# Carbohydrates

*Carbohydrates: polyhydroxy aldehydes or polyhydroxy ketones, or substances that give these compounds on hydrolysis.*

Carbohydrates or saccharides (Greek: sakcharon, sugar) are polyhydroxy aldehydes or polyhydroxy ketones or substances that give such molecules on hydrolysis. They are essential components of all living organisms and are, in fact, the most abundant class of biological molecules. The name carbohydrate, means "carbon hydrate", is derived from their chemical composition, which is roughly $(C-H_2O)_n$, where n ≥ 3 (many, but not all, carbohydrates have this general formula, some also contain nitrogen, phosphorus, or sulfur). Many of these compounds are synthesized from simpler substances in a process named gluconeogenesis. Others (and ultimately nearly all biological molecules) are the products of photosynthesis, through which plants and certain bacteria form carbohydrates. Carbohydrates account for approximately three-fourths of the dry weight of plants. Animals (including humans) get their carbohydrates by eating plants, but they do not store much of what they consume. In fact, less than 1% of the body weight of animals is made up of carbohydrates.

## Functions of carbohydrates

1. Carbohydrates (like glucose) serve as energy source in the living system. The metabolic breakdown of monosaccharides provides much of the energy used to power biological processes.
2. Carbohydrates serve as energy stores in the living system (like glycogen and starch).
3. Some carbohydrates are also principal components of a number of biomolecules like ribose and deoxy ribose in nucleic acids.
4. Insoluble carbohydrate polymers serve as structural and protective elements in the cell walls of bacteria and plants (like cellulose) and in the connective tissues of animals (acidic polysaccharides).

Depending on the number of sugar units in their molecules, carbohydrates can be divided into three classes:

1. Monosaccharides: consist of a single polyhydroxy aldehyde or ketone unit.
2. Oligosaccharides: consist of short chains of monosaccharide units, or residues, joined by glycosidic bonds. The most abundant are the disaccharides, with two monosaccharide units.
3. Polysaccharides: they are sugar polymers consist of more than 20 monosaccharide units (some have hundreds or thousands of units).

## Monosaccharides

*Monosaccharides:*
*Are aldehyde or ketone derivatives of straight-chain alcohols containing at least three carbon atoms and cannot be hydrolyzed to simpler compounds*

Monosaccharides are aldehyde or ketone derivatives of straight-chain alcohols containing at least three carbon atoms. They are simple sugars and cannot be hydrolyzed to form simpler saccharides. Monosaccharides are colorless, crystalline solids that are freely soluble in water but insoluble in nonpolar solvents. Most have a sweet taste.

The backbones of common monosaccharide molecules are unbranched carbon chains in which all the carbon atoms are linked by single bonds. In the open-chain form, one of the carbon atoms is double-bonded to an oxygen atom to form a carbonyl group; each of the other carbon atoms has a hydroxyl group.

*Aldose:*
*a monosaccharide containing an aldehyde group.*

 Monosaccharides are classified according to the chemical nature of their carbonyl group. If the carbonyl group is an aldehyde, as in glucose, the sugar is an aldose. If the carbonyl group is a ketone, as in fructose, the sugar is a ketose.

*Ketose:*
*a monosaccharide containing a ketone group.*

Monosaccharides can also be classified according to the number of carbon atoms in their backbones, smallest monosaccharides, those with three carbon atoms, are trioses. Those with four, five, six, seven, etc., C atoms are, respectively, tetroses, pentoses, hexoses, heptoses, etc. The two classifications may be combined to describe one sugar so that, for example, glucose is an aldohexose, whereas fructose is a ketopentose.

*Notes:*

*1. Examples of heptoses include the ketoses mannoheptulose and sedoheptulose.*

*2. Monosaccharides with eight or more carbons are rarely observed as they are quite unstable.*

## Stereochemistry of monosaccharides

Any tetrahedral carbon atom that has four different substituents is said to be asymmetric. In stereochemistry, the asymmetric carbons are called chiral centers while the symmetric carbons are called achiral atoms.

There are two facts about the molecule that contains one (or more) chiral center: **(1) it is optically active** and **(2) it occurs in more than one isomeric form**. Consequently, all monosaccharides except dihydroxyacetone (the simplest ketose) are **optically active isomeric forms** because they contain one or more chiral carbon atoms in their structures.

### Optical activity

*Optical activity: the ability of an asymmetric compound to rotate the plane of polarized light.*

 All monosaccharides (except dihydroxyacetone) are optically active due to the presence of chiral centers. Thus, they are able to rotate the plane of polarized light either clockwise or counter clockwise.

When a solution of an optically active compound rotates the plane of the polarized light clockwise, we say it is dextrorotatory; if it rotates the plane counter clockwise, we say it is levorotatory. A dextrorotatory compound is indicated by a plus sign (+) before its name, and a levorotatory compound is indicated by a minus sign (–) before its name. For example, D-glucose is dextrorotatory, it is written as (+)D-glucose, while D-Fructose is levorotatory written: (-)D-fructose.

The number of degrees by which an optically active compound rotates the plane of polarized light is called its **specific rotation** and is given the symbol [α] and can only be determined practically. The instrument used to measure the specific rotation is called polarimeter.

**Configuration about the chiral center**

There are two configurations about each chiral center, in other words, the atoms attached to a chiral center can exist in two spatial arrangements, and hence, the molecule can exist in two isomeric forms.

*Configuration:*
*the spatial relative*
*arrangement of the*
*substituents around the*
*chiral center.*

Accordingly, glyceraldehyde (the simplest aldose) has two different stereoisomers because it has one chiral center at the middle carbon atom as in figure (1.1). The two forms are mirror images of each other so they are called enantiomers. By convention, one of these two forms is designated the D isomer, the other the L isomer.
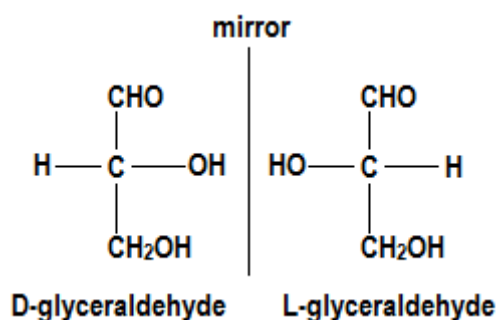


**Figure (1.1): The two stereoisomers of glyceraldehyde**

*Number of stereoisomers=*
*$2^n$, where n represents the*
*number of chiral atoms and*
*2 represents the number of*
*possible configurations*
*about each chiral atom.*

In general, a molecule with n chiral centers can have $2^n$ stereoisomers. Glyceraldehyde has $2^1 = 2$ stereoisomers; the aldohexoses, with four chiral centers, have $2^4 = 16$ stereoisomers.

