• **Carbohydrates** are a large class of naturally occurring polyhydroxy aldehydes and ketones.

• **Monosaccharides**, or simple sugars, have from three to seven carbon atoms, and one aldehyde or one ketone group.
  – If the sugar has an aldehyde group, it is an **aldose**.
  – If it has a ketone group, the sugar is classified as a **ketose**.
21.1 An Introduction to Carbohydrates

- Glucose, an aldohexose (monomer for starch and cellulose; major source of energy)
- Ribose, an aldopentose (a component of ATP, coenzymes, and RNA)
- Fructose, a ketohexose (present in corn syrup and fruit)
Monosaccharides undergo a variety of structural changes and chemical reactions. They form disaccharides and polysaccharides (complex carbohydrates), which are polymers of monosaccharides. Functional groups are involved in reactions with alcohols, lipids, or proteins to form biomolecules.
21.2 Handedness of Carbohydrates

- Chiral compounds lack a plane of symmetry and exist as a pair of enantiomers in either a “right-handed” $\text{D-}$ form or a “left-handed” $\text{L-}$ form.

\[\text{D-Glyceraldehyde (Right-handed)}\]
\[\text{L-Glyceraldehyde (Left-handed)}\]
21.2 Handedness of Carbohydrates
21.2 Handedness of Carbohydrates

- Aldotetraoses have two chiral carbon atoms and can exist in four isomeric forms.
21.2 Handedness of Carbohydrates

- By convention the carbonyl group and the terminal CH$_2$OH are drawn pointing to the right.
- In general, a compound with $n$ chiral carbon atoms has a maximum of $2^n$ possible stereoisomers and half that many pairs of enantiomers.
- In some cases, fewer than the maximum predicted number of stereoisomers exist because some of the molecules have symmetry planes that make them identical to their mirror images.
In a Fischer projection, the aldehyde or ketone group is always placed at the top. The result is that —H and —OH groups projecting above the page are on the left and right of the chiral carbons, and groups projecting behind the page are above and below the chiral carbons.

*Fischer projection of a glyceraldehyde enantiomer*
21.3 The D and L Families of Sugars: Drawing Sugar Molecules

- Monosaccharides are divided into **D sugars** and **L sugars** based on their structural relationships to glyceraldehyde.
21.3 The D and L Families of Sugars: Drawing Sugar Molecules

• In the D form, the —OH group on carbon 2 comes out of the plane of the paper and points to the right; in the L form, the —OH group at carbon 2 comes out of the plane of the paper and points to the left.
D and L derive from the Latin *dextro* for “right” and *levo* for “left.” In Fischer projections, the D form of a monosaccharide has the hydroxyl group on the chiral carbon atom farthest from the carbonyl group pointing toward the right, whereas the L form has the hydroxyl group on this carbon pointing toward the left.
The goal of modern drug development is creation of a drug molecule that binds with a specific hormone, enzyme, or cellular receptor.

Because most biomolecules are chiral, a chiral drug molecule (single isomer) is likely to meet the need most effectively.

The route to a chiral drug molecule begins with chiral reactants and an enzyme, or with chemical synthesis of a pair of enantiomers that are then separated from each other.

Enantiomers can have different effects. The active ingredient in the pain killer and anti-inflammatory Aleve, is sold as a single enantiomer. The other enantiomer causes liver damage.
21.4 Structure of Glucose and Other Monosaccharides

- Monosaccharides with five or six carbon atoms exist primarily in cyclic forms when in solution.
- Aldehydes and ketones react reversibly with alcohols to yield hemiacetals.

\[
\begin{align*}
\text{O} & \quad \text{H} \\
\text{R–C–H} & + \quad \text{O–R'} \quad \xlongleftrightarrow{} \quad \text{R–C–O–R'} \\
\text{An aldehyde} & \quad \text{An alcohol} \quad \text{A hemiacetal}
\end{align*}
\]
21.4 Structure of Glucose and Other Monosaccharides
21.4 Structure of Glucose and Other Monosaccharides

- D-Glucose can exist as an open-chain hydroxy aldehyde or as a pair of cyclic hemiacetals.
- The cyclic forms differ only at C1, where the —OH group is either on the opposite side of the six-membered ring from the CH₂OH (α) or on the same side (β).
- The —CH₂OH group in D sugars is always above the plane of the ring.
- Cyclic monosaccharides that differ only in the positions of substituents at carbon 1 are known as anomers, and carbon 1 is said to be an anomeric carbon atom.
21.4 Structure of Glucose and Other Monosaccharides

- Although the structural difference between anomers appears small, it has enormous biological consequences.

