose	Erythrulose
Pentoses	5	Ribose	Ribulose
Hexoses	6	Glucose	Fructose

According to chemical nature of the carbonyl group

According to chemical nature of the carbonyl group monosaccharides are further sub-divided into two groups, as aldoses and ketoses:

Aldoses

A sugar is referred to as aldose, when it has an **aldehyde (–CHO) group** on carbon-l, e.g. glucose.

Ketoses

The sugar is referred to as ketose when it has a **ketone (–CO) group** at carbon-2, e.g. fructose. Sometimes, a ketose sugar may be named by inserting '**-ul**' before the suffix '**-ose**' in the name of the corresponding aldose, e.g. **erythrulose**. Erythrulose is a ketose corresponding to erythrose, which is an aldose.

According to number of carbon atoms

According to number of carbon atoms, monosaccharides are further sub-classified as trioses, tetroses, pentoses, hexoses, etc.:

Trioses

Trioses are smallest monosaccharides, having **three carbon atoms**, e.g. **glyceraldehyde** (an aldotriose) and **dihydroxyacetone** (a ketotriose). Both of these trioses are of physiological significance, as their phosphate esters, i.e. glyceraldehyde-3-phosphate and dihydroxyacetone phosphate, occur as intermediates of the glycolytic pathway.

Tetroses

Tetroses have **four carbon atoms**, e.g. erythrose (an aldotetrose) and **erythrulose** (a ketotetrose). Erythrose, in the form of erythrose-4-phosphate, occurs as an intermediate in the hexose monophosphate (HMP) shunt.

Pentoses

Pentoses contain **five carbon atoms**, e.g. **ribose** (an aldopentose) and **xylulose** (a ketopentose). Both of them occur as intermediates of the HMP shunt. Ribose is also found as a constituent of nucleotides, commonly present in RNA.

Hexoses

Hexoses contain **six carbon atoms**, e.g. **glucose** (an aldohexose) and **fructose** (a ketohexose). Glucose, also known as dextrose, is used as a source of energy in the body. Galactose is found as a constituent of milk sugar, lactose. Fructose is found as a constituent of table sugar, also called sucrose.

Some monosaccharides of biological importance are shown in Fig. 1.2.

Properties of monosaccharides

Monosaccharides are **optically active** compounds, as they can rotate plane of the polarized light. This is a characteristic of the substances that have a tetrahedral carbon (asymmetric carbon), i.e. a carbon having four different atoms or groups attached to it.

Isomerism

A compound having an asymmetric carbon atom can occur in two isomeric forms, both of which are the **non-superimposable mirror**