The stereoisomers of monosaccharides (of each carbon-chain length) can be divided into two groups that differ in the configuration about the chiral center most distant from the carbonyl carbon. When the hydroxyl group at this reference carbon is on the right in the projection formula, the sugar is the D isomer; when on the left, it is the L isomer. The L sugars, in accordance with this convention, are mirror images of their D counterparts, as is shown below in Fischer projection for glucose (figure 1.2).

*D-Monosaccharide:*
*A monosaccharide that has the OH group at the last chiral atom to the right when drawn in Fischer projection.*

*L-Monosaccharide:*
*A monosaccharide in which the OH group at the last chiral atom is to the left when drawn in Fischer projection.*
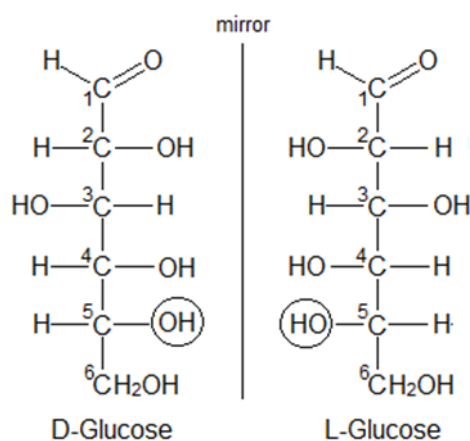


**Figure (1.2): Fischer projections for D-glucose and L-glucose, the reference hydroxyl groups are shown in cycles.**

*Diastereomers: pairs of stereoisomers that are non-superimposable, non-mirror images of one another.*

*Enantiomers: pairs of stereoisomers that are mirror images of one another.*

It is important to know that the carbons of a sugar are numbered beginning from the carbonyl group (the functional group). Stereoisomers that are mirror images of each other are called **enantiomers**. Pairs of stereoisomers that are not mirror images of each other are called **diastereomers**. To represent three-dimensional sugar structures on paper, we often use Fischer projection formulas. The stereochemistry and names of the D-aldoses are presented in figure (1.3).

*Epimers: pairs of monosaccharides that have the same molecular formula and bonding but differ in the configuration about one chiral center.*

Sugars that differ only by the configuration about one C atom are known as **epimers** of one another. Thus D-glucose and D-mannose are epimers with respect to C2, whereas D-glucose and D-galactose are epimers with respect to C4 .However, D-mannose and D-galactose are not epimers of each other because they differ in configuration about two of their carbon atoms.
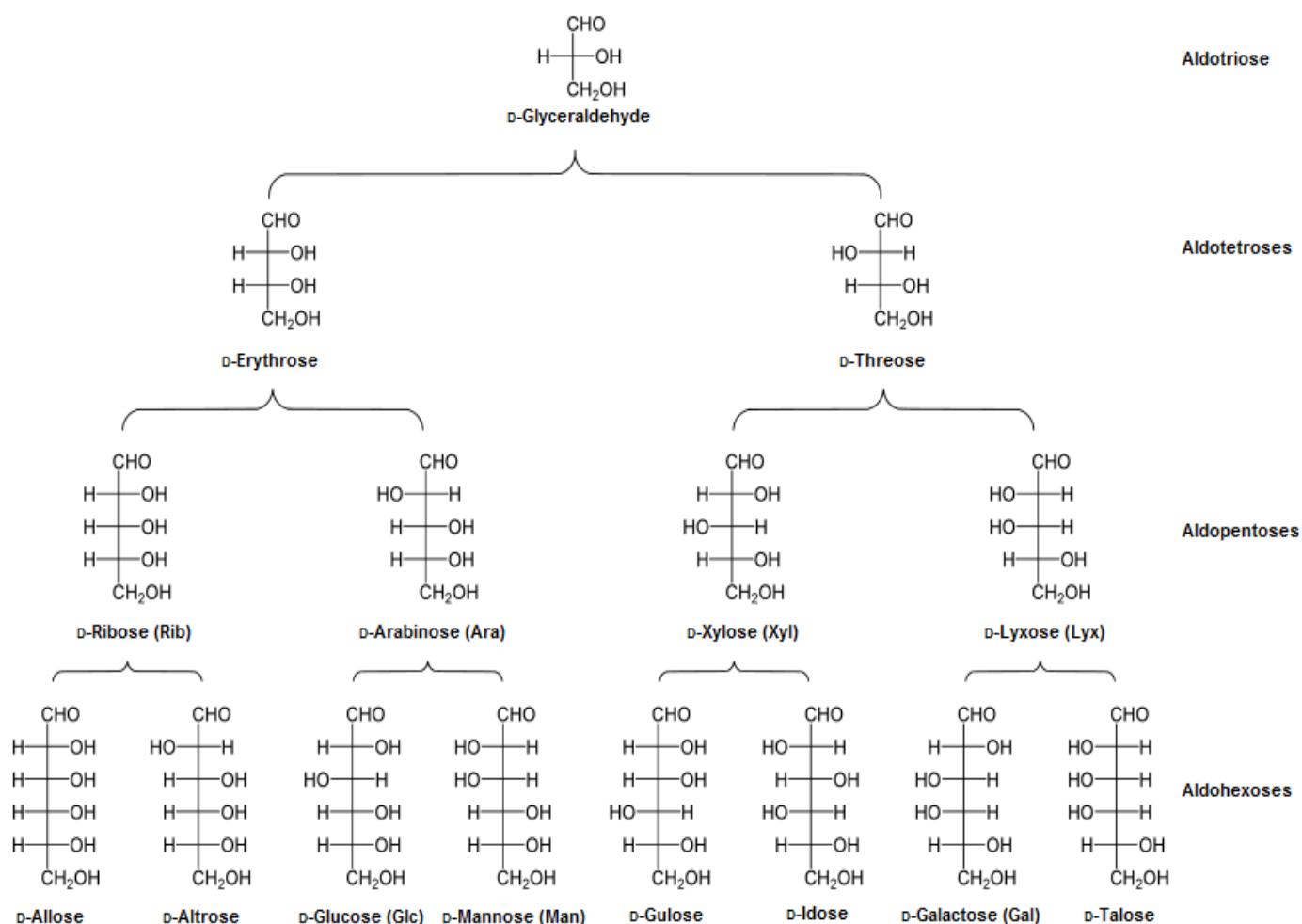
**Figure (1.3): Fischer projection formulas and names of the D-aldoses. Note: the L-aldoses are simply the mirror images of these D-aldoses.**

D-Glucose is the only aldose that commonly occurs in nature as a monosaccharide; however, it and several other monosaccharides including D-glyceraldehyde, D-ribose, D-mannose, and D-galactose are important components of larger biological molecules. L-sugars are biologically much less abundant than D sugars.

