Chapter 1

Carbohydrates

Carbohydrates, also called saccharides (Greek, Sakcharon: sugar), are the most abundant biological molecules containing C, H, and O, which are combined in the ratio of 2:1, i.e. as $(CH_2O)_n$, where n is 3 or more. They may be defined as the aldehyde or ketone derivatives of higher polyhydroxy-alcohols, or their anhydrides.

BIOLOGICAL IMPORTANCE OF CARBOHYDRATES

- Carbohydrates provide significant fraction of energy in the diet.
- They also act as the storage form of energy in the body.
- Carbohydrates also serve as component of a cell membrane that mediates intracellular communication.
- They also serve as structural component of many organisms, including cell wall of bacteria, exoskeleton of insects as well as the fibrous cellulose portion of the plants.

CLASSIFICATION OF CARBOHYDRATES

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

1. MONOSACCHARIDES

Monosaccharides are the simple sugars which can join in several ways to form disaccharides and polysaccharides. These are the aldehyde or ketone derivatives of the straight chain polyhydroxy-alcohols which contain 3 or more carbons.

Monosaccharides are **divided into different groups** either according to the chemical nature of the carbonyl group, or according to the number of the carbon atoms (Table 1.1).

Table 1.1: Classification of monosaccharides

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

According to the chemical nature of the carbonyl group

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

- **Aldoses:** A sugar is an aldose when it has an **aldehyde** (–CHO) **group** on carbon-l, e.g. **glucose**.
- **Ketoses:** The sugar is a ketose when it has a **ketone** (–CO) **group** at carbon-2, e.g. **fructose**.

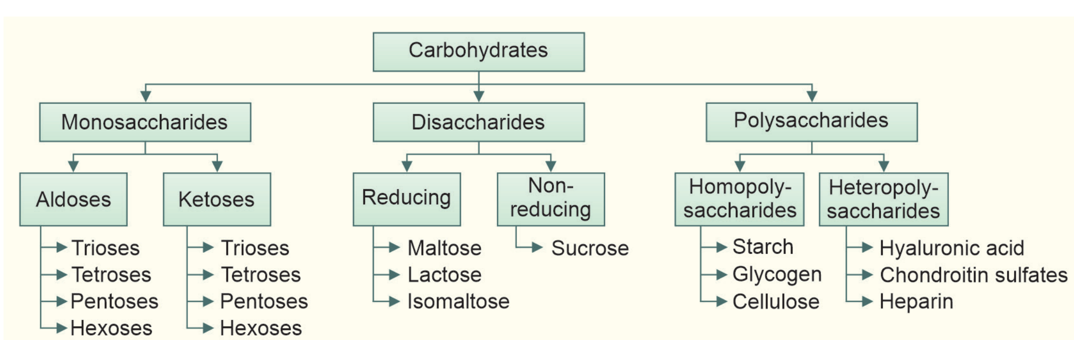

Fig. 1.1: Classification of carbohydrates

Some of the ketoses are named by inserting '**-ul**' before the suffix '**-ose**' with the name of the corresponding aldose, e.g. **erythrulose**. It is a ketose corresponding to erythrose, which is an aldose.

According to the number of the carbon atoms

According to the number of the carbon atoms monosaccharides are designated as trioses, tetroses, pentoses, hexoses, etc.:

