The organic macronutrients are carbon compounds synthesized by living organisms. They include carbohydrates, proteins or amino acids, and lipids. In the individual chapters in this unit on the structure and properties of the organic macronutrients, specific compounds in each class are described, from the viewpoint of both dietary macronutrients and of organic compounds formed in the human body during metabolism of carbohydrates, proteins and amino acids, and lipids. Compounds in the fourth group of organic nutrients, the vitamins, are micronutrients and are considered in Unit VI. Organic macronutrients are required in large amounts and are sources of energy for the body.

Like all organic compounds, proteins, carbohydrates, and lipids are made up largely of six elements: (1) hydrogen, (2) oxygen, (3) carbon, and (4) nitrogen along with some (5) phosphorus and (6) sulfur. These six relatively small elements, with atomic weights less than or equal to 32, make up the basic structures of proteins, carbohydrates, lipids, and vitamins, as well as nucleic acids and intermediates of metabolism. If water (H₂O), which makes up approximately 63% of the human body, is not considered, carbon, oxygen, hydrogen, and nitrogen (in organic compounds) make up 88.5% of the “dry weight” of the human body; these elements are present in about 11 kg of protein, 10 kg of fat, and 0.6 kg of carbohydrate (mainly glycogen) in a 65-kg man.

The ability of carbon to form carbon-to-carbon bonds, extended carbon chains, and cyclic compounds permits the formation of a myriad of organic compounds; the structures of a number of these compounds are considered in this unit. In organic molecules, the atoms of carbon, hydrogen, oxygen, phosphorus, and sulfur are held together by covalent bonds, which are formed when two atoms share a pair of outer orbital electrons. Each covalent bond of every molecule represents a small amount of stored energy, thereby allowing organic molecules to serve as a source of energy to the body. Units III, IV, and V describe the processes involved in the assimilation of dietary organic macronutrients, how these are used by the body for growth and maintenance via synthesis of the structural and functional components of the human body, and how these macronutrients are used as fuels with conversion of excess substrate to stored fuels for subsequent use.
**Structure, Nomenclature, and Properties of Carbohydrates**

Joanne L. Slavin, PhD, RD*

Carbohydrates are the most abundant organic components in most fruits, vegetables, legumes, and cereal grains, and they provide texture and flavor in many processed foods. They are the major energy source for humans by digestion and absorption in the small intestine and, to a lesser extent, by microbial fermentation in the large intestine. Food carbohydrates are often classified as available or unavailable carbohydrates. Available carbohydrates are those that are hydrolyzed by enzymes of the human gastrointestinal tract to monosaccharides that are absorbed in the small intestine and enter the pathways of carbohydrate metabolism. Unavailable carbohydrates are not hydrolyzed by human digestive enzymes, but they may be partially or totally fermented by bacteria in the large intestine, forming short-chain fatty acids that may be absorbed and contribute to the body’s energy needs.

Glucose is an essential energy source for human tissues; some types of cells such as red blood cells are not able to use other fuels. Glucose for the body’s use may be derived from dietary starches and sugars, from glycogen stores in the body, or by synthesis in vivo from gluconeogenic precursors such as amino acid carbon skeletons. Glucose also serves as a precursor for synthesis of all other carbohydrates including lactose produced by the mammary gland, the ribose needed for nucleic acid synthesis, and the sugar residues that are found as covalently bound constituents of glycoproteins, glycolipids, and proteoglycans in the body.

Carbohydrates are defined as polyhydroxy aldehydes and ketones and derivatives of these sugars. This definition emphasizes the hydrophilic nature of most carbohydrates and allows inclusion of sugar alcohols (alditols), sugar acids (uronic, aldonic, and aldaric acids), glycosides, and polymerized products (oligosaccharides and polysaccharides) among the classes of carbohydrates. The hydroxyl groups of carbohydrates may be modified by substitution with other groups to give esters and ethers or be replaced to give deoxy and amino sugars. Carbohydrates are also covalently bound to many proteins and lipids. These glycoconjugates include the glycoproteins, proteoglycans, and glycolipids.

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**MONOSACCHARIDES OR SUGAR RESIDUES**

Aldoses and ketones are monosaccharides or simple sugars. Monosaccharides are further classified by the number of carbon atoms in their structures (i.e., the trioses, tetroses, pentoses, hexoses, heptoses, octoses, and nonoses) and by their stereochemistry (i.e., D or L). For chains of sugar residues or “monosaccharide” units, the carbohydrates are classified by the degree to which the sugar units are polymerized (e.g., disaccharides, oligosaccharides, and polysaccharides).

**STRUCTURES AND NOMENCLATURE OF THE ALDOSES AND KETOSES**

Monosaccharides or simple sugars include the aldoses such as glucose and ketoses such as fructose. Aldoses contain one aldehyde group and hence are polyhydroxy aldehydes. Ketoses contain one ketone group and hence are polyhydroxy ketones. Both have the empirical chemical formula (CH₂O)ₙ.

**Chirality of Monosaccharides**

A chiral carbon atom is one that is bonded to four different groups. A property of chiral molecules that lack a plane of symmetry is optical activity, or their ability to rotate or turn the plane of linearly polarized light as the light travels through a solution of the compound. Several systems are used to designate the chirality or spatial configuration of atoms on a molecule. The d/l system is commonly used for designating the chirality of sugars and amino acids. In the d/l system, each molecule is named by its relation to glyceraldehyde. Glyceraldehyde is the simplest aldose sugar with a chiral atom, the C2 of glyceraldehyde. Thus, the three-carbon glyceraldehyde exists as both D- and L-enantiomers. The two-carbon aldehyde, glycolaldehyde does not have a chiral carbon atom and hence has no optical activity.

All D-aldoses are related to D-glyceraldehyde, and L-aldoses are similarly related to L-glyceraldehyde. The relation of D-aldoses to D-glyceraldehyde can be seen clearly by looking at a scheme for the chemical synthesis of the series of D-aldoses from D-glyceraldehyde. In the synthetic scheme shown in Figure 4-1, a nucleophilic cyanide ion (CN⁻) adds to the carbonyl double bond (C1) of glyceraldehyde, giving two cyanhydrin products. Selective reduction and hydrolysis of the CN group to an aldehyde completes the conversion of the triose D-glyceraldehyde to the pair of aldotetroses having...
a new chiral carbon at C2 (i.e., C1 of the glyceraldehyde precursor). Accordingly, this reaction scheme lengthens the carbon chain from the carbonyl end and gives two new aldoses, the last three carbons of which derive from glyceraldehyde. Therefore the configuration of the hydroxyl on the highest numbered chiral carbon of an aldose or ketose determines its D or L status. For a D-sugar, this hydroxyl is shown drawn to the right of the carbon chain in the Fischer formula.

Each cycle of the synthesis creates a new chiral center (i.e., at C2 of the successive aldoses) and a pair of stereoisomers. Accordingly, there are two tetrose, four pentoses, and eight hexoses in the D- (see Figure 4-1) and also in the L-series; not all of these occur commonly in nature. The nutritionally important glucose is one of the eight possible D-aldohexose monosaccharides. The L-sugars are mirror images (enantiomers) of the D-sugars, with the configuration of all chiral carbons reversed (e.g., D-glucose and L-glucose).

Similarly, D-ketoses are related to D-glyceraldehyde, and L-ketoses are related to L-glyceraldehyde. The simplest ketose sugar is the three-carbon dihydroxyacetone, which does not have a chiral carbon. The simplest ketose sugar with enantiomers is the four-carbon erythrose.

**Epimers**

 Sugars that vary in their configuration at only one carbon are epimers: for example, D-glucose and D-mannose are C2 epimers, whereas D-glucose and D-galactose are C4 epimers. Enzymes that catalyze epimer formation are called epimerases.

**Systematic Naming of Aldoses and Ketoses**

 The names of each of the two aldotetroses, four aldopen- toses and eight aldohexoses are shown in Figure 4-1. The carbonyl group in aldoses is always C1, but carbonyl groups
may occur at any internal carbon atom in ketoses. In the common ketoses (Figure 4-2), the carbonyl group is usually at C2. A few ketoses, such as fructose, are known by their trivial names, but ketoses also are named systematically with the suffix “-ulose” denoting a ketose sugar. In this nomenclature, a group of up to four consecutive chiral carbons is named after the corresponding aldose sugar (e.g., triose, tetrose, pentose, or hexose) that possesses the same chiral group, and the number of carbon atoms is designated also.

Fructose is the most common ketose, and its systematic name is D-arabino-hexulose, showing that the three chiral carbons in D-fructose have the same configuration as the three chiral carbons in D-arabinose. Frequently, the names ribulose and xylulose are used for the two ketopentoses. Their correct systematic names, however, are D-erythro-pentulose and D-threo-pentulose, respectively, showing that they have only two chiral carbons and the relationship of these chiral carbons to those of erythrose and threose (see Figure 4-1).