The position of their carbonyl group gives ketoses one less chiral center than their isomeric aldoses (e.g., compare D-fructose and D-glucose).Those with their ketone groups at C2 are the most common forms. Figure (1.4) shows structures and names of the D-ketoses.
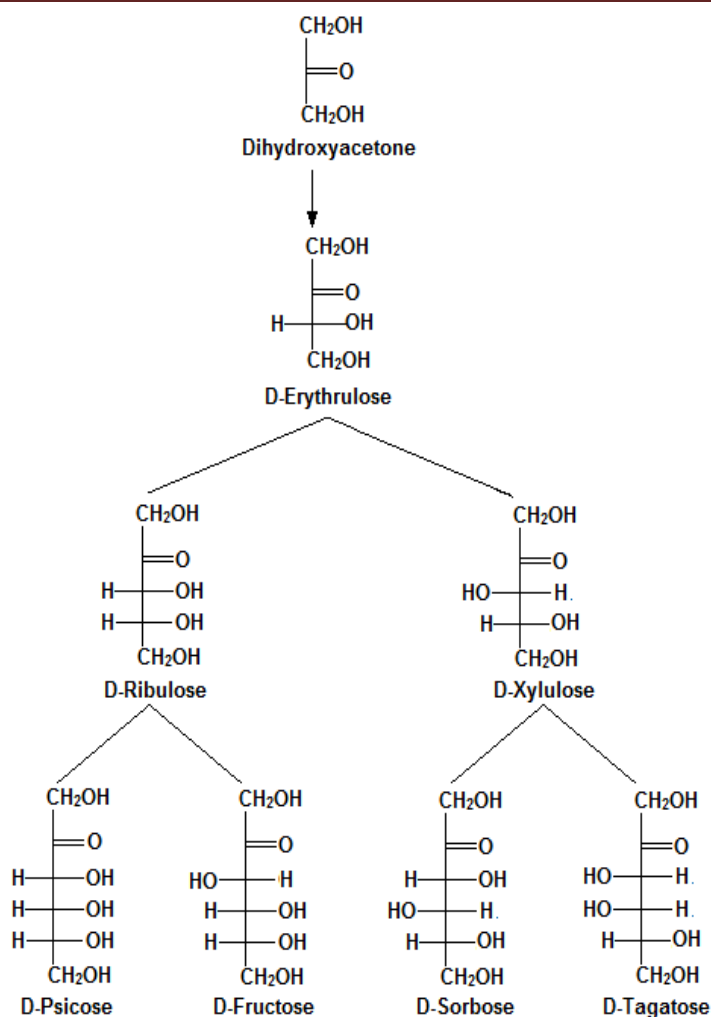
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**Figure (1.4): Fischer projection formulas and names of the D-ketoses. L-ketoses are the mirror images of them.**

Note that some of these ketoses are named by the insertion of -ul- before the suffix -ose in the name of the corresponding aldose; thus D-xylulose is the ketose corresponding to the aldose D-xylose. Dihydroxyacetone, D-fructose, D-ribulose, and D-xylulose are the biologically most prominent ketoses.

## Pyranose and Furanose rings formation

For simplicity, we have -until now- represented the structures of aldoses and ketoses as straight-chain molecules. In fact, in aqueous solution, aldotetroses and all monosaccharides with five or more carbon atoms in the backbone occur predominantly as cyclic (ring) structures in which the carbonyl group has formed a covalent bond with the oxygen of a hydroxyl group along the chain.

Aldehyde groups and ketone groups can react with the hydroxyl groups of alcohols to form hemiacetals and hemiketals respectively as shown below:
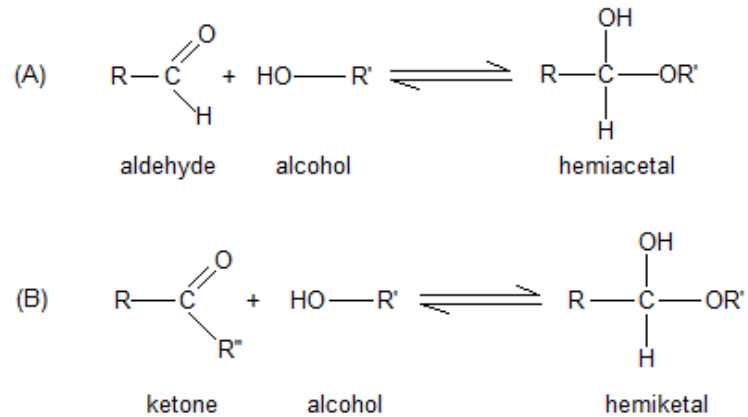


A similar reaction can occur intramolecularly in monosaccharides where the aldehyde or the ketone groups react with one of the hydroxyl groups in the same molecule.
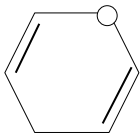


**Pyran**

In glucose, the aldehyde group (carbon number 1) reacts with the hydroxyl group at carbon number 5 to form a six-membered ring which is structurally similar to **pyran** (a simple heterocyclic compound) thus, it is called a **pyranose** ring. The cyclic form of glucose with a six-membered ring is therefore known as **glucopyranose**. Figure (1.5) shows the ring formation in glucose.

*Pyranose: A six-membered cyclic hemiacetal form of a monosaccharide.*

Ring formation gives glucose molecule one additional chiral center. The new chiral center is simply the former carbonyl carbon. Remember that two isomeric forms can exist for each chiral atom, so the resulting pair of stereoisomers is known as anomers and the carbonyl carbon is referred to as anomeric carbon atom.