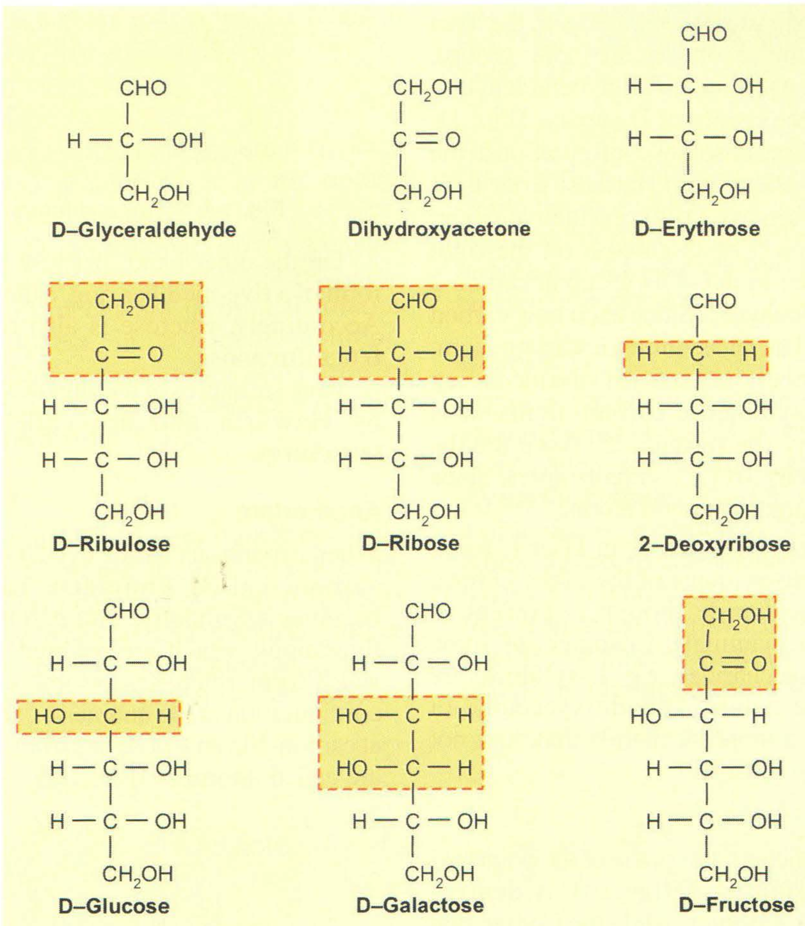

Fig. 1.2. Some monosaccharides of biological importance.

images of each other. These two isomers are referred to as **spatial isomers** or **stereoisomers** (enantiomers). Both the isomers rotate plane of the polarized light to the same degree but in opposite directions.

D-/L-isomerism

Fischer suggested that two isomers of the parent compound of the carbohydrate family, called glyceraldehyde, can exist in two forms, which are designated as D- and L-glyceraldehyde. The molecule which has –OH group around the asymmetric center (i.e. on the α carbon or the carbon adjacent to the one with the terminal primary alcoholic group) on the right hand side when –CHO group is at the top, is designated as D-glyceraldehyde. Its non-superimposable mirror image, which has –OH group around the asymmetric center on the left hand side, is designated as L-glyceraldehyde (Fig. 1.3).

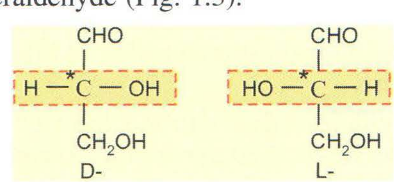

Fig. 1.3. D- and L-isomers of glyceraldehyde.

Addition of a successive carbon, in the form of –CHOH (the secondary alcoholic group), to the parent compound (D-glyceraldehyde), gives rise to the family of D-sugars. Thus, D-sugars have same absolute configuration at the asymmetric carbon atom (farthest from their carbonyl group), as D-glyceraldehyde (e.g. –OH at carbon 5 of D-glucose on the right hand, is similar to the –OH group at carbon 2 of D-glyceraldehyde). Since each new carbon atom is added as an asymmetric carbon atom, number of isomers increase with the increasing number of asymmetric carbon atoms. It is represented by the formula 2^n. Accordingly, glucose exhibits 16 (2^4) stereoisomers, since it has 4 asymmetric carbon atoms.

Every sugar, thus, exists in D or L form, each being mirror image of the other. D form of a monosaccharide though is present in abundance in mammals, L-isomers of some of the monosaccharides, e.g. L-xylulose, are also found in nature. Dihydroxyacetone (a ketotriose) is a monosaccharide that does not occur as D- or L-isomer.

Optical isomerism

An isomer which rotates plane of the polarized light to the right is designated as **dextrorotatory** (d or + isomer) while the isomer, that rotates plane of the polarized light to left, is designated as **levorotatory** (l or – isomer).

Thus, a chiral molecule with D configuration can either be dextrorotatory [D (+)] or levorotatory [D (–)], indicating its structural relationship to D-glyceraldehyde. A mixture containing equal amounts of the two isomers is called a **racemic mixture** or **dl-mixture**.

Formation of ring structure

Normally, monosaccharides exhibit ring structure.

D-glucose occurs in the form of a six-member ring, called **pyran** ring. Accordingly, glucose is also referred to as **glucopyranose** (Fig. 1.4).

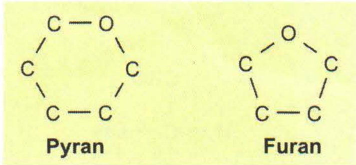

Fig. 1.4. Pyran and furan rings.

On the other hand, fructose occurs in the form of a five-member ring, called **furan** ring. Accordingly, fructose is also referred to as **fructofuranose**.

Ring structures of the sugars were proposed by Haworth and are called **Haworth structures**.

Anomerism

When a monosaccharide cyclizes, its carbonyl carbon, called **anomeric carbon**, also becomes asymmetric and exhibits two configurations, which are referred to as α-form and β-form. Such stereoisomers that differ in configuration at the anomeric carbon only, i.e. at carbon-1 in an aldose or carbon-2 in a ketose, are called **anomers** (Fig. 1.5).