Although the common monosaccharides are pentoses and hexoses, sugars with more than six carbon atoms also occur naturally. Some have trivial names, but most sugars having more than six carbons and possessing four or more chiral carbons are named systematically, as described in the preceding text for the aldoses and ketoses. Sedoheptulose (D-altro-heptulose), a seven-carbon sugar, and the other ketoses shown in Figure 4-2 are involved as phosphorylated intermediates in carbohydrate metabolism. N-Acetylneuraminic acid, a nine-carbon acidic ketose, is an important signaling epitope in glycoproteins.

The abbreviations or symbols for the sugars usually consist of the first three letters of their names (Table 4-1). The abbreviations of glucose (Glc) and some ketoses are exceptions to this rule.

**Cyclical and Conformational Structures for Monosaccharides and Sugar Residues**

Hemiacetals and hemiketals are compounds that are formed by addition of an alcohol to a carbonyl group of an aldehyde or ketone, respectively. Reaction of an intramolecular hydroxyl group with the carbonyl group of an aldose or ketose forms a cyclic hemiacetal or cyclic hemiketal, which are also called lactols. When a ring structure forms, the carbonyl carbon is transformed into a chiral carbon, giving rise to a new pair of isomers called α- and β-anomers. Aldoses and ketoses are more stable in their five- or six-membered cyclic forms than in their acyclic forms. Thus glucose, fructose, and many other sugars exist mainly in their cyclic forms.

**Cyclization of Aldoses and Ketoses to Pyranose and Furanose Ring Structures**

Cyclization of an aldose occurs via an intramolecular reaction of the nucleophilic hydroxyl group on C4 or C5 with the C1 aldehyde, as shown for glucose in Figure 4-3. This spontaneous reaction transforms the carbonyl carbon (i.e., C1 of an aldose) into a chiral carbon (the anomic carbon), giving the α- and β-anomers of both the furanose and pyranose ring forms. The same type of cyclization reaction occurs with the ketoses in which the C5 or C6 hydroxyl group reacts with the C2 ketose carbonyl. In the Fischer formula, the hemiacetal (anomeric) –OH of the α-anomer is drawn on the same side of the carbon chain as the designator oxygen (e.g., C5–O– of a hexose). In aqueous solution, the acyclic and cyclic isomers are in equilibrium, with the most energetically stable isomers predominating. For most aldoses, the six-membered pyranose ring is more stable than the five-membered furanose ring. However, some sugars (e.g., arabinose, ribose, and fructose) frequently occur in the furanose ring form in disaccharides, oligosaccharides, and polymers. The equilibrium nature of the hemiacetal reaction dictates that all hydroxyls

**Table 4-1: Abbreviated Names for Some Common Carbohydrates**

<table>
<thead>
<tr>
<th>NAME</th>
<th>ABBREVIATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arabinose</td>
<td>Ara</td>
</tr>
<tr>
<td>Fructose</td>
<td>Fru</td>
</tr>
<tr>
<td>Fucose</td>
<td>Fuc</td>
</tr>
<tr>
<td>Galactose</td>
<td>Gal</td>
</tr>
<tr>
<td>Galacturonic acid</td>
<td>GalA</td>
</tr>
<tr>
<td>N-Acetylgalactosamine</td>
<td>GalNAc</td>
</tr>
<tr>
<td>Glucose</td>
<td>Glc</td>
</tr>
<tr>
<td>Glucuronic acid</td>
<td>GlcA</td>
</tr>
<tr>
<td>N-Acetylglucosamine</td>
<td>GlcNAc</td>
</tr>
<tr>
<td>Iduronic acid</td>
<td>IdoA</td>
</tr>
<tr>
<td>Mannose</td>
<td>Man</td>
</tr>
<tr>
<td>N-Acetylneuraminic acid</td>
<td>NeuSAc</td>
</tr>
<tr>
<td>Rhamnose</td>
<td>Rha</td>
</tr>
<tr>
<td>Xylose</td>
<td>Xyl</td>
</tr>
</tbody>
</table>

Abbreviations for di-, oligo-, and polysaccharides often add α- or β- to indicate the enantiomeric form, or t or p to indicate the pyranose or furanose ring form, or α- or β- to indicate the stereochemistry of the glycosidic linkage, and carbon numbers to indicate the carbon atoms that are O-linked by the glycosidic bond. The designation is often omitted for the more common α-enantiomers and α-ring form.
and the carbonyl group can undergo reactions; that is, the sugar can react in acyclic or in ring form.

**Drawing Sugar Ring Structures**

Sugar ring structures are depicted in several ways, as shown for glucose and fructose in Figure 4-4. The Fischer projection formula is a convention used to depict a stereoformula in two dimensions. The Haworth formula was introduced as a more realistic depiction of the bond lengths in the cyclic sugars. Hydroxyl groups on the right of the carbon chain in the Fischer projection are below the plane of the ring in the Haworth formula, and those on the left of the carbon chain in the Fischer projection are above the plane of the ring in the Haworth formula. The exocyclic group (e.g., the $\text{−CH}_2\text{OH}$ group attached to C5 of hexoses such as glucose and fructose shown in Figure 4-4) is placed above or below the plane in the Haworth formula, depending on the stereochemistry of the ring oxygen. If the hydroxyl group that contributes the ring oxygen is on the right of the carbon chain in the Fischer structure, then the exocyclic group is above the plane in the Haworth structure. If the ring connects from a hydroxyl group on the left of the carbon chain in the Fischer structure, then the exocyclic group is drawn below the plane in the Haworth structure.

Because five- and six-membered rings are not planar but have a three-dimensional characteristic, the chair conformational formula is preferred for showing spatial relationships, such as in enzyme-catalyzed reactions where fit of substrate to enzyme binding site is important. In chair conformations, C2, C3, C5, and the ring oxygen are planar, and C1 and C4 are out of the plane and on opposite sides of the plane. The orientations of the hydroxyls are axial (almost perpendicular to the mean plane of the ring) or equatorial (almost parallel to the mean plane). Pyranose sugars assume a chair conformation based in part on maximizing the number of large groups ($\text{−OH}$ and $\text{−CH}_2\text{OH}$) at equatorial positions, which are less sterically hindered than are axial positions. Thus the $\text{4C}_1$ conformation, in which C4 is above and C1 is below the plane, is preferred (lower energy) for $\alpha$- and $\beta$-d-glucopyranose and most of the other aldohexoses.

**CHEMICAL REACTIVITY OF THE MONOSACCHARIDES AND SUGAR RESIDUES**

Sugars are relatively stable when pure and dry. In solution, their alcohol, aldehyde, and keto groups are involved in various reactions that are both nonenzymatic and enzymatic.

**General Reactivity of Sugars**

Aldoses are reducing agents, and the carbonyl group of an aldose is simultaneously oxidized to a carboxyl group when aldoses act as reducing agents. Ketoses are not good reducing agents because simultaneous oxidation of the carbonyl would require carbon chain cleavage. However, ketoses can isomerize to aldoses in an alkaline reducing sugar test and therefore result in a positive reducing sugar test even though they are nonreducing sugars. Formerly, glucose in urine was analyzed by an assay for reducing sugars, but more specific methods are now available. In vivo, oxidation of the aldehyde group of glucose is catalyzed enzymatically by a dehydrogenase, and this reaction yields the lactone (an intramolecular ester of the newly formed carboxylic acid) as the product. An example of this type of reaction is the conversion of glucose 6-phosphate to 6-phosphogluconolactone in the pentose phosphate pathway of metabolism (see Chapter 12, Figure 12-20).
The carbonyl group of an aldose or ketose is readily reduced to an alcohol by chemical catalysis, giving an alditol from an aldose or an epimeric pair of alditols from a ketose. These alditols (sugar alcohols), which lack a carbonyl group, are more stable than the aldoses and ketoses, and they are not reducing agents. Aldehyde reductases catalyze a similar reduction in vivo (e.g., in conversion of glucose to glucitol, which is also known as sorbitol).

The carbon proton adjacent to the carbonyl (i.e., the α-carbon proton) in aldoses is acidic and easily abstracted in basic solution, leading to epimerization of the aldoses at C2 as well as isomerization to ketoses. Thus glucose is epimerized to mannose and isomerized to fructose. Similar reactions occur in carbohydrate metabolism, as seen in the phosphoglucose isomerase–catalyzed conversion of glucose 6-phosphate to fructose 6-phosphate and in the phosphomannose isomerase-catalyzed conversion of mannose 6-phosphate to fructose 6-phosphate (see Chapter 12, Figures 12-4 and 12-5). Similar reactions occur with ketoses.