*Haworth projection:*
*A way to view furanose and pyranose forms of monosaccharides. The ring is drawn flat with the anomeric carbon on the right and the oxygen atom to the rear.*

The systematic names of the two anomers of D-glucose are α-D-glucopyranose (in which the hydroxyl group at the anomeric carbon is drawn below the ring) and β-D-glucopyranose (in which the hydroxyl group at the anomeric carbon is drawn above the ring). Note that the configurations of the substituents to each carbon atom of these sugar rings are usually represented by their **Haworth projection formulas**.

*Anomers: pairs of monosaccharides that differ in configuration only at the anomeric carbon.*

*Anomeric carbon: The hemiacetal or the hemiketal carbon (the former carbonyl carbon) of the cyclic form of a monosaccharide.*
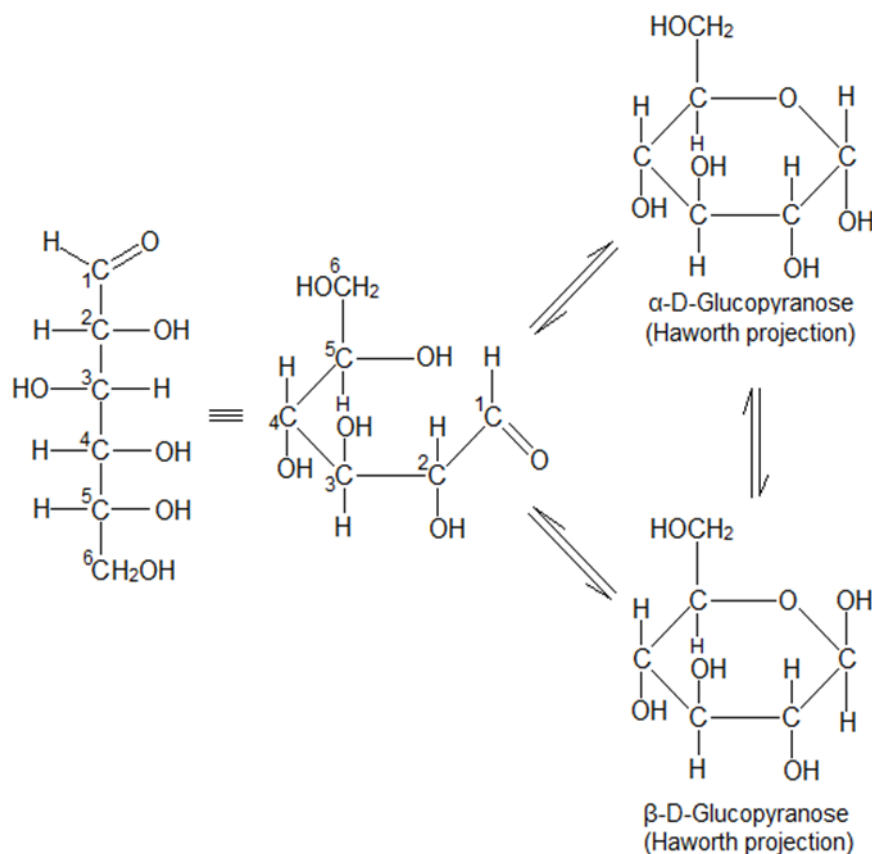


α-D-Glucopyranose
(Haworth projection)

β-D-Glucopyranose
(Haworth projection)

**Figure (1.5): Ring formation in D-glucose occurs via the reaction of carbonyl group with OH group at C 5 atom.**

*Mutarotation:*
*a phenomenon of the spontaneous change in specific rotation that accompanies the equilibration of α and β anomers in aqueous solution.*

The two anomers of D-glucose have different physical and chemical properties. For example, the values of the specific optical rotation for α-D-glucose and β-D-glucose are, respectively, +112.2° and +18.7°.When either of these pure substances is dissolved in water, however, the specific optical rotation of the solution slowly changes until it reaches an equilibrium value of +52.7°. This phenomenon is known as **mutarotation**.

*Interconversion: a process in which the α and β anomers convert into each other in aqueous solution via the linear structure.*

Mutarotation, in fact, occurs because the two anomers of D-glucose undergo **interconversion** in their aqueous solutions; in other words, when a pure sample of α anomer is dissolved in water it gradually converts into the β anomer via the linear form of glucose and vice versa. This interconversion leads to the formation of an equilibrium mixture consisting of 63.6% of the β anomer and 36.4% of the α anomer as shown in figure (1.6).
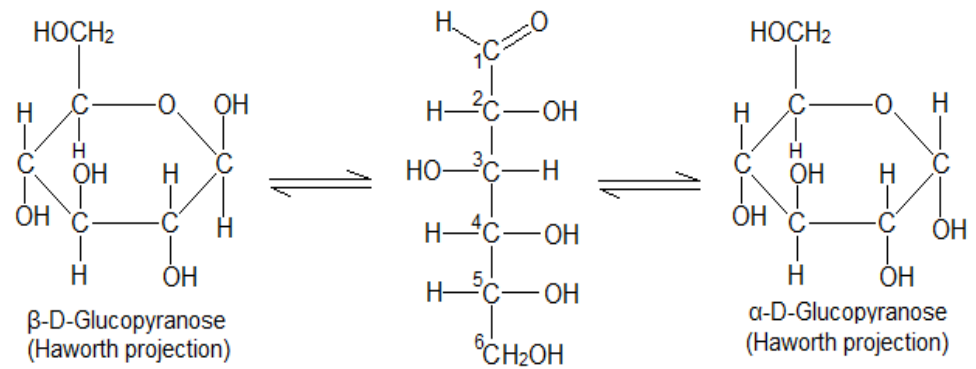
**Figure(1.6): Interconversion between the two anomers of D-glucose occurs via the linear form.**

Yet, since the linear forms of these monosaccharides are normally present in only small amounts, these carbohydrates are accurately described in  amounts, these carbohydrates are accurately described as cyclic polyhydroxy hemiacetals or hemiketals (cyclic forms).