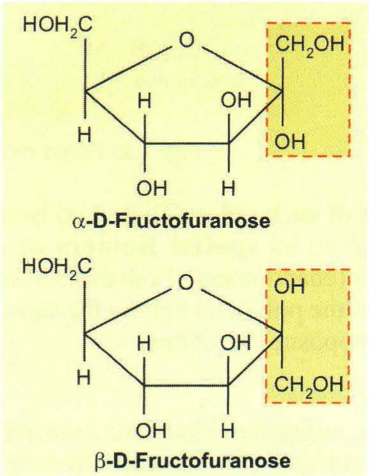

Fig. 1.5. α and β anomers of fructose.

Two anomers of glucose are freely interconvertible in an aqueous solution. At equilibrium, D-glucose occurs as a mixture of two anomers, when β and α anomers are found in the ratio of, approximately, 2:1.

Mutarotation

The α and β anomers have different physical and chemical properties, including optical rotation. During equilibrium, optical rotation of D (+) glucose slowly changes and reaches to a value of 52.5°. This phenomenon of change in optical rotation of D (+) glucose, in an aqueous solution, and reaching a constant value, due to interconversion of the two anomers, is called **mutarotation** (Fig. 1.6).

Epimerism

Sugars which differ in configuration of the –H and –OH groups around its one of the optically active carbons, are called **epimers**. For example, when compared with D-glucose, D-mannose differs in configuration at carbon 2 only. Similarly, D-galactose has different configuration at carbon 4. Thus, D-mannose and D-galactose are the two epimers of D-glucose (Fig. 1.7).

DISACCHARIDES

Disaccharides consist of two similar or dissimilar monosaccharides, which are linked together by a glycosidic bond. **Maltose**, **lactose** and **sucrose** are the disaccharides of biological importance.

Maltose

Maltose [α-D glucopyranosyl-(1,4)-α-D glucopyranose] consists of **two α-D glucose** units which are linked together by **α-1,4-glycosidic linkage**. The –OH group of carbon-4 of a glucose molecule is linked to the –OH group of carbon l (the anomeric carbon) of the other glucose molecule. This, in turn, leaves a free –OH at the anomeric carbon, i.e. carbon-l of the first glucose molecule, suggesting that maltose is a **reducing disaccharide** (Fig. 1.8).

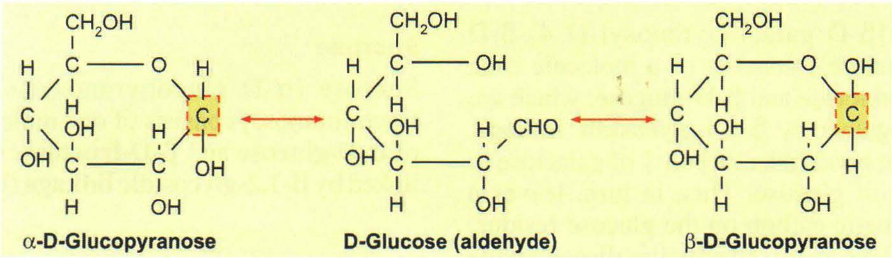

Fig 1.6. Mutarotation of glucose.

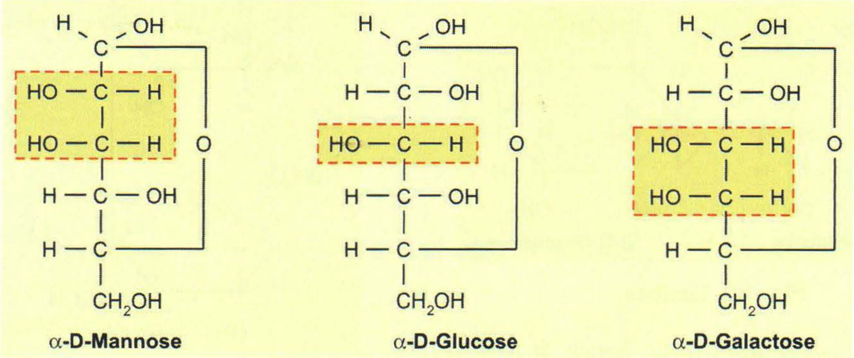

Fig. 1.7. Epimers of glucose.