Hydroxyl groups of carbohydrates are readily converted into a variety of esters, but the phosphate esters of the monosaccharides are particularly important as intermediates in metabolism. Sugar phosphates are also components of biological polymers. This is illustrated by the nucleic acids, which have ribose and 2-deoxyribose phosphates as key constituents. Other derivatives of hydroxyls, including ethers, are also important in modification of monosaccharides in living systems and contribute to the diversity of carbohydrate structure.

**Formation of Glycosidic Linkages**

The general term *glycoside* is used to describe any molecule in which a sugar group is bonded through its anomic carbon to another group via a glycosidic bond. As an example, the acid-catalyzed reaction of a sugar (glucose) with an alcohol (methanol) to form methyl d-glucopyranoside, which is an example of an O-glycoside, is shown in Figure 4-5. Although only the α-glycoside is shown, both α- and β-glycosides form in nonenzymatic reactions. When properly activated, sugars react with each other to form specific oligosaccharides and polysaccharides in which a sugar residue is linked by a new bond between its anomeric carbon and one of the hydroxyl groups of the second sugar residue. Thus the sugar residues in oligosaccharides and polysaccharides are linked by O-glycosidic bonds.

The terms *glycone* and *aglycone* are commonly used to refer to the two molecules linked by a glycosidic bond, particularly when the compound being described is not a chain of sugar residues (e.g., oligosaccharide or polysaccharide). The sugar group is the glycone and the nonsugar group is the aglycone part of the glycoside; for example, in Figure 4-5 glucose is the glycone and methanol is the aglycone portion of methyl d-glucopyranoside. The glycone can consist of a single sugar group (monosaccharide) or several sugar groups (oligosaccharide). Glycosides may be classified by the sugar group. If the sugar group is glucose, the molecule is a glucoside; if it is glucuronic acid (glucuronate), the molecule is a glucuronide. Various hydroxylated compounds are glycosylated in the liver by linkage to glucuronic acid,
which increases their water solubility; formation of β-D-glucuronides is a major means of detoxification and excretion of both endogenous (e.g., bilirubin) and exogenous (e.g., acetaminophen) compounds.

Sugars also react with amines or thiols to give N- or S-glycosides, respectively. For example, β-D-ribose and 2-deoxy-β-D-ribose in nucleic acids are bonded to purines and pyrimidines by N-glycosidic bonds. In uridine diphosphate (UDP)-glucose, the β-D-ribose is linked to uracil by an N-glycosidic bond, and the α-D-glucose unit is esterified to phosphate.

Maillard Reaction of Reducing Sugars with Amines

Aldoses and ketoses react with aliphatic primary and secondary amines, including amino acids and proteins, to form N-glycosides, which readily dehydrate to the respective Schiff base by the Maillard reaction, as shown in Figure 4-7 (reactions i and ii). The aldose Schiff base spontaneously undergoes an Amadori rearrangement at C1 and C2, giving a substituted 1-amino-1-deoxyketose (reaction iii). A ketone Schiff base will rearrange to a substituted 2-amino-2-deoxyaldose (not shown). These sugar amines undergo additional very complex reactions, leading to formation of highly reactive dicarbonyls (such as 3-deoxy-D-glucosone), cross-linking of proteins (as in reaction iv), formation of fluorescent compounds and brown pigments, and formation of low-molecular-weight compounds, some of which are useful flavoring agents. Although the Maillard complex of reactions has been studied extensively, the reactions are understood only in part. Lysine residues in proteins often react with sugars by the Maillard reaction, The reaction of glucose with hemoglobin was discovered first. Plasma glucose reacts with hemoglobins via the Maillard reaction, and the modified protein, detected by gel electrophoresis, is an indicator of plasma glucose levels in diabetics over the lifespan of the erythrocytes. The term “glycated” protein is used to distinguish these Maillard-derived, carbohydrate-modified proteins from true glycosylated proteins (glycoproteins). The Maillard and subsequent reactions also occur in food products exposed to heat, such as in powdered or evaporated milk during processing or storage, giving an off-white color to the product and decreasing the nutritive value of food proteins. Lysine residues in proteins are irreversibly modified by the Maillard reaction, and modification of lysine residues is partially responsible for the nonenzymatic browning and decrease in nutritive value.
OTHER CLASSES OF CARBOHYDRATE UNITS

Monosaccharides or monosaccharide residues may be modified or derived in several ways. Carbonyl groups can be reduced or oxidized, and terminal \(-\text{CH}_2\text{OH}\) groups can be oxidized. Hydroxyl groups on any of the carbons are subject to various modifications.

ALDITOLS

The alditols, or polyols, which occur naturally in plants and other organisms, are reduction products of aldoses and ketoses in which the carbonyl has been reduced to an alcohol. Two common alditols are shown in Figure 4-8, xylitol and sorbitol (glucitol). Reduction of ketoses gives an epimeric pair of alditols unless the reaction is enzyme-catalyzed and therefore stereospecific. The alditols, like the sugars, are soluble in water and vary in degree of sweetness. Xylitol, the sweetest, approaches the sweetness of sucrose. Because the alditols do not have a carbonyl group, they are considerably less reactive than their corresponding sugars. They do not undergo base-catalyzed reactions of epimerization and isomerization, the

![Figure 4-7](http://www.us.elsevierhealth.com/Nursing/Nutrition/book/9781437709599/Biochemical-Physiological-and-Molecular-Aspects-of-Human-Nutrition/)

**FIGURE 4-7** Initiation of the Maillard reaction of amines with aldoses. The aminoketose intermediate formed by reaction iii undergoes various reactions, including conversion to a highly reactive dicarbonyl compound (3-deoxy-\(\alpha\)-glucosone). When the amino group (\(R'\text{NH}_2\)) for reaction iv is from a protein, the reaction may result in cross-linked proteins.

**NUTRITION INSIGHT**

Sugar-Protein Reactions in Diabetes and Aging

The Maillard/Amadori reactions of sugars with amino acids and proteins lead to a cascade of reactions. Products of these reactions are referred to as advanced glycation end products. These reaction end products have been observed in collagen-rich tissues in vivo and in vitro, and they are associated with stiffening of artery walls, lung tissue, and joints and with other aging symptoms. Considerable evidence links hyperglycemia with increased formation of these end products; these products accumulate in the blood vessel wall proteins and may contribute to vascular complications of diabetes. Glycation of lens proteins increases somewhat with aging, but acceleration is associated with diabetes. Incubation of lens proteins with glucose or glucose 6-phosphate in vitro results in changes in the lens proteins that mimic most of those observed with age- and cataract-related changes in the lens. Drug-induced inhibition of the reactions leading to these end products in diabetic animals prevents various disease-associated pathologies of the arteries, kidneys, nerves, and retina.

![Figure 4-8](http://www.us.elsevierhealth.com/Nursing/Nutrition/book/9781437709599/Biochemical-Physiological-and-Molecular-Aspects-of-Human-Nutrition/)

**FIGURE 4-8** Structures of the common sugar alcohols (alditols), \(\alpha\)-xylitol and \(\alpha\)-glucitol.
passively absorbed in the small intestine and metabolized in the liver. Excessive amounts of alditols passing into the colon may induce diarrhea owing to their fermentation leading to increased luminal osmolarity (Grabitske and Slavin, 2009).

GLYCURONIC, GLYCONIC, AND GLYCARIC ACIDS
Sugar acids are sugars in which the carbonyl group and/or the terminal \(-\text{CH}_2\text{OH}\) group has been oxidized to a carboxyl group \((-\text{COOH})\). Uronic acids are formed when the terminal \(-\text{CH}_2\text{OH}\) group of an aldose or ketose is oxidized to a terminal carboxyl group \((-\text{COOH})\). Examples of several uronic acids are shown in Figure 4-9. \(\alpha\)-Glucuronic and \(\alpha\)-iduronic acids are shown as their \(\beta\) anomers; uronic acids are important constituents of glycosaminoglycans. The acids are shown in their anionic forms (gluconate, glucuronate, and iduronate), which are the major species at physiological pH.

DEOXY AND AMINO SUGARS
Several common sugars lack the complete complement of hydroxyl groups; examples of these are shown in Figure 4-10. Deoxy sugars, in which a hydroxyl group is replaced by a hydrogen, include 2-deoxy-d-ribose, \(\alpha\)-fucose (6-deoxy-l-galactose), and \(\alpha\)-rhamnose (6-deoxy-l-mannose). \(\alpha\)-Fucose is a constituent of many glycoproteins and serves as a signaling epitope for physiological events (e.g., in the inflammatory response). The presence of fucose in crucial oligosaccharides of cell-surface glycoproteins is required for recruitment of leukocytes to sites of inflammation and injury. \(\alpha\)-Rhamnose occurs in plant polysaccharides, and...
2-deoxy-\(\text{d}\)-ribose is the sugar constituent of deoxyribonucleotides that make up DNA.