In D-fructose, the carbonyl group (ketone group) reacts with the hydroxyl group at carbon number 5 to form a five-membered ring that structurally resembles **furan** (a simple heterocyclic compound) so the ring is named **furanose** and D-fructose in its cyclic form is called **D-fructofuranose** as shown in figure (1.7).
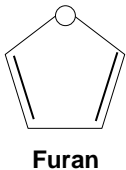


**Furan**

*Furanose: A five-membered cyclic hemiacetal form of a monosaccharide.*
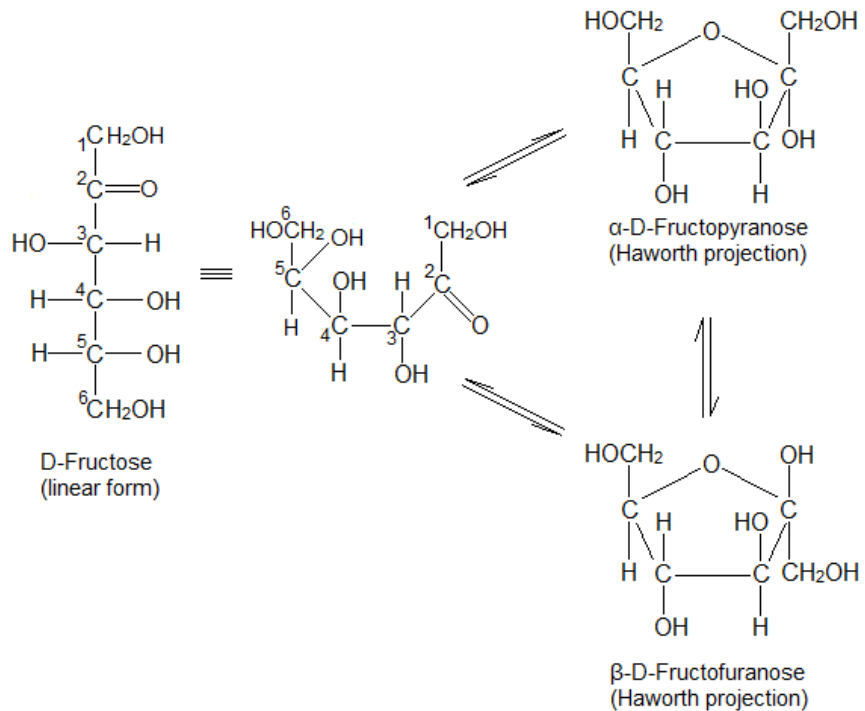


**Figure (1.7): Ring formation in D-fructose occurs via the reaction of carbonyl group with OH group at C 5 atom.**

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## The real conformations of monosaccharides

The use of Haworth formulas to represent monosaccharides may lead to the incorrect impression that furanose and pyranose rings are planar. This cannot be the case, however, because all of the atoms in these rings are tetrahedral (they are ($sp$3) hybridized).

The Pyranose ring, like the cyclohexane ring, may assume a **boat** or a **chair** conformation as shown below (fig.1.8).

*Note:*
*Although, in principle, hexoses and larger sugars can form rings of seven or more atoms, such rings are rarely observed because of the greater stabilities of the five- and six-membered rings that these sugars can also form. The internal strain of three- and four-membered sugar rings makes them unstable with respect to linear forms.*
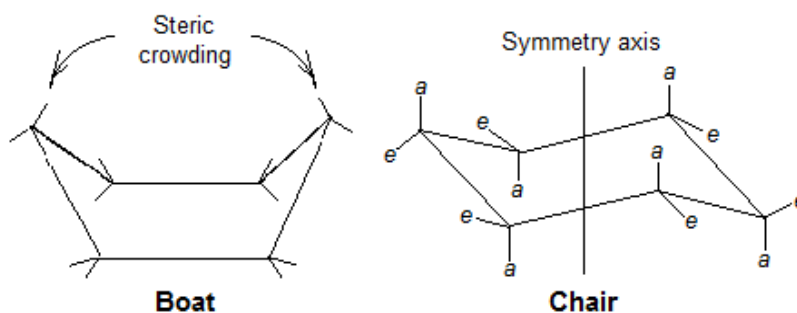


**Figure (1.8): Conformations of the six-membered ring. Axial position (a) where the substituents extend parallel to the symmetry axis. Equatorial position (e) the substituents extend nearly perpendicular to the axis.**

Note:
A five-membered furanose ring is so close to being planar and, in fact, it may assume two possible conformations: the envelope that has four atoms in a plane and the twist that has only three in a plane.

The relative stabilities of the two conformations depend on the stereochemical interactions between the substituents on the ring. The boat conformation is less stable due to crowding of the substituents (resulting in steric hindrance among them).

The ring substituents on the chair conformation (fig. 1.8) fall into two geometrical orientations: they may be either axial (ax), projecting parallel to the vertical axis through the ring, or equatorial (eq), projecting nearly perpendicular to this axis.

Since the axial and equatorial groups on a cyclohexane ring are conformationally interconvertible, pyranose ring has two alternative chair forms (fig. 1.9); the one that predominates usually has the lesser crowding among its axial substituents.
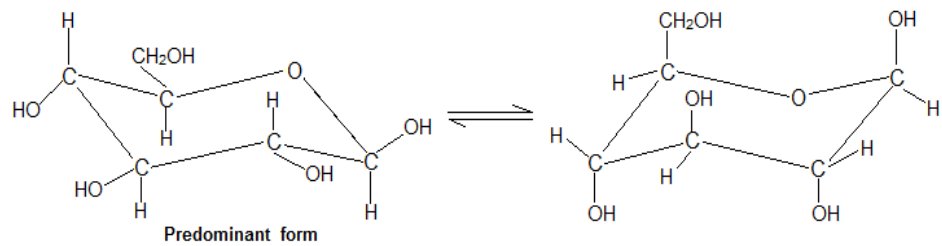
**Figure (1.9): The two alternative chair conformations of β-D-glucopyranose. In the conformation on the left, which predominates, the relatively bulky OH and CH$_2$OH substituents all occupy equatorial positions, whereas in that on the right they occupy the more crowded axial positions.**

The majority, about 64% of D-glucose exist in β form because when the molecule is in chair conformation, all the bulky hydroxyl groups will be placed in equatorial position which have lesser steric hindrance between the bulky groups. Thus, β-D-glucose is more stable than α-D-glucose that occupied typically 35% of D-glucose molecules, whereas the remaining 1% is in the open-chain form.