- **Trioses:** Trioses are the smallest monosaccharides having **three carbon atoms**, e.g. **glyceraldehyde** (an aldo-triose) and dihydroxyacetone (a keto-triose). Both, of these are of physiological significance as their phosphate esters, which are referred to as glyceraldehyde-3-phosphate and dihydroxyacetone phosphate. They occur as intermediates of glycolysis.
- **Tetroses:** Tetroses have **four carbon atoms**, e.g. **erythrose** (an aldo-tetrose) and erythrulose (a keto-tetrose). Erythrose, as erythrose-4-phosphate, occurs as an intermediate in the hexose monophosphate (HMP) shunt.
- **Pentoses:** Pentoses contain **five carbon atoms**, e.g. **ribose** (an aldo-pentose) and **xylulose** (a keto-pentose). Both of them are found as intermediates of the HMP shunt. Ribose is also a constituent of the nucleotides present in RNAs.
- **Hexoses:** Hexoses contain **six carbon atoms**, e.g. **glucose** (an aldo-hexose) and fructose (a keto-hexose). Glucose, commonly known as dextrose, is used as a source of energy in the body. Galactose is a constituent of milk sugar lactose. Fructose is a constituent of the common sugar called sucrose.

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

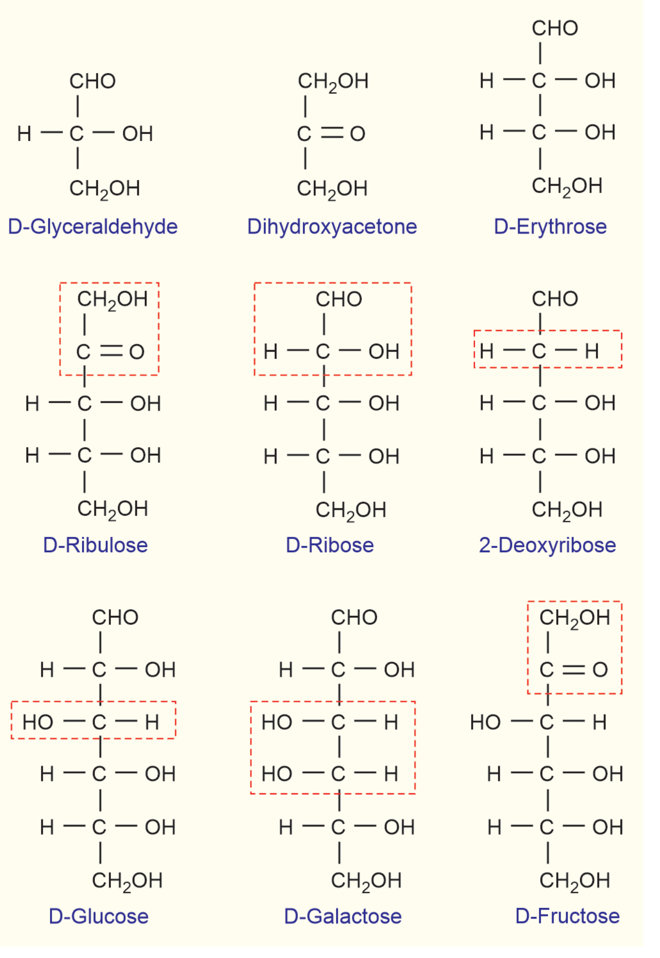

Fig. 1.2: Some monosaccharides of biological importance

PROPERTIES OF MONOSACCHARIDES

Carbohydrates exhibit different types of isomerism, such as stereoisomerism, optical isomerism, etc.

Stereoisomerism

Carbon-containing compounds commonly exist as stereoisomers, the molecules with the same chemical bonds but different stereochemistry, i.e. different configurations (the fixed spatial arrangement of atoms). This configuration is conferred by the presence of either:

- **Double bond** around which there is no freedom of rotation, or
- **Chiral centers** around which substituent groups are arranged in a specific sequence.

Asymmetric carbon: Asymmetric carbon refers to the carbon having four different atoms or groups attached to it. It is also referred to as **asymmetric center** or **chiral center** (Fig. 1.3).

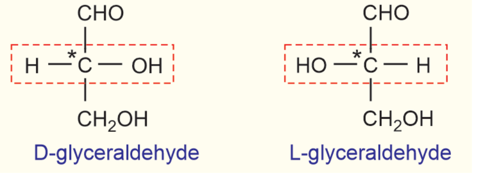

Fig. 1.3: Asymmetric carbon atom (*C)

All the monosaccharides except dihydroxyacetone, contain one or more asymmetric carbon atoms.