In the common amino sugars, the C2 hydroxyl group is replaced by an amino group. These common amino sugars are \(\text{d}\)-glucosamine (2-amino-2-deoxy-\(\text{d}\)-glucose) and \(\text{d}\)-galactosamine (2-amino-2-deoxy-\(\text{d}\)-galactose), which usually occur as the N-acetyl derivatives (N-acetyl-\(\text{d}\)-glucosamine and N-acetyl-\(\text{d}\)-galactosamine). They are constituents of glycosaminoglycans and of many glycoproteins.

Glycoproteins and a class of glycolipids known as gangliosides may also contain derivatives of neuraminic acid. Neuraminic acid is a unique nine-carbon amino deoxy keto sugar that has an unsubstituted anomeric \(-\text{OH}\) group at their reducing end, this sugar residue can essentially undergo any of the reactions that the simple sugars undergo, including reduction, oxidation, and base-catalyzed epimerization and isomerization.

Disaccharides and oligosaccharides are readily hydrolyzed to their constituent monosaccharides by acid or enzymatic hydrolysis of their glycosidic linkages, with enzymes showing strong specificity for the sugar units and their anomeric forms involved in the glycosidic bonds. As a result of this specificity, humans digest only a subset of the carbohydrates present in foods. The structures of the three major dietary disaccharides (sucrose, lactose, and maltose) are shown in Figure 4-11.

**DISACCHARIDES**

Disaccharides are composed of monosaccharides covalently linked by glycosidic bonds. They can be classified as either reducing or nonreducing.

A disaccharide or oligosaccharide terminating with a residue that has an unsubstituted anomeric \(-\text{OH}\) group is reducing. An oligosaccharide that has the final sugar unit joined by linkage of its anomeric carbon to the anomeric carbon of preceding sugar so that the oligosaccharide does not have a free anomeric \(-\text{OH}\) is nonreducing. If the disaccharide or oligosaccharide has a free anomeric carbon (i.e., not involved in a glycosidic bond), the hemiacetal or hemiketal is in equilibrium with the free aldehyde or ketone form. Because reducing oligosaccharides have an unsubstituted anomeric \(-\text{OH}\) group at their reducing end, this sugar residue can essentially undergo any of the reactions that the simple sugars undergo, including reduction, oxidation, and base-catalyzed epimerization and isomerization.

Disaccharides and oligosaccharides readily hydrolyzed to their constituent monosaccharides by acid or enzymatic hydrolysis of their glycosidic linkages, with enzymes showing strong specificity for the sugar units and their anomeric forms involved in the glycosidic bonds. As a result of this specificity, humans digest only a subset of the carbohydrates present in foods. The structures of the three major dietary disaccharides (sucrose, lactose, and maltose) are shown in Figure 4-11.

**FIGURE 4-11** Reducing (lactose and maltose) and nonreducing (sucrose and trehalose) disaccharides. The free anomeric \(-\text{OH}\) of the glucosyl unit of lactose and of maltose indicates the reducing nature of these disaccharides. In sucrose and trehalose, both anomeric carbons are involved in the glycosidic bond, and these disaccharides are nonreducing. The small arrows point to the glycosidic bonds. Two abbreviated structural notations are shown for these disaccharides. Notation \(A\) defines the complete structure, whereas \(B\) assumes the more common ring form and \(\alpha\)-configuration for each sugar unit.
is produced commercially from sugar cane and sugar beets, but is typically called cane sugar regardless of its source. It is easily hydrolyzed to glucose and fructose in acid solution and rapidly digested by sucrase, an α-glucosidase of the intestinal villi. Sucrose is a major caloric sweetener for commercial or home use, and the term “sugar” on food labels refers to sucrose.

**NUTRITION INSIGHT**

**Derivatives of Sucrose Used by the Food Industry: Noncaloric Fat and Sugar Substitutes**

The low cost and purity of sucrose and the eight hydroxyl groups in its structure make sucrose an appealing starting material for chemical modification. In 1968, Procter & Gamble, while searching for a way to increase the fat intake of premature babies, created a fat substitute, sucrose polyester. Sucrose polyester, which is known as olestra or Olean, is a sucrose molecule to which as many as eight fatty acid residues (usually six to eight long-chain fatty acids) derived from vegetable oil have been esterified. It has so many fatty acid “spokes” around the central sucrose core that digestive enzymes and bacteria in the intestinal tract cannot find an entry point to break down the molecule. Thus it passes through the body largely unhydrolyzed. Olestra was approved by the U.S. Food and Drug Administration (FDA) in 1996 as a replacement for regular cooking oil in production of savory snack foods such as crackers, potato chips, and corn chips.

In 1976, Tate & Lyle, in conjunction with researchers at Queen Elizabeth College, University London, discovered that chlorination of three hydroxyl groups on sucrose produced a modified sucrose that is about 600 times as sweet as sucrose. They subsequently developed the product in partnership with McNeil Nutrionals. Use of this chlorinated sucrose derivative, which is known as sucralose or Splenda, was approved by Canada in 1991. In 1998, the FDA granted approval for use of sucralose as a tabletop sweetener in the United States, and in 1999 the FDA granted approval for use of sucralose as a general purpose sweetener in food products. Sucralose is currently used as a sugar substitute in numerous food products, including beverages, baked goods, dairy products, canned fruits, syrups, and condiments, and it is also sold to consumers, under its trade name Splenda, for use as a table and baking sugar substitute.

Additional sugar substitutes continue to enter the marketplace. A relative newcomer is stevia, an extract from *Stevia rebaudiana*, also known as sweetleaf. The sweetleaf plant contains sweet glycosides that are not digested and absorbed. The leaves of the sweetleaf plant have been used in medicinal teas by the Guarani tribes of Paraguay and Brazil for centuries, but stevia extract has been approved for use as a food additive in the United States only since 2008.

**CLINICAL CORRELATION**

**Sugars and Dental Caries**

Sugars are readily metabolized by oral bacteria, leading to production of organic acids in sufficient concentration to lower the pH of dental plaque. Most studies have focused on the contribution of sucrose, but monosaccharides are also readily fermented by the bacteria in the dental plaque. The acids demineralize (dissolve) the nearby tooth enamel. If the degree of demineralization exceeds remineralization over repeated cycles of changing acid concentrations, dissolution of the tooth enamel leads to tooth decay.

Although many studies done in the past clearly demonstrated the relationship between sucrose consumption and dental caries at the population level (e.g., association between sugar consumption and dental caries among countries) and at the individual level (e.g., persons with hereditary fructose intolerance who strictly limit sugar consumption), the apparent relationship between sugar consumption and dental caries has weakened in industrialized countries in recent decades. The weakening of the observed relationship is due, at least partially, to the decreased prevalence of caries in children owing to widespread use of fluoride, which raises the threshold of sugar intake at which caries will progress to cavitation. Furthermore, studies have shown that the amount of carbohydrate consumed is not as significant in the formation of dental caries as is the frequency of consumption. The form of the carbohydrate is also important because sticky carbohydrates are retained on the teeth and allow acid production to be prolonged. The American Dental Association recommends that the number of between-meal snacks eaten each day be minimized, that sweet consumption be limited to meal time, and that infants not be allowed to sleep with bottles containing sweetened liquids, fruit juices, milk, or formula.
from the watery part of milk that remains after the manufacture of cheese. Lactose has about one third the sweetness of sucrose. It is readily digested to glucose and galactose by a β-galactosidase (lactase) of the small intestine. Lactose is a reducing disaccharide and therefore susceptible to reactions of the glucose carbonyl group, including the Maillard reaction. Alkaline isomerization of lactose gives lactulose \[4-O-β-D-glucopyranosyl-(1,4)-D-fructofuranoside\], in which the glucose unit has been isomerized to fructose. This isomerization also occurs to some extent during heating of milk. Lactulose is not digested or absorbed from the small intestine and it therefore acts as substrate for fermentation and, hence, as a colonic acidifier and an osmotic laxative.

Trehalose

α,α-Trehalose \[α-D-glucopyranosyl-(1,1)-α-D-glucopyranoside\] is a nonreducing disaccharide found in fungi, such as young mushrooms and yeasts, and in invertebrates, such as insect hemolymph. It is digested by an intestinal α-glucosidase called trehalase. Trehalose is a rather insignificant dietary disaccharide in most modern diets.