## Monosaccharides as reducing agents:

A reducing sugar is any sugar that either has an aldehyde group or is capable of forming one in solution through isomerism. The aldehyde functional group allows the sugar to act as a reducing agent, for example in the Tollens' test or Benedict's reagent.

Reducing sugars can be oxidized by relatively mild oxidizing agents such as cupric ion (Cu$^{2+}$) (Fig. 1-10). The carbonyl carbon (aldehyde group) is oxidized to a carboxylic acid, at the same time; cupric ion (Cu$^{2+}$) is reduced to cuprous ion (Cu$^{1+}$).

*Reducing sugar: A carbohydrate that reacts with a mild oxidizing agent under basic conditions to give an aldonic acid; the carbohydrate reduces the oxidizing agent.*
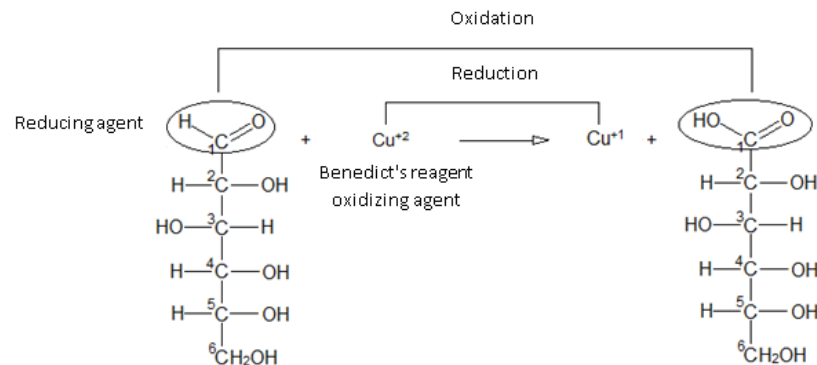


**Figure (1.10): Oxidation process by reducing sugar.**

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In fact, a sugar is classified as a reducing sugar only if it has an open-chain form with an aldehyde group or a free hemiacetal group. Monosaccharides which contain an aldehyde group are known as aldoses, and those with a ketone group are known as ketoses. The aldehyde can be oxidized via a redox reaction in which another compound is reduced. Thus, a reducing sugar is one that reduces certain chemicals. Sugars with ketone groups in their open chain form are capable of isomerizing via a series of tautomeric shifts to produce an aldehyde group in solution. Therefore, ketone-bearing sugars like fructose are considered reducing sugars but it is the isomer containing an aldehyde group which is reducing since ketones cannot be oxidized without decomposition of the sugar. This type of isomerization is catalyzed by the base present in solutions which test for the presence of aldehydes. Under the basic conditions of the oxidation process, Carbon 1 (a $CH_2OH$ group) of a ketose is not oxidized directly. Instead, a 2-ketose exists in equilibrium with an aldose by way of an enediol intermediate (Fig. 1.11).
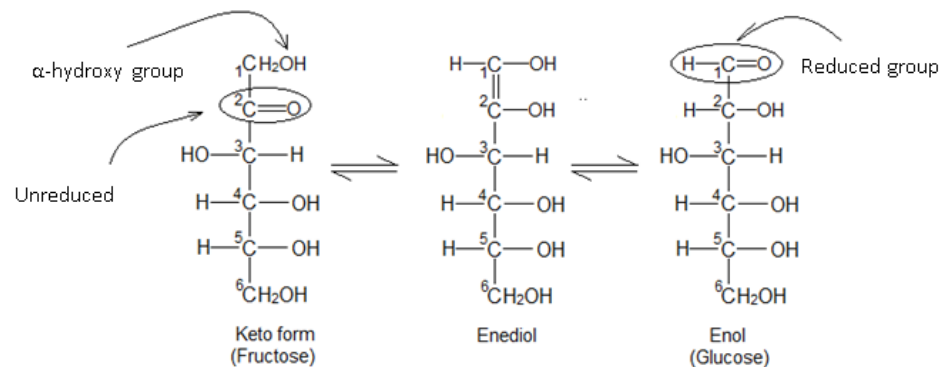


**Figure (1.11): Equilibrium between ketose and aldose by way of an enediol intermediate.**

### Disaccharides and Oligiosaccharides:

*Disaccharide: A carbohydrate containing two monosaccharide units joined by a glycosidic bond.*

Most carbohydrates in nature contain more than one monosaccharide unit. Those that contain two units are called disaccharides; those that contain three units are called trisaccharides, and so forth. We use the general term oligosaccharide to describe carbohydrates that contain from three to ten monosaccharide units, which can be hydrolyzed by enzymes or acid to give the constituent monosaccharide units. Carbohydrates containing larger numbers of monosaccharide units are called polysaccharides.

Figure (1.12) represents the chemical structure of Raffinose, which is a trisaccharide composed of galactose, glucose and fructose. Raffinose can be found in peas, beans, cabbage, brussels sprouts, broccoli, asparagus, other vegetables and whole grains.

*Oligosaccharide: A carbohydrate containing from three to ten monosaccharide units, each joined to the next by a glycosidic bond.*

*Polysaccharide: A carbohydrate containing a large number of monosaccharide units, each joined to the next by one or more glycosidic bonds.*
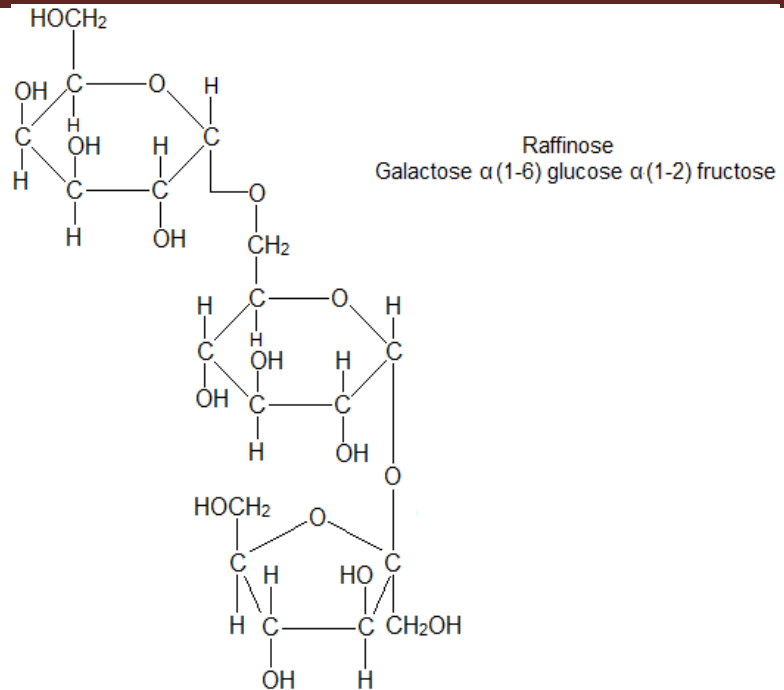
**Figure (1.12): Chemical structure of Raffinose.**

In a disaccharide, two monosaccharide units are joined by a glycosidic linkage between the anomeric carbon of one unit and an OH group of the other unit. Three important disaccharides are sucrose, lactose, and maltose.