A molecule with one chiral center can have two stereoisomers. When two or more chiral carbons, suppose **'n'** are present, there can be $\mathbf{2^n}$ stereoisomers.

Enantiomers

As discussed above, a compound having one asymmetric carbon atom may occur in two forms, both of which are the non-super-imposable mirror images of each other. These are called enantiomers. For example, **D-glyceraldehyde** and **L-glyceraldehyde**.

- D- or L-form of a monosaccharide, in turn, is determined with respect to its spatial relationship with glyceraldehyde, which is referred to as the parent compound of carbohydrate family.

- In the Fischer projection, glyceraldehyde molecule with –OH group around the asymmetric center (i.e., the α-carbon atom or the carbon atom adjacent to the carbon atom 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**.
- Any successive addition of a carbon atom, in the form of –CHOH (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 center, farthest from their carbonyl group, as does D-glyceraldehyde (e.g. –OH at fifth carbon of D-glucose is on the right hand, similar to the –OH at the second carbon of D-glyceraldehyde).
- Since each new carbon atom (as a secondary alcoholic group) is added as an asymmetric center, the number of isomers increase with the increasing number of carbon atoms. The number of isomers so formed, thus, depends upon the number of the asymmetric carbon atoms. For example, as we know that the number of the asymmetric carbon atoms in a glucose molecule are four (i.e. n = 4), hence glucose has 2^4 (16) stereoisomers.

Optical Isomerism

Enantiomers have nearly identical chemical properties but differ in a characteristic physical property, i.e. their interaction with the plane-polarized light.

- In separate solutions, two enantiomers rotate the plane of the polarized light in the opposite direction.
- An isomer which rotates the plane of the polarized light to the right is designated as **dextrorotatory** (**d** or +).
- On the other hand, another isomer which rotates the plane of the polarized light to the left is designated as **levorotatory** (**l** or –).
- A chiral molecule with D-configuration can be either dextrorotatory [D (+)] or levorotatory [D (–)], indicating its structural relationship to D- or L-glyceraldehyde but exhibiting different types of optical rotations.
- An equimolar solution of the two enantiomers shows no optical rotation and is called a **racemic mixture (dl-mixture)**.

Epimerism

Sugars that differ in configuration of its –H and –OH groups around only one of the optically active carbon atoms are called **epimers**. For example:

- D-Mannose differs in configuration around the second carbon atom (C2) with respect to D-glucose.
- D-galactose has a different configuration than D-glucose around the fourth carbon atom (C4).
- **D-Mannose** and **D-galactose**, therefore, are the **epimers of D-glucose** (Fig. 1.4).

Formation of the Ring Structure

Generally, monosaccharides have a ring conformation.

- Cyclization of D-glucose forms a six-membered ring, which has a hemiacetal bond between the aldehyde carbonyl group of carbon-1 and the hydroxyl group of carbon-5. The ring structure, so formed, is analogous to the structure of **pyran**, which is a six-membered ring that has five carbon atoms and one oxygen atom (Fig. 1.5).