Maltose

Only small amounts of maltose \[α-D-glucopyranosyl-(1,4)-D-glucopyranose\] are consumed as such in the diet. Maltose occurs naturally in the seeds of starch-producing plants, and small amounts are used in processed foods. Isomaltase \[α-D-glucopyranosyl-(1,6)-D-glucopyranose\] probably does not occur naturally, but both maltose and isomaltose are formed by acidic hydrolysis of starch; the isomaltose results from the structural branch points of amylpectin. Digestion of starch by α-amylases in the lumen of the gastrointestinal tract yields maltose, maltotriose, and α-dextrins containing the isomaltose moiety. Digestion of these glucose disaccharides and oligosaccharides is accomplished by intestinal α-glucosidases (maltase-glucamylase and sucrase-isomaltase). Digestion of carbohydrates is discussed in detail in Chapter 8.

OLIGOSACCHARIDES

Although disaccharides are common components of the diet, oligosaccharides containing 3 to 10 sugar residues are not abundant.

α-Galactosides

A series of α-galactosides, known as raffinose, stachyose, verbascose, and ajucose, occur in relatively large amounts in soybeans, lentils, and other legume seeds. As shown in Figure 4-12, these oligosaccharides contain a sucrose moiety to which one or more residues of α-galactose are attached by a 1,6 linkage to the glucose moiety of sucrose. Raffinose, stachyose, verbascose, and ajucose contain one, two, three, or four residues of α-D-galactose, respectively. Multiple residues of α-D-galactose are attached by 1,6 linkages; for example, stachyose contains an α-D-galactopyranosyl-(1,6)-D-galactopyranosyl unit attached to C6 of the glucose unit of sucrose. During plant seed development, a galactosyl derivative of inositol [i.e., α-D-galactosyl-(1,3)-D-myoo-inositol, or galactinol], serves as the donor of the galactose residues in the galactosyltransferase reactions that catalyze the synthesis of raffinose family oligosaccharides. Because humans do not have a digestive α-D-galactosidase, these oligosaccharides pass into the lower gut to be metabolized by the anaerobic bacteria. Excessive flatulence may result from fermentation of these oligosaccharides.

β-Fructans

Fructose oligosaccharides are produced by hydrolysis of inulin, which is a β-fructan obtained from chicory roots. Inulin is a polymer of fructose residues with the fructose residues present as furanose rings joined by β(2,1)-glycosidic linkages. The partial hydrolysate of inulin (oligofructose) is used as a food ingredient. Although pyranose rings are more stable thermodynamically and occur more frequently in polymers than do furanose rings, furanose rings are found in inulin and in sucrose because the biosynthesis of these molecules in plants involves the 6-phosphate ester of fructose as the fructose donor. In fructose 6-phosphate, the −OH on C6 is tied up and not free to cyclize with the carbonyl carbon to form a pyranose ring, so fructose 6-phosphate forms only furanose rings. The food industry also produces synthetic fructose oligosaccharides that are sucrose molecules to which fructose

\[
\text{Raffinose} \quad \text{An oligofructose}
\]

\[\text{FIGURE 4-12 Structures of two oligosaccharides; raffinose} \ [α-D-galactopyranosyl(1,6)-α-D-glucopyranosyl(1,2)-D-fructofuranosyl] \text{and an oligofructose product of inulin hydrolysis} \ [β-D-fructofuranosyl(2,1)-D-fructofuranosyl].\]
Polysaccharides of Nutritional Importance

Polysaccharides are polymers composed of sugars linked by glycosidic bonds. They vary in size from approximately 20 to more than 10^7 sugar units. The structural diversity includes molecular size, kinds and proportions of sugars, ring size (furanose or pyranose), anomeric configuration (α or β), and linkage site of the glycosidic bonds, as well as the sequence of sugars and linkages and the presence of noncarbohydrate components.

General Characteristics of Polysaccharides

Polysaccharides may be linear or branched, and the latter exhibit various branching modes that range from a single sugar unit to longer extensions carrying additional branches, as illustrated in Figure 4-13. Polysaccharides may be classified by whether they are polymers of only one type of sugar residue (homopolysaccharides) or of two or more different sugar residues (heteropolysaccharides). Homopolysaccharides are designated either by a trivial name, such as starch and cellulose, or by a systematic name constructed from the constituent sugar names and the suffix “an.” Thus α(1,4)-d-glucan is the systematic name for amylose, and β(1,4)-d-glucan is the systematic name for cellulose, both of which are made up of glucose units linked C1–C4 but with different stereoisomers (anomers) of the C1 of the glucose residues in the polymer.

In heteropolysaccharides composed of more than one kind of sugar, the sugar units may be linked in many different arrangements. Repeating units of a two- or three-sugar sequence is common. The physical properties of polysaccharides depend highly on their chemical and conformational structures. In general, polysaccharides that are highly branched are water soluble, whereas linear polysaccharides tend to be insoluble. However, linear polysaccharides possessing structural irregularities that hinder intermolecular hydrogen bonding may be soluble and give viscous

NUTRITION INSIGHT

Corn Syrups: A Major Source of Dietary Sugars

The development of various types of corn syrups and maltodextrins from cornstarch sources has brought about major changes in the food industry. Starch is separated from other parts of the corn kernels and is then hydrolyzed by acid- or enzyme-catalyzed processes to produce a mixture of glucose and glucose oligosaccharides. Corn syrups or maltodextrins with various degrees of hydrolysis are produced and classified according to reducing sugar content; the higher the reducing sugar value, the greater the degree of hydrolysis and the smaller the oligosaccharides.

More recently, a glucose isomerase has been used to convert some of the glucose in corn syrup to fructose to produce high-fructose corn syrups. If a higher percentage of fructose is desired, fructose is chromatographically separated and then back mixed to produce a syrup with the desired fructose concentration. High-fructose corn syrup is classified according to its fructose content (e.g., 42%, 55%). High-fructose corn syrup is listed as Generally Recognized as Safe (GRAS) for use by the food industry in the United States on the basis that its succharide composition (glucose to fructose ratio) is approximately the same as that of honey, invert sugar, and the disaccharide sucrose. Several features of high fructose corn syrup have led to its widespread use as a sweetening agent in processed foods. On a weight basis, glucose is less sweet than sucrose, whereas fructose is sweeter. Fructose is also twice as soluble as glucose at low temperatures. Thus conversion of half of the glucose to fructose produces a syrup that is more stable and sweeter than a glucose solution of the same sugar concentration. In addition, high fructose corn syrup is less expensive than sucrose (sugar).

Because fructose is processed differently in the body than glucose, which is the more common sugar unit in dietary carbohydrates, fructose bypasses many of the regulatory points that control glucose uptake and metabolism. There is concern that high intakes of either sucrose or high-fructose corn syrup may have adverse effects in terms of obesity and diabetes beyond those associated with the intake of calories from refined products. The basis of these concerns is addressed more fully in Chapters 8 and 12.
solutions. Hyaluronic acid, a linear polysaccharide with two different sugars in alternating sequence, shows this mucilaginous characteristic. In contrast, glycogen, which is highly branched and very soluble, gives relatively nonviscous solutions. Many different polysaccharide structures are represented in the plant kingdom, whereas only a few have been identified in vertebrates. Bacteria synthesize many unusual sugars, thereby greatly increasing the diversity of their polysaccharide antigens.

**DIGESTIBLE POLYSACCHARIDES**

Starch and glycogen are digestible polysaccharides of glucose. Both linear and branched forms of starch are found in plant cells. Glycogen has a highly branched structure and is found in animal tissues, particularly muscle and liver.

**Starch: Amylose and Amylopectin**

Starch is one of the most abundant polysaccharides in plants, where it is stored in the seeds, tubers, roots, and some fruits. It is composed of two families of polymers, a mostly linear amylose [α(1,4)-d-glucan] and the branched amylopectin [α(1,4)-d-glucan with branches linked to C6]. Starches from different sources vary in structure, but typically amylopectin has an average chain length between branch points of 20 to 25 glucose units. Typical starches contain 20% to 30% amylose and 70% to 80% amylopectin; however, high amylopectin (e.g., waxy corn, 98% amylopectin) and high amylose (e.g., high amylose corn, 55% to 85% amylose) starches are also available. Starches for food processing are produced from many sources. The most important sources are corn (regular, waxy, and high amylose), potato, rice, tapioca, and wheat. The physical properties and, to some extent, the digestibility of the starches vary with their fine structure and reflect their source.

Amylose and amylopectin molecules are laid down in plants during biosynthesis in highly organized particles called granules. The highly organized or crystalline structure of starch granules makes amylose and amylopectin less susceptible to digestion by α-amylases. The linear molecular structure of amylose results in more tightly packed granules, which are more insoluble and more resistant to digestion than those containing more of the branched and less tightly packed amylopectin. Therefore, certain raw starch granules with high amylose content, particularly those in raw potatoes and green bananas, resist digestion.