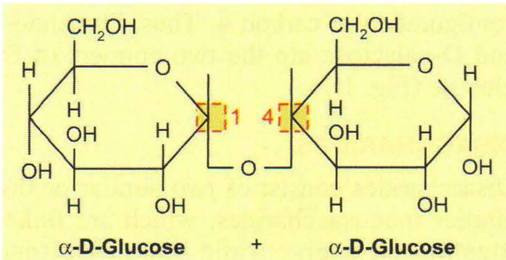

Fig. 1.8. Maltose.

Maltose is obtained as a hydrolyzed product of polysaccharides, such as starch and glycogen. It is further hydrolyzed to two glucose units by the enzyme **maltase** in the intestinal lumen.

Isomaltose

Partial hydrolysis of starch and glycogen also produces isomaltose. It is also a reducing sugar and contains two glucose units but they are linked by the **α-1,6-glycosidic linkage**.

Lactose

Lactose [β-D galactopyranosyl-(1,4)-β-D glucopyranose)] consists of a molecule each of **β-D galactose** and **β-D-glucose**, which are linked together by **β-1,4-glycosidic linkage**. Glycoside bond links carbon-1 of galactose to carbon-4 of glucose. This, in turn, leaves a free anomeric carbon on the glucose residue. Thus, lactose is also a **reducing disaccharide** (Fig. 1.9).

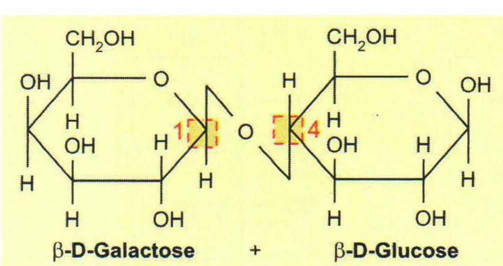

Fig. 1.9. Lactose.

Lactose is found in milk, hence, it is also called as **milk sugar**. It is synthesized in mammary glands, during lactation, from where it is secreted into milk.

Lactose is hydrolyzed by the intestinal enzyme **lactase** (β-D-galactosidase), to glucose and galactose.

Some individuals cannot metabolize lactose and experience gastrointestinal disturbances after they consume milk or milk products. This is referred to as **lactose intolerance**. It is caused by the **deficiency of the enzyme lactase**, which cleaves lactose into glucose and galactose. Lactose is a good energy source for micro-organisms present in the colon. They ferment lactose to lactic acid (lactate). In addition, there is also production of methane and hydrogen gas, which produce uncomfortable feeling, gut distension and flatulence. Lactate is also osmotically active, which, in turn, draws water into the intestine and results in diarrhea. Production of gas and diarrhea, in turn, hinder absorption of other nutrients, such as fat and protein. Its treatment includes avoidance of consumption of milk and milk products.

Sucrose

Sucrose [α-D glucopyranosyl-(1,2)-β-D fructofuranose] consists of one molecule each of **α-D-glucose** and **β-D-fructose**, which are linked by **β-1,2-glycosidic linkage** (Fig. 1.10).

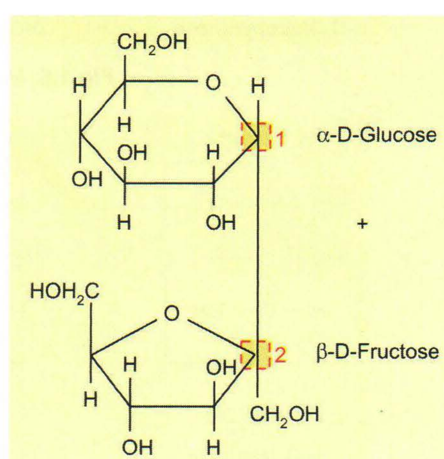

Fig. 1.10. Sucrose.

The carbonyl groups of both the monosaccharides, i.e. carbon-l of glucose and carbon-2 of fructose, participate in the formation of glycosidic bond. Since there is no free carbonyl carbon on any of its monosaccharides, sucrose, thus, is a **non-reducing sugar**.

Sucrose, also known as **invert sugar**, is the most abundant disaccharide found in plants. It is also referred to as **table sugar** or **cane sugar**. It is hydrolyzed to glucose and fructose by the intestinal enzyme **sucrase**, also referred to as **invertase**.