- Crystalline glucose is entirely in the cyclic $\alpha$ form. In water, equilibrium is established among the open-chain form and the two anomers through mutarotation.
21.4 Structure of Glucose and Other Monosaccharides

Monosaccharide Structures—Summary

- Monosaccharides are polyhydroxy aldehydes or ketones.
- Monosaccharides have three to seven carbon atoms, and a maximum of $2^n$ possible stereoisomers, where $n$ is the number of chiral carbon atoms.
- D and L enantiomers differ in the orientation of the $-\text{OH}$ group on the chiral carbon atom farthest from the carbonyl. In Fischer projections, D sugars have the $-\text{OH}$ on the right and L sugars have the $-\text{OH}$ on the left.
- D-Glucose (and other 6-carbon aldoses) forms cyclic hemiacetals conventionally represented so that $-\text{OH}$ groups on chiral carbons on the left in Fischer projections point up and those on the right in Fischer projections point down.
- In glucose, the hemiacetal carbon (the anomeric carbon) is chiral, and $\alpha$ and $\beta$ anomers differ in the orientation of the $-\text{OH}$ groups on this carbon. The $\alpha$ anomer has the $-\text{OH}$ on the opposite side from the $-\text{CH}_2\text{OH}$ and the $\beta$ anomer has the $-\text{OH}$ on the same side as the $-\text{CH}_2\text{OH}$. 
• Monosaccharides can form multiple hydrogen bonds, and are generally high-melting, white, crystalline solids that are soluble in water and insoluble in nonpolar solvents.
• Most monosaccharides and disaccharides are sweet-tasting, digestible, and nontoxic.
• Except for glyceraldehyde (an aldotriose) and fructose (a ketohexose), the carbohydrates of interest in human biochemistry are all aldohexoses or aldopentoses.
• Most are in the D family.
21.5 Some Important Monosaccharides

Glucose

• Glucose is the most important simple carbohydrate in human metabolism.

• It is the final product of complex carbohydrate digestion and provides acetyl groups for entry into the citric acid cycle as acetyl-CoA.

• Maintenance of an appropriate blood glucose level is essential to human health.
21.5 Some Important Monosaccharides

Galactose

- D-Galactose is widely distributed in plant gums and pectins, and is a component of the disaccharide lactose.
- Galactose is an aldohexose; it differs from glucose only in the spatial orientation of the —OH group at carbon 4.
- In the body, galactose is converted to glucose to provide energy and is synthesized from glucose as needed.
Fructose

- D-Fructose, often called *levulose* or *fruit sugar*, occurs in honey and many fruits.
- It is one of the two monosaccharides combined in the disaccharide sucrose.
- It is a ketohexose rather than an aldohexose. In solution, fructose forms five-membered rings:
Ribose and 2-Deoxyribose

- Ribose and its relative 2-deoxyribose are both 5-carbon aldehyde sugars. These two sugars are most important as parts of larger biomolecules.
- Ribose is a constituent of coenzyme A, ATP, oxidizing and reducing agent coenzymes and cyclic AMP.
- 2-deoxyribose differs from ribose by the absence of one oxygen atom, that in the —OH group at C2.
CELL-SURFACE CARBOHYDRATES AND BLOOD TYPE

- Human blood can be classified into four blood group types, called A, B, AB, and O, based on the presence of three different oligosaccharide units, designated A, B, and O.
- Among the targets of antibodies are cell-surface molecules that are not present on the individual’s own cells, thus “foreign blood cells.”
- Type O cell-surface oligosaccharides are similar in composition to those of types A and B. People with blood types A, B, and AB all lack antibodies to type O cells making individuals with type O blood “universal donors.”
- People with type AB blood have both A and B molecules on their red cells. Their blood contains no antibodies to A, B, or O, and they can, if necessary, receive blood of all types.
21.6 Reactions of Monosaccharides