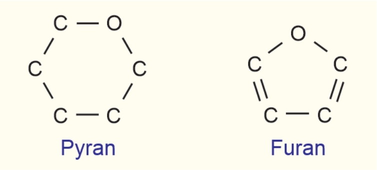

Fig. 1.5: Pyran and furan rings

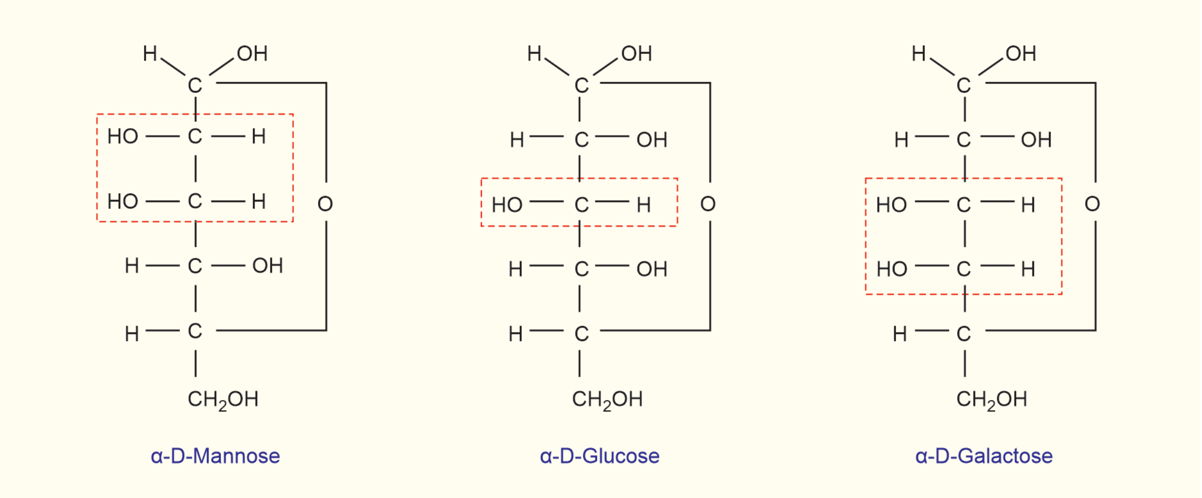

Fig. 1.4: Epimers of glucose

- Monosaccharides having a pyran ring are designated as pyranoses. Accordingly, glucose is referred to as **glucopyranose**.
- On the other hand, cyclization of D-fructose forms a five-membered ring, which has a hemiketal bond between the carbonyl group of carbon-2 and the alcoholic group of carbon-5. The ring structure, so formed, is analogous to the structure of **furan**, which is a five-membered ring that has four carbon atoms and one oxygen atom (Fig. 1.5).
- Monosaccharides having furan rings are designated as furanoses. Accordingly, fructose is referred to as **fructo-furanose**.
- The smallest monosaccharide having a furan ring is ribose.
- Ring structures of monosaccharides were proposed by Haworth and, thus, are also called **Haworth structures**.
- When a monosaccharide cyclizes, its carbonyl carbon, called anomeric carbon, also becomes asymmetric and exhibits two configurations, which are referred to as α and β **anomers**.

Anomerism

Isomeric forms of the monosaccharides that differ only in their configuration at the anomeric carbon, i.e. the first carbon (C1) in an aldose (e.g. glucopyranose) or the second carbon (C2) in a ketose (e.g. fructofuranose) are called **anomers**.

- An α-**anomer** has –OH group (at the anomeric carbon) below the plane.
- The other anomer, which has –OH group at the anomeric carbon above the plane is designated as β-**anomer** (Fig. 1.6).
- Two anomers of D-glucose, i.e. α-D-glucopyranose and β-D-gluco-pyranose have different physical and chemical properties, including optical rotation.
- They are, however, freely interconvertible in an aqueous solution.

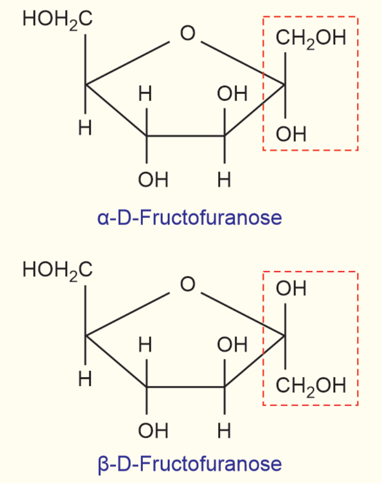

Fig. 1.6: α- and β-anomers of fructose

- During equilibrium, optical rotation of D-glucose also changes with time and reaches a constant value of 52.5°.
- At equilibrium, D-glucose is a mixture of β-anomer and α-anomer in a ratio of nearly 2:1.