OLIGOSACCHARIDES

Oligosaccharides are carbohydrates built by linking of more than two (generally three to ten) monosaccharide units by glycosidic bonds, e.g. maltotriose, raffinose, etc. Most of these are not digested in human beings.

High contents of O-linked oligosaccharides occur in mucin. Oligosaccharides are usually attached to proteins at the sequences that form surface loops or turns. Some oligosaccharides also play a structural role. A single protein may contain several N- as well as O-linked oligosaccharide chains. Glycosylation may affect structure, stability, or activity of the protein.

POLYSACCHARIDES

Polysaccharides, also called **glycans**, are the polymers containing large number of monosaccharides (usually more than ten), which are linked together by glycosidic bonds. They are sparingly soluble in cold water but form a colloidal solution in hot water. Polysaccharides are neither sweet in taste nor have reducing properties.

Polysaccharides are classified into two groups, as homopolysaccharides and heteropolysaccharides:

HOMOPOLYSACCHARIDES

Homopolysaccharides or **homoglycans** are the polymers which contain identical monosaccharide units. Some homopolysaccharides of biological importance include starch, glycogen and cellulose (polymers of glucose), and inulin (a polymer of fructose).

Starch

Starch is found as a reservoir of glucose in plants, such as in cereal grains (wheat and maize), tubers (potato), etc.

Starch, structurally, comprises of two subunits, called **α-amylose** and **amylopectin**, and has both, **α-(1→4)** as well as **α-1→6**, linkages (Fig. 1.11).

α-Amylose

It is a linear polymer of glucose, where glucose residues are linked by **α-(1→4) glycosidic bonds**.

Amylopectin

It is a branched polymer of glucose. It has both, **α-1→4** (in the straight chain) and **α-1→6** (at the branching point), linkages. Branching occurs after every 24 to 30 glucose units.

Starch is the main source of carbohydrate in a human diet. **Amylase**, present in saliva and pancreatic juice, randomly, hydrolyses

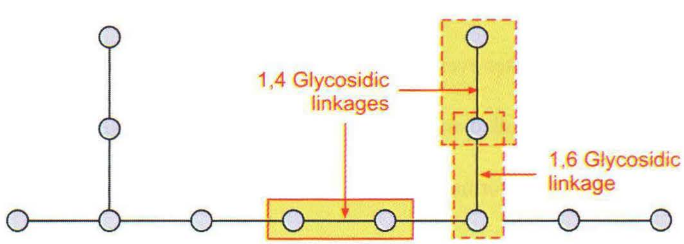

Fig. 1.11. Starch (–O– a glucose molecule).

α-1→4 glycosidic bonds in starch and yields a mixture of **maltose**, **maltotriose** and **dextrins**.

Glycogen

Glycogen is a polysaccharide **found in animals,** hence, it is also called as **animal starch**. Though, glycogen is found in all types of cell in the body but **muscle and liver are rich in glycogen**. Liver glycogen is used as a readily available source of glucose during starvation.

Glycogen also has both **α-1→4** and **α-1→6 glycosidic bonds**. It is highly branched. Branching occurs more frequently than starch, i.e. nearly after every 10 to 12 glucose units (Fig. 1.12).

Table 1.2 lists differences between starch and glycogen.

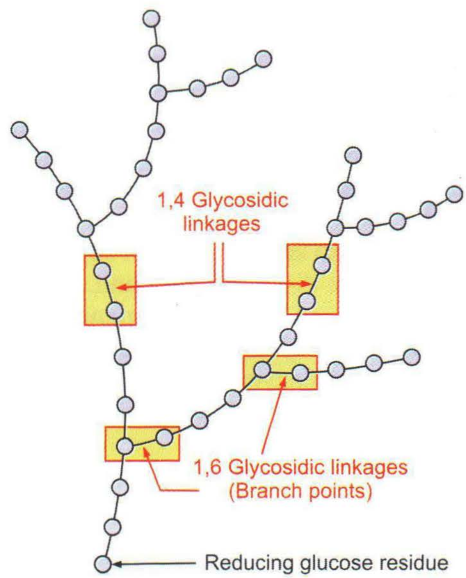

Fig. 1.12. Glycogen.