Although hydrogen bonding of the starch components renders the granules insoluble in water below approximately 55°C, cooking or heating in the presence of water breaks the intermolecular hydrogen bonds and the starch takes up water or swells, causing a transition to a disorganized amorphous structure. Upon further heating and further swelling, the granules rupture, releasing starch into the liquid. This process is called starch gelatinization. The hydration and disruption of starch granule structure that normally occurs during cooking and food processing makes the starch more accessible. Thus, in contrast to the raw starches, cooked potato and green banana starch are readily digested.

Gelatinized starch is hydrolyzed to glucose in the gastrointestinal tract by the combined action of salivary and pancreatic α-amylases and the intestinal mucosal α-glucosidases (glucoamylase, sucrose/isomaltase). The α-amylases, which cleave the α(1,4)-linkages only, catalyze hydrolysis of starch to maltose, maltotriose, maltotetrose, and oligosaccharides called α-limit dextrins, that contain at least four glucose units and include a α(1,6)-linked branch point. These disaccharides and oligosaccharides are then converted to glucose by the α-glucosidases. Figure 4-14 shows a fragment of the amylopectin structure and the α(1,4)- and α(1,6)-glucosidic linkages that can be hydrolyzed by human digestive enzymes. The human upper digestive tract does not possess an endogenous (1,4)-β-d-glucanase, and therefore cellulose, with its β-linkages, is not digestible.

**Resistant Starch**

Although starch is highly digestible, it appears that about 15% of dietary starches may not be well digested and absorbed in the small intestine (Sajilata et al., 2006). This starch is called “resistant starch.” Several factors may cause starch to be resistant to digestion and absorption in the small intestine. One of these factors is the physical structure or food matrix. Starch granules in whole or partly ground grains, seeds, cereals, and legumes may be resistant to digestion due to trapping of starch inside intact plant cells. Digestive enzymes may be unable to penetrate or break down the plant cell walls. Furthermore, the starch trapped inside these plant cell walls may not be easily gelatinized during cooking. Milling, grinding, and other types of food processing that

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**FIGURE 4-13** Branching structures of polysaccharides. A, Linear polysaccharide. Circles represent sugar units linked by glycosidic bonds. B, Alternating branches consisting of a single sugar unit. C, Blocks of consecutive single sugar unit branches. D, Ramified structure (branches on branches). Reducing end, Ø; Nonreducing end, ●; one sugar of a sequence of sugar units.
disrupt the food matrix may make starch more accessible to the digestive enzymes in the gastrointestinal tract.

Another factor that affects starch digestion by the gastrointestinal tract is the tight packing of starch in crystalline structures in starch granules. As discussed earlier, certain raw starch granules with high amylose content, particularly those in raw potatoes and green bananas, are very resistant to digestion. High-amylose corn starches have high gelatinization temperatures and typically resist digestion, even after cooking. Legumes are also a rich source of resistant starch.

A third physical process that affects starch availability is retrogradation. When a starch is cooked and then cooled, a gel is formed from the starch and trapped water. Because of the limited solubility of amylose and amylopectin in water, however, there is a tendency for the solubilized amylose chains, and to a lesser extent the branched amylopectin chains, to realign or reaggregate through hydrogen bonding over time in the process known as retrogradation. Starches that have a high amylose to amylopectin ratio tend to have an earlier onset of retrogradation and to form firmer gels that are more resistant to dispersion in water and digestion by α-amylase. Retrogradation occurs in foods that have been cooked and then cooled (e.g., potatoes, bread, or pasta) and in food products that undergo repeated moist heat treatments during food processing (e.g., canned beans and peas). Retrogradation in starch-based products is frequently undesirable, as in the staling or undesirable hardening of bread or in the syneresis (expulsion of liquid from the gel) of starch-thickened puddings.

Finally, certain chemically modified and cross-linked starches that are used in processed foods such as cakes and breads are resistant to digestion by human digestive enzymes.

**Glycogen**

Glycogen, like starch amylopectin, is an α(1,4)-D-glucan with branches on branches that are α(1,6)-linked. Glycogen has a high molecular mass, in the range of 10⁶ to 10⁷ Da. The average length of the α(1,4)-linked chain between branch points is 10 to 14 glucose units. Because of its greater degree of branching compared with amylopectin, glycogen is readily soluble in cold water and gives solutions of relatively low viscosity, which facilitate its use as a readily available endogenous energy source. The branching pattern interferes with intramolecular and intermolecular hydrogen bonding of the glycogen chains, thereby permitting rapid solvation and easy access to enzymes. A low viscosity of the solution facilitates diffusion of the substrate to the enzymes and diffusion of products away from the enzymes that hydrolyze glycosidic bonds in glycogen.

Glycogen is present in most animal tissues, with the highest content in liver and skeletal muscle. It may constitute up to 10% (wet weight) of the human liver. Mammalian tissue levels of glycogen are highly variable and affected by factors such as nutritional status and time of day. By electron microscopy of native glycogen in mammalian cells has revealed glycogen particles (β-particles) with diameters of about 10–30 nm. In liver, but not in muscle, supramolecular complexes called α-particles with diameters as large as...
Nondigestible Food Polysaccharides of Plant, Algal, and Bacterial Origin

<table>
<thead>
<tr>
<th>POLYSACCHARIDE</th>
<th>MAIN CHAIN OR REPEAT UNIT</th>
<th>BRANCHES, OTHER SUBSTITUENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLANTS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cellulose</td>
<td>-Glc(β1,4)Glc</td>
<td>None</td>
</tr>
<tr>
<td>Arabinoxylan</td>
<td>-Xyl(β1,4)Xyl</td>
<td>l-Araf(α1,2 or α1,3)- or Acetate at C2 or C3 of Xyl</td>
</tr>
<tr>
<td>Xyloglucan</td>
<td>Glc(β1,4)Glc</td>
<td>Xyl(α1,6)-; Gal (β1,2) or Araf(α1,3) linked to Xyl(α1,6)-; Fuc(α1,2)Gal (β1,2)]Xyl(α1,6)-; or Araf(α1,3)Araf(α1,3)Xyl(α1,6)-</td>
</tr>
<tr>
<td>Galactomannan</td>
<td>-Man(β1,4)Man</td>
<td>Gal(α1,6)-</td>
</tr>
<tr>
<td>Cereal β-glucan</td>
<td>-[Glc(β1,4)]βGlc(β1,3)-</td>
<td>None</td>
</tr>
<tr>
<td>Rhamnogalacturonan-1</td>
<td>[GalA(α1,4)-Rha(α1,2)]-</td>
<td>Oligosaccharide side chains (rich in Gal and l-Araf) attached to l-Rha at C4; main chain contains some methyl esters of GalA</td>
</tr>
<tr>
<td>ALGAE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alginic acid</td>
<td>-[ManA(β1,4)]βL-GulA(α1,4)]-</td>
<td>None</td>
</tr>
<tr>
<td>Carrageenan</td>
<td>-[Gal(β1,4)3,6-anhydroGal(α1,3)]-</td>
<td>-SO$_3$ at C4, C2†</td>
</tr>
<tr>
<td>BACTERIA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xanthan gum</td>
<td>-Glc(β1,4)Glc</td>
<td>4,6-Pyr-Man(β1,4)Glc(β1,2)6-Ac-Man(α1,3)- side chains attached to alternate glucose residues in the main chain. Pyr (pyruvate) is linked by glycosidic bonds between its C2 and the C4 and C6 of the terminal Man of some of the side-chains. Ac (acetate) is linked to the C6 of many internal Man residues of the side-chain</td>
</tr>
</tbody>
</table>

* Sugars are α isomers and pyranose ring forms unless otherwise indicated.
† The substituent group replaces the proton of the −OH of a sugar unit in the main chain.
‡ Alternating glucose units are substituted at C3 by the trisaccharide branch. The nonreducing terminal Man carries a pyruvate substituent, and the other Man is substituted at C6 by an acetyl group.

300 nm are also observed. These α-particles consist of several covalently linked β-particles (Sullivan et al., 2010).

**Nondigestible Plant Polysaccharides (Dietary Fiber)**

Polysaccharides are the major components of plant cell walls and interstitial spaces. Plants also synthesize storage polysaccharides other than starch, including galactomannans, the β(1,3)(1,4)-d-glucans of cereal grains, and the fructans of grasses and some tubers. All of these nonstarch polysaccharides present in plants, as well as those added during food processing, constitute dietary fiber (Table 4-2).