SUGAR DERIVATIVES

Several derivatives of monosaccharides such as acids, alcohols, amines and methyl-glycosides are known to occur.

Acids

Monosaccharides have reducing (oxidation–reduction) properties. They act as reducing agents because they have a free aldehyde or ketone group. Due to the presence of this group, they reduce some other compound and, in turn, get oxidized.

- 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 the Fehling's reaction, a qualitative test used to show the presence of a reducing sugar.
- Oxidation of the carbonyl (aldehyde) carbon of an aldose (C1) 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 at C6 forms **uronic acid**, such as **D-glucuronic acid**, which is formed from glucose (Fig. 1.7).
- Oxidation of both the carbon atoms (i.e. C1 as well as C6) forms **saccharic acid** or **aldaric acid**.

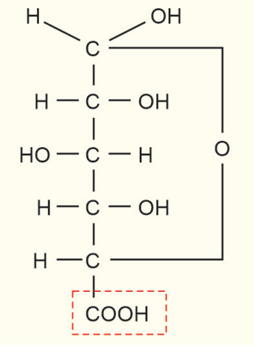

Fig. 1.7: D-Glucuronic acid

Alcohols

Sugars reduce under mild conditions and produce cyclic polyhydroxy alcohols called **alditols**, e.g. **ribitol** (a component of FMN and FAD) and **xylitol** (a sweetener used in the formation of gums and candies).

Amines

Amines, such as **glucosamine** and **galactosamine**, are formed when the —OH group at carbon-2 is substituted by the $-NH_2$ group.

- Some of the amines also **occur** as their **acetylated derivatives**.
- Several derivatives of these amines are **found in glycosaminoglycans**, such as in hyaluronic acid, chondroitin sulfates, erythromycin, etc.
- N-acetyl-neuraminic acid and its derivatives are called **sialic acids**. They are important constituents of glycoproteins and glycolipids.

Methyl-glycosides

A glycoside is a molecule that is formed by the condensation reaction, between a sugar and the hydroxyl group of some other compound, which may be another sugar (glycone) or some non-sugar molecule (aglycone).

- Glycosides can be linked by O- (an O-glycoside), N- (a glycosylamine), S- (a thio-glycoside), or C- (a C-glycoside) glycosidic bond.
- If the carbohydrate portion is glucose, the resulting glycoside is a **glucoside**; if galactose, it is referred to as a **galactoside**, etc.
- Carbon atom number-1 of a monosaccharide can also react with an alcohol, such as methanol and form **methyl-glycosides**. Methyl-glycosides are **found in glycosaminoglycans**.
- Molecules containing N-glycosidic bonds are known as **glycosyl-amines**.

2. DISACCHARIDES

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

Maltose

Maltose consists of **two glucose** (α-D-glucopyranose) **units**, which are linked together by α-1, 4-glycosidic linkage.

- In maltose, **C1** of a glucose molecule is linked to **C4** of the other molecule of glucose.
- Since –OH group at C4 of a glucose molecule is linked to the –OH group at C1 (the anomeric carbon) of the other glucose molecule, there remains the free –OH group at the anomeric carbon (C1) of the first glucose molecule. Thus, maltose is a **reducing disaccharide** (Fig. 1.8).

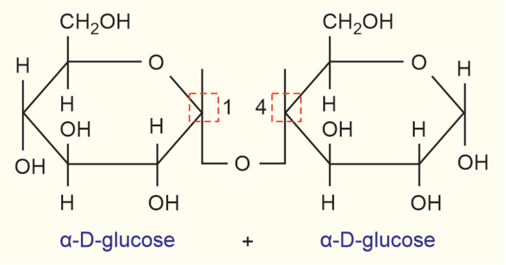

Fig. 1.8: Maltose

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

Lactose

Lactose consists of **galactose** (β-D-galacto-pyranose) and **glucose** (β-D-glucopyranose), which are linked together by α-1,4-glycosidic linkage.