Cellulose

Cellulose is a component of plant cell wall. It is a linear polymer having **β-D glucosyl-(1→4)-α-D glucose** disaccharide units. Cellulose, thus, has β-1(1→4) glycosidic bonds.

Cellulose cannot be digested by human beings because we lack enzyme cellulase, which is capable of hydrolyzing β-(1→4) linkages. Cellulose, though cannot be utilized by human beings, it forms considerable part of the vegetarian diet and adds bulk to the feces.

Inulin

Inulin is a linear homopolymer of β-D fructose. It is found in bulbs of dahlia, onion and garlic. It is also not utilized by human beings but has a biological significance. It is clinically used for the determination of glomerular filtration rate (GFR).

Dextrans

Dextrans are highly branched homopolymers of glucose, having 1→6, 1→4 and 1→3 glycoside linkages. Various microorganisms grown

Table 1.2. Differences between starch and glycogen

Starch	Glycogen
It is a plant reserve food, mainly stored in grains.	It is animal reserve food, mainly stored in the liver and muscle.
It is less branched. Branching occurs after every 24 to 30 glucose units.	It is highly branched. Branching occurs after every 10 to 12 glucose units.
Its structure consists of two subunits, called amylose and amylopectin.	No such structural subunits are found.
It is sparingly soluble in cold water but forms paste in hot water.	It forms an opalescent solution in water.
It gives violet color with iodine.	It gives brown to red color with iodine.

in a sucrose medium produce dextrans. They have molecular weight ranging between 1 to 4 millions. They are used for intravenous infusion, as volume expanders, in the treatment of hypovolemic shock.

Chitin

Chitin is present in exoskeleton of insects. It is composed of *N*-acetylglucosamine residues, which are linked by β-1→4 glycosidic bonds.

HETEROPOLYSACCHARIDES

Heteropolysaccharides, also called **hetero-glycans**, contain repeating disaccharide units, which have negatively charged groups. They are present in the connective tissue, e.g. cartilage, tendon, skin and blood vessel walls. Since they are linked to proteins, they are also called **glycosaminoglycans**. Glycosamino-glycan-protein complexes are referred to as **proteoglycans**. Various glycosaminoglycans include hyaluronic acid, chondroitin sulfates, heparin, etc.

Hyaluronic acid

Hyaluronic acid is composed of repeating disaccharide units of **D-glucuronic acid** and ***N*-acetyl-D-glucosamine**. This polysaccharide chain is the longest of the glycosaminoglycans (GAG) and is different from others, as it is the only GAG which is non-sulfated. It is not covalently attached to protein and is not limited to animal tissues but is also found in bacteria. It is an important component of the connective tissue, synovial fluid and vitreous humor in eye. Visco-elastic behavior of hyaluronate solution, makes it an excellent biological shock absorber and lubricant.

Chondroitin sulfates

Chondroitin sulfates contain **glucuronic acid** and ***N*-acetylgalactosamine** with sulfate on the hydroxyl group of either carbon-4, (called chondroitin-4-sulfate) or carbon-6 (chondroitin-6-sulfate). They are the major components of the cartilage. They bind to collagen and hold fibers in a tight and strong network. They are also found in the aorta, tendons and ligaments.

Dermatan sulfate

Dermatan sulfate is derived from chondroitin sulfate, by enzymatic epimerization of carbon-5 of glucuronate which, in turn, forms iduronate. Thus, dermatan sulfate contains **L-iduronic acid** (with variable amounts of glucuronic acid) and ***N*-acetylgalactosamine**. It is found in skin, blood vessels, and tendon and heart valves.

Heparan sulfate

Heparan sulfates exhibit structural diversity, as these are not formed of identical disaccharides. They consist of **glucuronic** or **iduronic acid**, and **glucosamine**. Some glucosamines are also acetylated, and may have N- and/or O-sulfate groups. It is a ubiquitous cell-surface component as well as extracellular substance present in blood vessel walls and brain. Heparan sulfates, which function directly at the cell surface, interact with a variety of proteins, including some growth factors and growth factor receptors (such as fibroblast growth factors and their receptors). Formation of the ternary complexes of heparan sulfate with fibroblast growth factor and fibroblast growth factor-receptor, initiates signaling processes.