Reaction with Oxidizing Agents: Reducing Sugars

- Aldehydes can be oxidized to carboxylic acids (RCHO $\rightarrow$ RCOOH).
- As the open-chain aldehyde is oxidized, its equilibrium with the cyclic form is displaced, so that the open-chain form continues to be produced.
- Carbohydrates that react with mild oxidizing agents are classified as **reducing sugars**.
21.6 Reactions of Monosaccharides

Reaction with Oxidizing Agents: Reducing Sugars

- In *basic* solution, ketones can undergo rearrangement and will also act as reducing sugars.
- Keto–enol tautomerism is an equilibrium that results from a shift in position of a hydrogen atom and a double bond. It is possible whenever there is a hydrogen atom on a carbon adjacent to a carbonyl carbon.
Reactions of Monosaccharides

21.6 Reaction with Alcohols: Glycoside and Disaccharide Formation

- Hemiacetals react with alcohols with the loss of water to yield acetals, compounds with two —OR groups bonded to the same carbon.

- Because glucose and other monosaccharides are cyclic hemiacetals, they also react with alcohols to form acetals, which are called **glycosides**.
21.6 Reactions of Monosaccharides

- In larger molecules monosaccharides are connected to each other by glycosidic bonds.

Formation of a glycosidic bond between two monosaccharides

![Formation of a glycosidic bond between two monosaccharides](image)

- The reverse of this reaction is a hydrolysis.

Hydrolysis of a disaccharide

![Hydrolysis of a disaccharide](image)
Formation of Phosphate Esters of Alcohols

- Phosphate esters of alcohols contain a \(-\text{PO}_3^{-2}\) group bonded to the oxygen atom of an \(-\text{OH}\) group.
- The \(-\text{OH}\) groups of sugars can add \(-\text{PO}_3^{-2}\) groups to form phosphate esters in the same manner.
- Phosphate esters of monosaccharides appear as reactants and products throughout the metabolism of carbohydrates.
Disaccharide Structure

- The two monosaccharides in a disaccharide are connected by a glycosidic bond. The bond may be $\alpha$ or $\beta$ as in cyclic monosaccharides.
- The structures include glycosidic bonds that create a 1,4 link between C1 of one monosaccharide and C4 of the second monosaccharide.
Maltose

- Maltose can be prepared by enzyme-catalyzed degradation of starch.
- Two $\alpha$-D-glucose molecules are joined in maltose by an $\alpha$-1,4 link.
- It is both an acetal (at C1 in the glucose on the left) and a hemiacetal (at C1 in the glucose on the right), making maltose a reducing sugar.
Lactose

- Lactose, or milk sugar, is the major carbohydrate in mammalian milk. Human milk, for example, is about 7% lactose.
- Structurally, lactose is composed of D-galactose and D-glucose. The two monosaccharides are connected by a $\beta$-1,4 link. Like maltose, lactose is a reducing sugar because the glucose ring (on the right in the following structure) is a hemiacetal at C1.
21.7 Disaccharides

Sucrose

- Hydrolysis of sucrose yields one molecule of D-glucose and one molecule of D-fructose. The 50:50 mixture of glucose and fructose that results, invert sugar, is sweeter than sucrose.

- Sucrose has no hemiacetal group because a 1,2 link joins both anomeric carbon atoms (C1 on glucose, C2 on fructose). The absence of a hemiacetal group means that sucrose is not a reducing sugar.
Carbohydrates and Fiber in the Diet

- The major monosaccharides in our diets are fructose and glucose from fruits and honey. The major disaccharides are sucrose and lactose.
- Our diets contain large amounts of the complex carbohydrate starch and the indigestible polysaccharide cellulose.
- Cellulose and all other indigestible carbohydrates are collectively known as dietary fiber.
- Consumption of the more easily digested carbohydrates results in rapid elevation of blood glucose levels followed by lower-than-desired levels a few hours later.
- Carbohydrates that are digested and absorbed more slowly are associated with healthier blood sugar responses.
- The Nutrition Facts labels on packaged foods give percentages based on a recommended 300 g per day of total carbohydrate and 25 g per day of dietary fiber.
- Pectins and vegetable gums comprise the “soluble” portion of dietary fiber.
- Hemicellulose and lignin are the major components of “insoluble” fiber.
21.8 Variations on the Carbohydrate Theme

- Variations on carbohydrates often incorporate modified glucose molecules.

\[
\begin{align*}
\beta\text{-d-Glucuronate} & & \beta\text{-d-Glucosamine} & & \text{N-Acetyl}\beta\text{-d-Glucosamine}
\end{align*}
\]
Chitin