### Maltose:

Maltose derives its name from its presence in malt, the juice from sprouted barley and other cereal grains. It consists of two units of D-glucopyranose joined by a glycosidic bond between carbon 1 (the anomeric carbon) of one unit and carbon 4 of the other unit. Because the oxygen atom on the anomeric carbon of the first glucopyranose unit is alpha, the bond joining the two units is an α-1,4-glycosidic bond.



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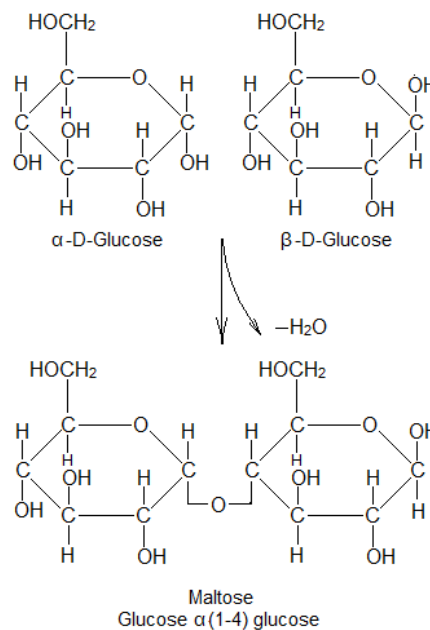
Maltose has been recorded occasionally in plants. It is usually obtained as a product of the enzyme hydrolysis of starch during germination or malting process. It is used as a sweetener and as a substrate for fermentation. Maltose is a reducing sugar; the hemiacetal group on the right unit of D-glucopyranose is in equilibrium with the free aldehyde and can be oxidized to a carboxylic acid (Fig. 1.13).

*Note: If two monosaccharides are linked through their anomeric centers the disaccharide formed is a non-reducing disaccharide. If one monosaccharide is linked by one of its other hydroxyl groups, then the anomeric center is unsubstituted and a reducing disaccharide occurs.*
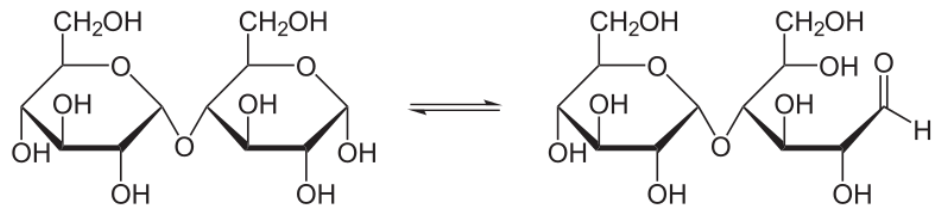


**Figure (1.13): Equilibrium between cyclic and open-chain form in one ring of maltose.**

**Lactose:**

Lactose is the principal sugar present in milk. It accounts for 5 to 8% of human milk and 4 to 6% of cow's milk. It is digested by the enzyme Lactase. Pure lactose is found in whey, the watery byproduct of cheese production.

Lactose consists of D-galactopyranose bonded by a β-1,4-glycosidic bond to carbon 4 of D-glucopyranose. It is a reducing sugar, because the cyclic hemiacetal of the D-glucopyranose unit is in equilibrium with its open-chain form and can be oxidized to a carboxyl group.
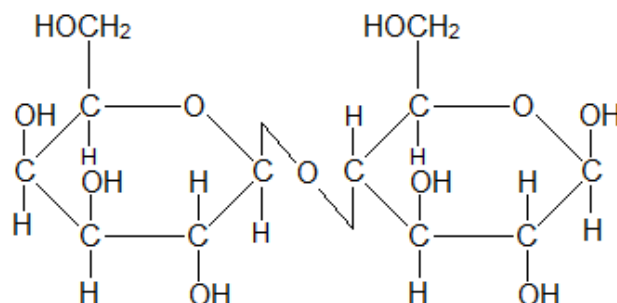


Lactose
Galactose β(1-4) glucose

**Sucrose:**

Sucrose (table sugar, $10^8$ tons of sucrose are produced annually for consumption) is the most abundant disaccharide in the biological world. It is found in fruits, nectar, sugar cane, and sugar beets; maple syrup contains about 65% sucrose, with glucose and fructose present as well. Caramel is the solid residue formed from heating sucrose. A flavoring agent called invert sugar is produced by the hydrolysis of sucrose under acidic conditions, which breaks it apart into glucose and fructose; invert sugar is sweeter than sucrose because of the fructose. Some of the sugar found in honey is formed in this fashion; invert sugar is also produced in jams and jellies prepared from acid-containing fruits.

In sucrose, carbon 1 of α-D-glucopyranose bonds to carbon 2 of D-fructofuranose by an α-1,2-glycosidic bond. Because the anomeric carbons of both the glucopyranose and fructofuranose units are involved in formation of the glycosidic bond, neither monosaccharide unit is in equilibrium with its open-chain form. Thus sucrose is a non-reducing sugar.