- In lactose, glycoside bond links C1 of galactose to C4 of glucose.
- There is a free –OH group at the anomeric carbon (C1) of β-D-glucose. Thus, lactose is a **reducing disaccharide** (Fig. 1.9).
- Lactose **occurs** naturally **in milk**; hence lactose is also called **milk sugar**.
- In females, lactose is **synthesized during lactation** and is **secreted in milk**.
- During late pregnancy and lactation, lactose may be excreted in urine. This is referred to as **physiological lactosuria**.
- Lactose is **hydrolyzed by** the intestinal enzyme, called **lactase** (β-D-galactosidase) to **glucose and galactose**.

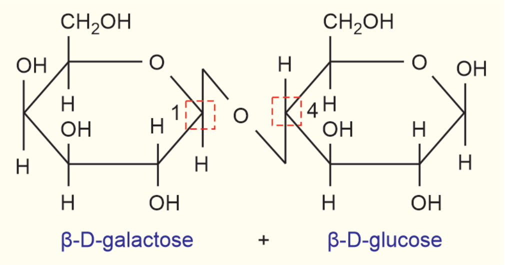

Fig. 1.9: Lactose

Sucrose

Sucrose consists of **glucose** (α-D-glucopyranose) and **fructose** (β-D-fructo-furanose), which are linked by the β-1,2-glycosidic linkage (Fig. 1.10).

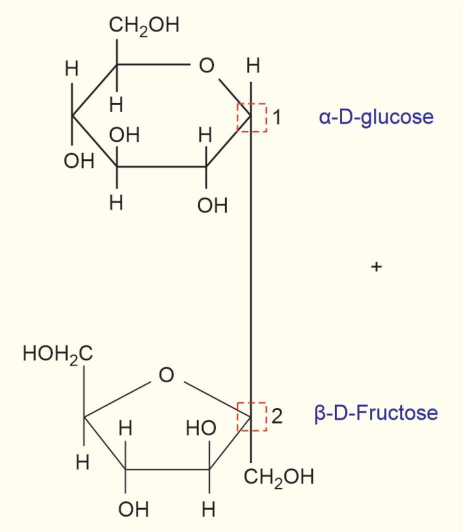

Fig. 1.10: Sucrose

- As carbonyl groups of both the monosaccharides, i.e. C1 of glucose and C2 of fructose, participate in the synthesis of the glycosidic bond and there is no free carbonyl carbon on any of its monosaccharides, thus, sucrose is a **nonreducing sugar**.
- Sucrose is also known as **table sugar, cane sugar** or **invert sugar**.
- It is the most abundant disaccharide **found in plants**.
- Sucrose is **hydrolyzed to glucose** and **fructose** by the intestinal enzyme, called **sucrase**, also referred to as **invertase**.

3. POLYSACCHARIDES

Polysaccharides are the carbohydrates which are built by the linking several monosaccharide units.

When three to ten monosaccharide units are linked by the O-glycosidic bonds, e.g. **malto-triose, raffinose**, etc. these **are** referred to as **oligosaccharides**. Most of the oligosaccharides are not digested in human. Oligosaccharides are, usually, attached to proteins, at the sequences that form surface loops or turns. Some oligosaccharides also play structural roles. A single protein may contain several N- or O-linked oligosaccharide chains. High extent of O-linked oligosaccharides occurs in mucin. Glycosylation may affect structure, stability, or activity of a protein.

Polymers of **large number of monosaccharides**, usually more than ten, are **called polysaccharides** or **glycans**.

Polysaccharides are **sparingly soluble in cold water**, but **form a colloidal solution in hot water**. They are **neither sweet in taste nor have reducing properties**.