- The shells of lobsters, beetles, and spiders are made of chitin, the second most abundant polysaccharide in the natural world. (Cellulose is the most abundant.)
- Chitin is a hard, structural polymer. It is composed of $N$-acetyl-$D$-glucosamine rather than glucose but is otherwise identical to cellulose.
21.8 Variations on the Carbohydrate Theme

Connective Tissue and Polysaccharides

- Connective tissues are composed of protein fibers in a matrix that contains unbranched mucopolysaccharides.
- The gel-like mixtures of these polysaccharides with water serve as lubricants and shock absorbers.
- *Hyaluronate* molecules contain up to 25,000 disaccharide units. It forms the *synovial fluid* that lubricates joints and is present within the eye.
- *Chondroitin 6-sulfate* (also the 4-sulfate) is present in tendons and cartilage, where it is linked to proteins.
Heparin

- Heparin is valuable medically as an anticoagulant (an agent that prevents or retards the clotting of blood).
- Heparin is composed of a variety of different monosaccharides, many of them containing sulfate groups.
Glycoproteins

- Proteins that contain short carbohydrate chains (oligosaccharide chains) are glycoproteins.
- The carbohydrate is connected to the protein by a glycosidic bond between an anomeric carbon and a side chain of the protein.
- The oligosaccharide chains function as receptors or, in one case, antifreeze.
21.9 Some Important Polysaccharides

- Polysaccharides are polymers of tens, hundreds, or even many thousands of monosaccharides linked together through glycosidic bonds.
Cellulose

- Cellulose provides structure in plants.
- Each molecule consists of several thousand \(\text{D}-\text{glucose}\) units joined in a long, straight chain by \(\beta-1,4\) links.
- Because of the tetrahedral bonding at each carbon atom, the carbohydrate rings bent up at one end and down at the other in what is known as the *chair conformation*.
21.9 Some Important Polysaccharides

- The hydrogen bonds within chains and between chains (shown in red) contribute to the rigidity and toughness of cellulose fibers.
- Grazing animals, termites, and moths are able to digest cellulose because microorganisms colonizing their digestive tracts produce enzymes that hydrolyze $\beta$-glycosidic bonds.
- Humans neither produce such enzymes nor harbor such organisms, and therefore cannot hydrolyze cellulose.
Starch

- In starch, individual glucose units are joined by $\alpha$-1,4 links rather than by the $\beta$-1,4 links of cellulose.

- Starch is fully digestible and is an essential part of the human diet. It is present only in plant material; our major sources are beans, wheat and rice, and potatoes.
21.9 Some Important Polysaccharides

Starch

• *Amylose*, accounts for about 20% of starch. It is somewhat soluble in hot water and consists of several hundred to a thousand D-glucose units linked in long chains.

• Amylose tends to coil into helices.
Starch

- *Amylopectin* accounts for about 80% of starch. It has up to 100,000 glucose units per molecule and $\alpha$-1,6 branches approximately every 25 units along its chain. It is not soluble.
Glycogen

- Glycogen stores energy in animals in the liver and muscles.
- Structurally, glycogen is similar to amylopectin in being a long polymer of D-glucose with the same type of branch points in its chain.
- Glycogen has many more branches and contains up to one million glucose units per molecule.
Cell Walls: Rigid Defense Systems

• Bacteria and higher plants surround the plasma membrane with a rigid cell wall. The rigidity of the wall prevents the cell from bursting due to osmotic pressure, gives shape to the cell, and protects it from pathogens.

• Plant cell walls are composed of fibrils of cellulose in a polymer matrix of pectins, lignin, and hemicellulose.

• Bacterial cell walls provide a rigid platform for the attachment of flagella and pilli. They do not contain cellulose. A majority of bacterial cell walls are composed of a polymer of peptidoglycan.

• Animals have developed natural defenses that can control many bacteria. For example, lysozyme—an enzyme found naturally in tears, saliva, and egg white—hydrolyzes the cell wall of pathogenic bacteria.

• Penicillin contains a beta-lactam ring that acts as a “suicide inhibitor” of the enzymes that synthesize the peptidoglycan cross-linking peptide chain. Unfortunately, many bacteria have developed enzymes that destroy the ring, granting resistance to penicillin.