**Cellulose and Hemicelluloses**

Cellulose is a linear β(1,4)-d-glucan with a flat, ribbonlike conformation in which alternate glucose units are flipped 180 degrees and hydrogen bonded intramolecularly (see Figure 4-14). These ribbonlike chains are aligned in parallel arrays called microfibrils, in which the chains are strongly hydrogen bonded to each other. The microfibrils are similarly packed together into strong fibers, which are very insoluble and stiffen the plant cell wall. Associated with cellulose in the cell wall are several other insoluble polysaccharides, the hemicelluloses. These include the xyloglucans, which have a cellulose-like backbone with α-d-xylose units linked to C6 of the glucosyl unit, and arabinoxylans, in which the β(1,4)-d-xylan chain has α-L-arabinofuranose and d-glucuronic acid branches at C2 or C3.

**Pectic Polysaccharides**

Pectic polysaccharides [α(1,4)-D-galacturonans with occasional α-L-rhamnose units] and other associated polysaccharides (galactans and arabinans) are present in the cell walls of immature plant tissues and in the interstitial spaces. Native pectic galacturonan in the plant tissue is relatively insoluble, but isolated commercial pectin is soluble in hot water. Calcium ions form complexes with the galacturonic acid units of pectin, cross-linking the chains into a gel network. This is thought to account partially for the insolubility of native pectin in the plant tissue. The calcium–pectin complex is also the basis for dietary low-sugar, low-calorie fruit jams and jellies, whereas jellies prepared without calcium require a high sugar content to form a gel structure.

**Natural and Modified Polysaccharides for Use in Processed Foods**

Several natural polysaccharides are used in processed foods for their functional properties. These natural polysaccharides include guar and locust bean galactomannans, alginic
acid and carrageenan from seaweed, xanthan gum, and starches from several sources. Polysaccharides are also modified physically and chemically to enhance their functionality (Tharanathan, 2005). Some examples of modified starch cellulose are listed in Table 4-3. Starch and cellulose are alkylated or esterified to convert a very small proportion of the hydroxyls into ethers or esters for increased solubility. Starches are also subjected to partial acid or enzymatic hydrolysis, yielding starch dextrins with greater solubility. Industrial production of starch dextrins by pyrolysis (dry heat under acidic conditions) promotes further alteration of the structure, including new linkages, increased branching, and some decrease in size. Maltodextrins, which are smaller than the dextrins, usually in the oligosaccharide range, are formed by enzymatic hydrolysis of gelatinized starch without structural alterations. Modified starch products designed for enhanced solubility would be expected to favor rapid their digestion and absorption, whereas those designed for greater cross-linking may result in starch that is resistant to digestion. In general, the modified starches are digestible by human digestive enzymes, whereas the other polysaccharides added to foods contribute to dietary fiber. The interest in functional foods aimed at obesity and diabetes control may lead to the use of more resistant starches by the food industry (Zhang and Hamaker, 2009; Grabitske and Slavin, 2008).

### TABLE 4-3  Modified Polysaccharides Added to Processed Foods

<table>
<thead>
<tr>
<th>POLYSACCHARIDE</th>
<th>MODIFYING GROUP OR TREATMENT*</th>
<th>PRODUCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starch</td>
<td>−COCH₃</td>
<td>Starch acetate (ester)</td>
</tr>
<tr>
<td></td>
<td>−CH₂CHOHCH₃</td>
<td>Hydroxypropyl starch (ether)</td>
</tr>
<tr>
<td></td>
<td>−PO₂⁻</td>
<td>Phosphate cross-linked starch (diester)</td>
</tr>
<tr>
<td>Acid, heat</td>
<td>Dextrins</td>
<td></td>
</tr>
<tr>
<td>Water, heat</td>
<td>Cold water–soluble starch</td>
<td></td>
</tr>
<tr>
<td>Cellulose</td>
<td>−CH₂COOH</td>
<td>Carboxymethylcellulose (CMC)</td>
</tr>
<tr>
<td></td>
<td>−CH₂CHOHCH₃</td>
<td>Hydroxypropylcellulose</td>
</tr>
<tr>
<td></td>
<td>−CH₃</td>
<td>Methylcellulose</td>
</tr>
<tr>
<td>Acid, heat</td>
<td>Microcrystalline cellulose</td>
<td></td>
</tr>
</tbody>
</table>

*The modifying group replaces the proton of one of the three free hydroxyls of the glucose units at a degree of substitution usually less than 1 per 10 glucose units.

Conjugates of sugars and oligosaccharides play essential physiological roles. These glycoconjugates include the glycosaminoglycans and proteoglycans, the glycoproteins, and the glycolipids.

### GLYCOCONJUGATES OF PHYSIOLOGICAL INTEREST

Glycosaminoglycans (Table 4-4) are linear polysaccharides that have a disaccharide repeat unit composed of a hexosamine and a uronic acid. They are constituents of the extracellular spaces of mammalian tissues and vary in molecular mass and in fine structure. Many are sulfated and thus more highly charged. Most glycosaminoglycans are covalently bound to proteins, and the resulting proteoglycans vary considerably in the number and types of bound glycan chains.

#### Hyaluronic Acid

Hyaluronic acid (hyaluronan) is a negatively charged, soluble, high-molecular-weight, linear glycan composed of β-glucuronic acid and N-acetyl-β-glucosamine. It is found in the extracellular matrix, especially in soft connective tissue. Unlike most glycosaminoglycans, it is not covalently linked to protein but binds physically to receptor proteins on many different cells. Hyaluronic acid is noted for its ability to form highly viscous solutions, and some of its clinical applications depend on this rheology. The viscosity stems from the extended helical conformation, high molecular weight, and network of aggregated chains. Thus hyaluronic acid may have a role in water and protein homeostasis in the intercellular matrix. Interaction between hyaluronic acid and its cell receptors is involved in cell locomotion and migration, as shown for lymphocytes. Hyaluronic acid is synthesized by transfer of sugar units from their nucleotide diphosphate derivatives to the reducing end of the growing hyaluronic acid chain. This is in contrast to the usual mode of chain lengthening of oligosaccharides and polysaccharides, which involves addition of sugar units to the nonreducing end of the growing chain.

#### Chondroitin Sulfate

Chondroitin sulfate has a disaccharide repeat unit of β-glucuronic acid and N-acetyl-β-galactosamine, with sulfate ester groups being added at C2 of glucuronic acid units and C4 or C6 of the galactosamine units. This sulfation adds sequence heterogeneity, defined by the amount and positions of the sulfate esters along the chain. The large number of ionized sulfate groups and the weaker carboxyl groups ensure that this large polysaccharide will attract counter cations and water for osmotic balance and hydration of the polysaccharide.

#### Dermatan Sulfate

Dermatan sulfate is synthesized from chondroitin sulfate by intracellular C5 epimerization of some of the β-glucuronic acid units to l-iduronic acid. This both produces
a new uronic acid and increases structural diversity relative to the proportion and sequence of each acid. The other major differences between dermatan sulfate and chondroitin sulfate reside in the number of sulfate groups and their positions.

Heparin and Heparan Sulfate

Heparin and heparan sulfate have disaccharide repeat units of D-glucuronic acid and D-glucosamine with some L-iduronic acid. The glucosamine units may be N-acetylated or N-sulfated, and all sugar residues may be O-sulfated. Heparin is extensively epimerized and thus has many iduronic acid residues. Heparin also has a high proportion of N-sulfates and total sulfate. Heparin is found predominantly in the secretory granules of mast cells. Heparan sulfate chains vary widely in extent of epimerization and sulfation, with some chains having little iduronic acid or sulfate. Despite its name, heparan sulfate has less sulfate than heparin. Heparan sulfate is found linked to many cell surface proteins and as a component of matrix proteoglycans. Lipoprotein lipase in the capillaries of muscle and adipose tissue is closely associated with a heparan sulfate proteoglycan.

Keratan Sulfate

Keratan sulfate, composed of alternating D-galactose and N-acetyl-D-glucosamine units, lacks a uronic acid constituent, but it is heavily sulfated. The N-acetyl-D-glucosamine units carry sulfate groups at C6, and some of the galactose units are sulfated also at C6.

PROTEOGLYCANS

Proteoglycans are large, complex macromolecules that consist of a protein core to which glycosaminoglycans are covalently linked. These proteoglycans are found in the plasma membrane and extracellular matrices of most eukaryotic cells, where they have many functions. They may play a role in cell–cell and cell–matrix interactions and bind to a variety of ligands. The size and complexity of proteoglycans varies. A proteoglycan may carry more than one covalently linked glycosaminoglycan as well as additional oligosaccharides that are N- and O-linked to the core protein. Heparan sulfate/heparin proteoglycans contain at least one heparin sulfate chain, and usually O- and N-linked oligosaccharides in addition. The proteoglycans containing chondroitin sulfate, dermatan sulfate, and heparan sulfate frequently share a common tetrasaccharide-linkage region (GlCA-Gal-Gal-Xyl-) by which the glycosaminoglycan is covalently O-linked to a serine residue of the protein. Keratan sulfate is an exception and is found both O-linked and N-linked to serine/threonine or asparagine residues of core proteins. The biosynthesis of proteoglycans occurs posttranslationally and takes place in the lumen of the endoplasmic reticulum and Golgi apparatus.