Polysaccharides are further classified into two groups as homopolysaccharides and heteropolysaccharides.

A. Homopolysaccharides

Homopolysaccharides, also called **homoglycans**, are polymers, which have **identical monosaccharide units**.

Homopolysaccharides of biological significance include:

- Homopolymers of glucose, i.e. starch, glycogen and cellulose, and
- Homopolymer of fructose, called inulin.

i. Starch: Starch is stored as a **reservoir of food**, commonly **found in cereals** and **tubers of plants**.

- Starch **consists of two polysaccharide subunits**, referred to as α-amylose and amylopectin.
- **α-Amylose** is a **linear polymer of glucose**. Glucose molecules are linked together by α-(1→4) glycosidic bonds.
- **Amylopectin** is a **branched molecule** having, both α-(1→4) (straight chain) and α-(1→6) (branch points). Branching occurs after every 24 to 30 glucose residues (Fig. 1.11).

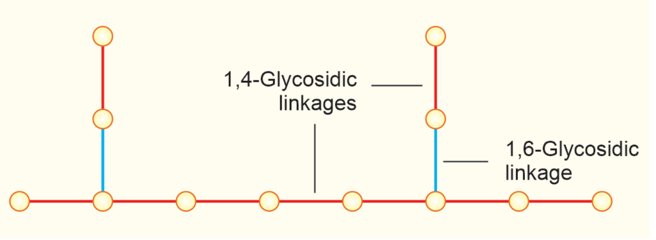

Fig. 1.11: Starch

- Starch is a **main source of carbohydrate in the human diet**.
- **Amylase**, found **in saliva and pancreatic juice**, randomly **hydrolyses α-(1→4) glycosidic bonds of amylose** (starch) and degrades starch **to** give a mixture of **maltose, malto-triose** and **dextrins**.

ii. Glycogen: Glycogen is a **polysaccharide found in animals**; hence, it is also **called animal starch**.

- Although, glycogen is found in all the cells in animals, it is **most prevalent in skeletal muscle and liver**.
- In the liver, glycogen is **degraded by the enzyme phosphorylase** and **serves as a readily available source of glucose**, especially, during initial 18–24 hours of fasting.
- Structure of glycogen is similar to amylopectin having both, a linear chain consisting of α-(1→4) glycosidic bonds and the branch points consisting of α-(1→6) glycosidic bonds. However, compared to amylopectin, in glycogen, branching occurs more frequently, i.e. after every 10–12 glucose residues. Thus, glycogen is **highly branched**, having a tree-like structure (Fig. 1.12).
- In the **liver glycogen is used as a** readily available **source of glucose during starvation**.

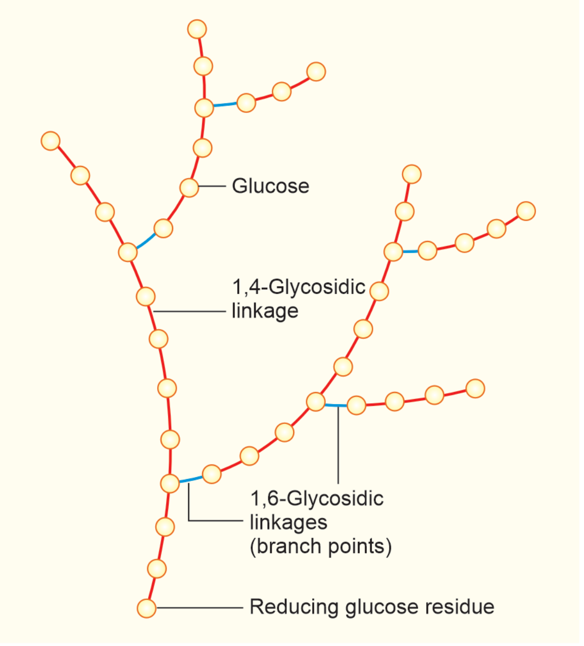

Fig. 1.12: Glycogen

Differences between starch and glycogen are shown in Table 1.2.