Heparin

Heparin consists of **glucuronic** or **iduronic acid** and **glucosamine**. Most of its glucosamine units are *N*-sulfated. Sulfate is also bound to the hydroxyl group on carbon-2 of uronic acid residues and carbon-3 or 6 of glucosamine. It is a highly charged polymer found in the intracellular granules of mast cells that occur in arterial walls, especially in liver, lungs and skin. Heparin is widely used clinically, to inhibit blood clotting in post-surgical patients.

Keratan sulfate

Keratan sulfate is the most heterogeneous group of glycosaminoglycans, as its sulfate content is variable. It also contains small amounts of **fucose**, **mannose**, ***N*-acetylglucosamine** and **sialic acid**. The repeating disaccharide, generally, is *N*-acetylglucosamine and galactose. Sulfate content is variable and may be present on hydroxyl group at carbon-6. Keratan sulfates are linked to proteins either by N-linked (keratan sulfate I) or O-linked (keratan sulfate II) oligosaccharides. Keratan sulfate I is found in **cornea** while keratan sulfate II occurs in loose connective tissue proteoglycan aggregates with chondroitin sulfate.

CHEMICAL NATURE AND PROPERTIES OF CARBOHYDRATES

Carbohydrates are organic molecules comprising of carbon, hydrogen and oxygen (C, H and O). Due to the presence of hydrogen and oxygen, they have reducing properties. All monosaccharides and disaccharides (except sucrose) are reducing substances and participate in **oxidation-reduction** reactions. They act as reducing agents because they have a free aldehyde or ketone group. They reduce some other compound and, in turn, get oxidized, themselves.

Monosaccharides can be oxidized by relatively mild oxidizing agents, such as ferric (Fe^{3+}) or cupric (Cu^{2+}) ions. This property forms the basis of Fehling's test, a qualitative test for reducing sugar.

- **Oxidation of the carbonyl (aldehyde) carbon** of an aldose (i.e. C-1) to the carboxyl group produces **aldonic acid**, such as D-gluconic acid, which is formed by the oxidation of D-glucose.
- **Oxidation of the carbon-6** forms **uronic acid**, such as **D-glucuronic acid,** which is formed from glucose (Fig. 1.13).

Oxidation of the carbon atoms 1 and 6 forms saccharic acid.

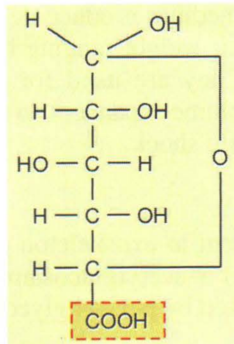

Fig. 1.13. D-glucuronic acid.

- **Reduction of monosaccharides** under mild conditions produces cyclic polyhydroxy-alcohols, called **alditols**, e.g., ribitol (from ribose), xylitol (from xylose), sorbitol (from glucose), etc.

BIOLOGICAL ROLE OF CARBOHYDRATES

Carbohydrates perform numerous functions in living organisms:

1. Polysaccharides serve as the **storage form of energy**, e.g. starch and glycogen, and as structural components, e.g. cellulose, in plants and chitin in arthropods.
2. The 5-carbon monosaccharide, ribose, is an important **component of coenzymes**, such as ATP, FAD and NAD. Ribose is also the backbone of **RNA**. The related compound, deoxyribose is a component of **DNA**.
3. Saccharides and their derivatives also play **key role in the immune system**, fertilization, preventing pathogenesis, blood clotting and development.
4. **Galactose is a component of milk sugar**, lactose. It is also found in galactolipids (in plant cell membranes) and glycoproteins (in many tissues in men and animals).
5. **Fructose** or fruit sugar, **is a component of sucrose** (cane sugar, also called table sugar). It is found in many plants. In human beings, it is absorbed in the intestine and is found in semen.

SOME IMPORTANT QUESTIONS

1. Define carbohydrate. Give their classification.
2. What are polysaccharides? Classify them.
3. Explain biological roles of carbohydrates.
4. Differentiate between starch and glycogen.
5. Write note on:
   i. Cellulose
   ii. Anomers
   iii. Epimers
   iv. Mutarotation
   v. Inulin
   vi. Homopolysaccharides
   vii. Heteropolysaccharides
   viii. Hyaluronic acid
   ix. Chondroitin sulfates
   x. Heparin
   xi. Glycosaminoglycans
   xii. Optical isomerism