GLYCOPROTEINS

Many proteins carry covalently linked oligosaccharides as minor components. The number and size of the oligosaccharide chains vary. The N-linked oligosaccharides tend to have a common core and are β-glycosidically linked from the N-acetyl-D-glucosamine unit to the nitrogen of the β-carboxamide of asparagine. Mucin-type glycoproteins have an α-D-galactosyl unit O-linked to the hydroxyl group

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**TABLE 4-4** Structural Repeating Units of the Glycosaminoglycans, Showing Sulfation Patterns and Structural Variation

<table>
<thead>
<tr>
<th>Glycosaminoglycan</th>
<th>Repeat Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyaluronan</td>
<td>[GlcNAc(β1,4)GlcA(β1,3)]n</td>
</tr>
<tr>
<td>Chondroitin 4-sulfate and 6-sulfate</td>
<td>[GalNAc(β1,4)GlcA(β1,3)4]2SO3−</td>
</tr>
<tr>
<td>Dermatan sulfate</td>
<td>[GalNAc(β1,4)-IdoA(α1,3)2]n R</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Keratan sulfate</td>
<td>[Gal(β1,4)GlcNAc(β1,3)]66</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Heparan sulfate and heparin</td>
<td>[GlcNR(α1,4)GlcA(β1,4)]6 R = Ac or SO3−</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

With the exception of hyaluronan and keratan sulfate, the glycosaminoglycans are glycosidically linked to the core protein chain by the disaccharide repeat unit -4GlcA(β1,3)GlcA(β1,4)-serine. Keratan sulfate is glycosidically linked to core proteins by either N-linked to an asparagine residue or O-linked to a serine/threonine residue. Hyaluronan is not covalently linked to proteins. Sugars are α unless noted as β.

* R in the abbreviated structure format refers to the proton of an –OH or –NH₂ group or a substitution for the proton (e.g., esterification of the sugar residue with sulfate or acetate).
of serine or threonine. Collagen is unique in that the carbohydrate chains are O-linked to the C5 of 5-hydroxylsine. The carbohydrate moieties of glycoproteins may help stabilize proteins, thus inhibiting denaturation, and may be involved in protein folding in addition to other specific biological roles (Figure 4-15).

**GLYCOLIPIDS**

Glycolipids are widespread in nature but only as minor components of the lipid fraction and usually in association with proteins. The common glycolipids of mammalian systems include cerebrosides and gangliosides, which are glycosyl (glucosyl or galactosyl) derivatives of sphingolipids (Table 4-5). These glycosphingolipids contain a base such as sphingosine, which has an 18-carbon monounsaturated chain substituted with two hydroxyl groups and an amine group. The amine nitrogen of the sphingosine unit is acylated with an 18-carbon monounsaturated chain substituted with two hydroxyl groups and an amine group.

**Additional Sugar Residues**

Additional sugar residues (usually glucose, galactose, L-fucose, or N-acetylgalactosamine) are attached to cerebrosides (usually to glucosylceramide) to form globosides and gangliosides. Neutral ceramide oligosaccharides (globosides) and acidic, sialic acid–containing ceramide oligosaccharides (gangliosides) are also sphingoglycolipids. Globosides are ceramides with two or more neutral sugar residues. The neutral diglycosylceramide, called lactosylceramide, is the precursor of other globosides and of gangliosides; lactosylceramide is also found in the membrane of red blood cells. Tetrasyglycosylceramides (“aminoglycolipids”) are globosides. These glycosphingolipids contain a base such as sphingosine, which has an 18-carbon monounsaturated chain substituted with two hydroxyl groups and an amine group. The amine nitrogen of the sphingosine unit is acylated with an 18-carbon monounsaturated chain substituted with two hydroxyl groups and an amine group.

**Figure 4-15** Structural variations in oligosaccharide chains of glycoproteins and their attachment site in the protein. A. A core of five sugar units, common to all three types of N-linked glycans, is linked to asparagine (Asn). High-mannose N-glycans contain up to nine mannose units in addition to N-acetylglucosamine. Other sugars, including galactose and sialic acid, also may be linked to the nonreducing ends of the antennary (branch) chains in the complex N-glycans. B. Examples of O-linked oligosaccharides, linked to serine (Ser) or threonine (Thr) residues of various proteins or to 5-hydroxylysine residues in posttranslationally-modified collagen. O-Linked oligosaccharides in the mucins and O-GlcNAc type in glycoproteins may be extended at the nonreducing end by addition of N-acetylglucosamine, galactose, L-fucose, and sialic acid. Sugars are α-enantiomers unless noted otherwise.

**Table 4-5** The Major Neutral and Acidic Glycolipids of Bovine and Human Milk

<table>
<thead>
<tr>
<th>NEUTRAL GLYCOLIPIDS</th>
<th>ACIDIC GLYCOLIPIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gal(β1,1)Cer</td>
<td>Neu5Ac(α2,3)Gal(β1,4)Cer</td>
</tr>
<tr>
<td>Glc(β1,1)Cer</td>
<td>Neu5Ac(α2,8)Neu5Ac(α2,3)Gal(β1,4)Cer</td>
</tr>
<tr>
<td>Gal(β1,4)Glc(β1,1)Cer</td>
<td></td>
</tr>
</tbody>
</table>

Cer, Ceramide. HOCH2-C(H)(NHR)-(C(H)(OH)-CH=CH-C13H27, with R representing a long-chain acyl group.
that contain an additional sugar (i.e., galactose) and an N-acetylhexosamine unit (i.e., N-acetylgalactosamine); certain globo sides are antigenic determinants of blood group types. Gangliosides are formed by the addition of sialic acid (N-acetylneuraminic acid) to diglycosylceramides; additional sugar residues such as galactose, N-acetylgalactosamine, and N-acetylglucosamine may also be added to form a variety of gangliosides, many containing branches formed by the addition of one or two sialic acid units to the linear portion of the oligosaccharide chain. Gangliosides are found on the surface membranes of most cells, and they make up about 6% by weight of total brain lipids. Gangliosides are most highly concentrated in the ganglion cells of the central nervous system.

Aberrant glycosylation expressed in glycosphingolipids in tumor cells is strongly implicated as an essential mechanism in tumor progression. Abnormal accumulation of specific glycosphingolipids in specific cancers has been correlated with altered cell–cell or cell–substratum interactions, and reagents that block glycosylation have been shown to inhibit tumor cell metastasis.

Plants and microorganisms synthesize several simple glycolipids, which include fatty acid esters of the sugars and glycosides of diglycerides, hydroxy fatty acids, and myo-inositol–containing phospholipids. Highly complex lipopolysaccharides of cell walls of pathogenic gram-negative bacteria act as endotoxins, inducing a strong response from the animal immune system, and as pyrogens, inducing fever. The lipopolysaccharides, or endotoxins, are composed of three domains: the terminal carbohydrate chain, which defines the O-specific antigenicity; the lipid A, which is embedded in the outer membrane and is the source of the endotoxin activity (probably after it is released from the cell in soluble form); and an oligosaccharide core, which is sandwiched between. Endotoxins are responsible for many of the clinical manifestations of infections with pathogenic gram-negative bacteria such as Neisseria meningitidis, Escherichia coli, and Salmonella spp.

**THINKING CRITUICALLY**

Most of the substrates for bacterial fermentation in the colon, leading to production of short-chain fatty acids and gases (hydrogen, carbon dioxide, and methane), are carbohydrates rather than proteins or fats. Some dietary carbohydrates that promote gas production include raffinose and related oligosaccharides found in legume seeds, sorbitol and other sugar alcohols, lactose (particularly in lactose-intolerant individuals), resistant starches, and dietary fiber.

1. What is the chemical or structural basis for the lack of digestion and/or absorption of each of these carbohydrates in the human small intestine?
2. Dietary supplements or digestive aids contain α-galactosidase (e.g., Beano) or β-galactosidase (e.g., Lactaid). What are the substrates for each of these enzymes? How do these supplements reduce gas production in the lower gastrointestinal tract?
3. What are common sources of dietary resistant starch? How can food processing and/or food preparation techniques alter the amount of total starch that is resistant to digestion in the human small intestine?

**REFERENCES**


**RECOMMENDED READINGS**