Table 1.2: Differences between starch and glycogen

Starch	*Glycogen*
It is a plant reserve food, mainly stored in grains	It is an 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
It consists of two subunits, called amylose and amylopectin	No such structural subunits are found
It is sparingly soluble in cold water and forms a 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

iii. Cellulose: Cellulose is found in plants. It is a **linear polymer of β-D-glucose**, and, thus, has β-(1→4) glycosidic bonds.

Though cellulose cannot be utilized by human beings, it forms a considerable part of the vegetarian food and adds to the bulk of the feces.

iv. Inulin: Inulin is found in plants such as in the bulbs of dahlia, onion and garlic.

- It is also not utilized by human beings.
- However, it is of biological significance as it is used for determining glomerular filtration rate (GFR).

v. Dextrans: Dextrans are produced by various microorganisms that are grown in sucrose media.

- Dextrans have high molecular weight.
- These are the highly branched homopolymers of glucose, having 1–6, 1–4 and 1–3 linkages.
- They are used for intravenous infusion, as plasma volume expanders in the treatment of hypovolemic shock.
- Dextrans are also used as food additives and cryopreservatives

B. Heteropolysaccharides

Heteropolysaccharides **(heteroglycans)** are the **polymers of nonidentical monosaccharide units**, also referred to as **glycosaminoglycans** (GAGs). Glycosaminoglycans, **originally designated as mucopolysaccharides**, are large complexes of negatively charged heteropolysaccharides associated with a small amount of protein, forming proteoglycans. These are the gel-forming components of the extracellular matrices. According to their monomeric composition, type of glycosidic linkage, and degree and location of sulfate units, GAGs are divided into several classes.

i. 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 (GAGs).
- 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 the eye**.
- Viscoelastic behavior of hyaluronate solution makes it an excellent biological shock absorber and lubricant.
- Its concentration is decreased in osteoarthritis.

ii. Chondroitin sulfates: Chondroitin sulfates **contain glucuronic acid and N-acetyl-galactose with sulfate** on the hydroxyl group of either carbon-4 **(chondroitin-4-sulfate)** or carbon-6 **(chondroitin-6-sulfate)**.

- These are the major components of the cartilage, where they bind to collagen and hold fibers in a tight and strong network.
- They are also **found in the aorta, tendons and ligaments**.

iii. Dermatan sulfate: Dermatan sulfate is derived from chondroitin, by enzymatic epimerization of carbon-5 of its glucuronate residues to iduronate residues.

- Dermatan sulfate **contains L-iduronic acid** (with variable amounts of glucuronic acid) and **N-acetyl-galactosamine**.
- It is **found in skin, blood vessels, tendon and heart valves**.

iv. Heparan sulfate: Heparan sulfates consist of **glucuronic or iduronic acid and glucosamine**. Some glucosamines are acetylated and may also have N- or O-sulfate groups.

- It is a ubiquitous cell-surface component as well as an extracellular substance **present in blood vessel walls and brain**.
- Some 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 initiate signaling processes.

v. 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 carbon-6 of glucosamine residues.

- It is a highly charged polymer that is **found in the intracellular granules of the mast cells** that occur in arterial walls, especially in liver, lungs and skin.

- Heparin is widely **used clinically**, to inhibit blood clotting, e.g. in postsurgical patients.
- Suitably modified low-molecular weight heparin is used in the prophylaxis and **treatment of deep vein thrombosis**.

vi. Keratan sulfates: 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.

Some Important Questions

1. Define carbohydrate. Giver their classification explain stereoisomerism of carbohydrates.

2. What are polysaccharides? Classify them.

3. Differentiate between starch and glycogen.

4. Write notes on:

I. Cellulose
II. Anomerism
III. Epimerism
IV. Inulin
V. Homopolysaccharides
VI. Heteropolysaccharides