Sucrose
Glucose α(1-2)β -fructose
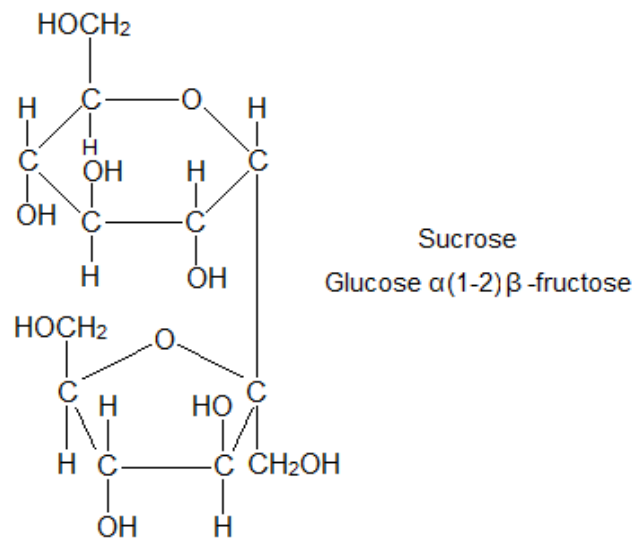
**Polysaccharides:**

Polysaccharides consist of large numbers of monosaccharide units bonded together by glycosidic bonds. The polysaccharides found in nature either serve a structural function (structural polysaccharides) or play a role as a stored form of energy (storage polysaccharides). They are not reducing sugars, since the anomeric carbons are connected through glycosidic linkages. Three important polysaccharides, all made up of glucose units, are starch, glycogen, and cellulose.

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**Starch (Amylose and Amylopectin):**

Starch is used for energy storage in plants. It is found in all plant seeds and tubers and is the form in which glucose is stored for later use. Starch can be separated into two principal polysaccharides: amylose and amylopectin. Although the starch from each plant is unique, most starches contain 20 to 25% amylose and 75 to 80% amylopectin.

Complete hydrolysis of both amylose and amylopectin yields only D-glucose. Amylose is composed of continuous, unbranched chains of as many as 4000 D-glucose units joined by α-1,4-glycosidic bonds. Amylopectin contains chains of as many as 10,000 D-glucose units also joined by α-1,4-glycosidic bonds. In addition, considerable branching from this linear network occurs. New chains of 24 to 30 units are started at branch points by α-1,6-glycosidic bonds (Fig. 1.14).
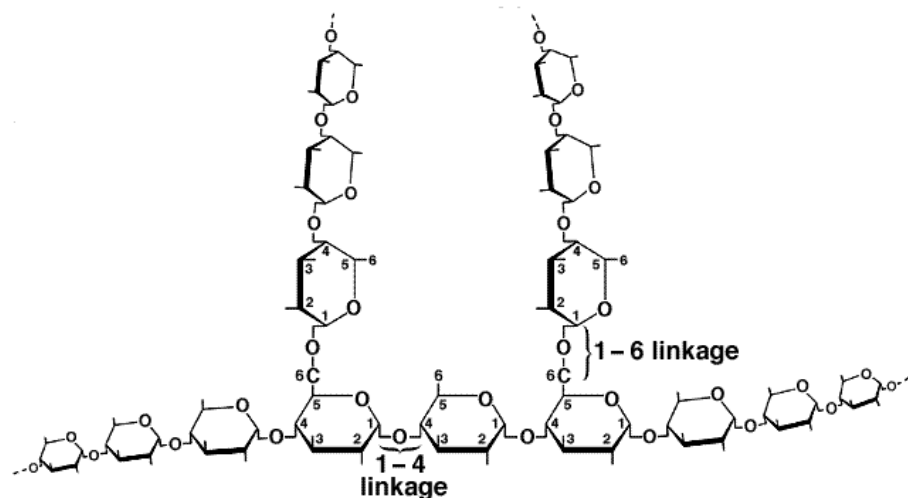


**Figure (1.14): Amylopectin is a branched polymer of approximately 10,000 D-glucose units joined by α-1,4-glycosidic bonds. Branches consist of 24-30 D-glucose units started by α-1,6-glycosidic bonds.**

*Starches (plants):*
*Amylose – unbranched,*
*Amylopectin – branched*
*Glycogen (animals):*
*highly branched*

**Glycogen:**

Glycogen acts as the energy-reserve carbohydrate for animals. Like amylopectin, it is a branched polysaccharide containing approximately $10^6$ glucose units joined by α-1,4- and α-1,6-glycosidic bonds. The total amount of glycogen in the body of a well-nourished adult human is about 350 g, divided almost equally between liver and muscle.

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### Cellulose:

Cellulose, the most widely distributed plant skeletal polysaccharide, constitutes almost half of the cell-wall material of wood. Cotton is almost pure cellulose. Cellulose is a linear polysaccharide of D-glucose units joined by β-1,4- glycosidic bonds (Fig. 1.15). It has an average molecular weight of 400,000 g/mol, corresponding to approximately 2200 glucose units per molecule.
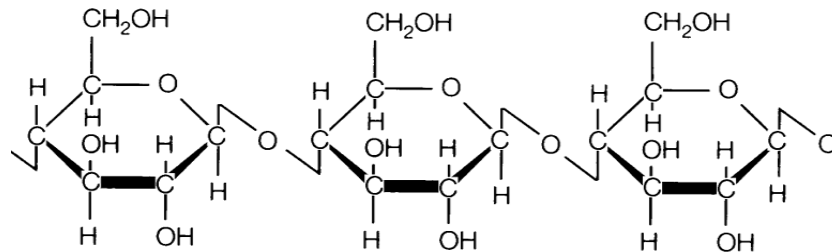


**Figure (1.15): Cellulose is a linear polysaccharide containing as many as 3000 units of D-glucose joined by β-1,4-glycosidic bonds.**

Cellulose molecules act much like stiff rods, a characteristic that enables them to align themselves side by side into well-organized, water-insoluble fibers in which the OH groups form numerous intermolecular hydrogen bonds. This arrangement of parallel chains in bundles gives cellulose fibers their high mechanical strength. It also explains why cellulose is insoluble in water. When a piece of cellulose-containing material is placed in water, there are not enough OH groups on the surface of the fiber to pull individual cellulose molecules away from the strongly hydrogen-bonded fiber.

Humans and other animals cannot use cellulose as food because our digestive systems do not contain β-glucosidases, enzymes that catalyze the hydrolysis of β-glucosidic bonds. Instead, we have only α-glucosidases; hence, we use the polysaccharides starch and glycogen as sources of glucose. In contrast, many bacteria and microorganisms do contain β-glucosidases and so can digest cellulose. Termites (much to our regret) have such bacteria in their intestines and can use wood as their principal food. Ruminants (such as cows and sheep) and horses can also digest grasses and hay because β-glucosidase-containing microorganisms are present in their alimentary systems.