

Chapter 8

Carbohydrates

This chapter is concerned with the structures and properties of carbohydrates. These molecules contain just three elements, namely carbon, hydrogen and oxygen. Carbohydrates are not only important metabolic energy sources, as detailed in Chapters 14 and 15, but they also have key functions in molecular and cellular recognition events. You will first learn the structures and chemical characteristics of monosaccharides and some of their derivatives, and then of oligosaccharides and polysaccharides. This is followed by a presentation of the composition, structure, and function of molecules in which carbohydrate are covalently linked to polypeptides, including proteoglycans, bacterial cell wall components, and glycoproteins. It is important to realize that a large proportion of proteins contain covalently attached carbohydrates and that the structures of these carbohydrate chains can vary enormously.

Essential Concepts

Monosaccharides

1. Monosaccharides can be defined as aldehyde or ketone derivatives of straight-chain polyhydroxy alcohols containing a minimum of three carbon atoms. Sugars that have aldehyde groups are called aldoses, whereas those with ketone moieties are termed ketoses. Depending on the number of carbon atoms, monosaccharides are referred to as trioses, tetroses, pentoses, hexoses, etc.
2. D-glucose has four chiral centers and is therefore one of 16 possible aldohexose stereoisomers. D sugars have the same absolute configuration at the asymmetric center most distant from the carbonyl group as does D-glyceraldehyde. Epimers are sugars in which the configuration around one carbon atom differs. Ketoses, which have a ketone function at C2, have one less chiral center than aldoses with the same number of carbons. Therefore, a ketohexose has only 8 possible stereoisomers.
3. Sugars can be represented in their cyclic hemiacetal and hemiketal forms as planar Haworth projections. Sugars that form six-membered rings are known as pyranoses, whereas those with five-membered rings are known as furanoses. A cyclic monosaccharide exists as either an α or a β anomer. Anomers freely interconvert in aqueous solution via the linear (open chain) form.
4. Five- and six-membered sugar rings are most abundant because of their stability. The tetrahedral bonding angles of carbon prevent the rings from being truly planar. The pyranose ring prefers the chair conformation and exists predominantly in the form that minimizes steric interactions among bulky ring substituents (i.e., bulky groups tend to occupy equatorial rather than axial positions).
5. Sugars can undergo reactions characteristic of aldehydes and ketones:

- (a) Oxidation of the aldehyde group of an aldose yields an aldonic acid. Thus, D-glucose oxidation results in D-gluconic acid.
 - (b) Oxidation of the primary hydroxyl group produces a uronic acid, such as D-glucuronic acid from D-glucose.
 - (c) Reduction of aldoses and ketoses yields polyhydroxy alcohols called alditols. Thus, D-glucose reduction gives glucitol (also known as sorbitol).
6. Monosaccharides in which an OH group is replaced by an H are called deoxy sugars. The most important of these is β -D-2-deoxyribose, a component of DNA.
 7. In amino sugars, an OH group is replaced by an amino group that is usually acetylated. A common amino sugar is *N*-acetylglucosamine. *N*-acetylneuraminic acid, an important constituent of glycoproteins (see below), is composed of an acetylated amino sugar, *N*-acetylmannosamine, covalently linked to pyruvic acid.
 8. The anomeric carbon of a sugar can form a covalent bond with an alcohol to form an α or β glycoside. The bond is called a glycosidic bond. An *N*-glycosidic bond links an anomeric carbon and a nitrogen atom, as in the covalent bond between ribose and a purine or pyrimidine.

Polysaccharides

9. Polysaccharides are made up of monosaccharides covalently linked by glycosidic bonds. A homopolysaccharide contains one type of monosaccharide, whereas a heteropolysaccharide can contain diverse monosaccharides. Polysaccharides may be linear or branched, because glycosidic bonds can form between an anomeric carbon and any of the hydroxyl groups of another monosaccharide. Naturally occurring polysaccharides incorporate only a few types of monosaccharides and glycosidic linkages.
10. Disaccharides consist of two sugars linked by a glycosidic bond. One example is lactose, in which C1 of galactose is linked to C4 of glucose by an α -glycosidic bond. Lactose is a reducing sugar because the free anomeric carbon on the glucose residue can reduce a mild oxidizing agent. Another disaccharide is sucrose, common table sugar, in which the C1 anomeric carbons of glucose and fructose are joined by an α -glycosidic bond. Sucrose is therefore a nonreducing sugar.
11. Cellulose, the most abundant polysaccharide, is a large, linear polymer in which glucose units are linked by $\beta(1\rightarrow4)$ glycosidic bonds. Cellulose forms a highly hydrogen bonded structure of enormous strength that contributes to the rigidity of plant cell walls. Cows and other herbivores can utilize cellulose as a nutrient because they harbor microbes that produce cellulases which cleave the glycosidic bonds. Another widely distributed polysaccharide is chitin, which comprises the exoskeletons of many invertebrates. It is a homopolymer of *N*-acetylglucosamine residues linked in $\beta(1\rightarrow4)$ fashion.

12. Starch is the principal food reserve in plants. It has two structural forms: α -amylose, a linear polymer of $\alpha(1\rightarrow4)$ linked glucose units, and amylopectin, an $\alpha(1\rightarrow4)$ linked glucose polymer bearing periodic branches linked by $\alpha(1\rightarrow6)$ bonds. Digestion of starch by animals begins with the action of salivary amylase, an enzyme that cleaves $\alpha(1\rightarrow4)$ glycosidic bonds, and is continued by pancreatic amylase, which produces $\alpha(1\rightarrow4)$ linked di- and trisaccharides, as well as oligosaccharides containing the $\alpha(1\rightarrow6)$ bonds. These latter polymers, known as dextrans, are further degraded by a debranching enzyme that can cleave $\alpha(1\rightarrow6)$ links. These oligosaccharides are eventually converted to glucose, which can be absorbed by the intestine.
13. Glycogen is a polysaccharide that is synthesized and stored by animals, primarily in skeletal muscle and liver. The structure of glycogen resembles that of amylopectin but is more highly branched. When needed for metabolic energy, glycogen is broken down through the combined action of glycogen phosphorylase, which cleaves $\alpha(1\rightarrow4)$ bonds, and glycogen debranching enzyme.
14. Glycosaminoglycans are major constituents of the extracellular matrix. Most of these rigid, linear polysaccharides are composed of alternating uronic acid and hexosamine residues. For example, hyaluronic acid is composed of D-glucuronate linked $\beta(1\rightarrow3)$ to *N*-acetylglucosamine which in turn is linked $\beta(1\rightarrow4)$ to the next glucuronate residue. Because of its polyanionic nature, hyaluronic acid forms viscoelastic solutions, a property that makes it an effective biological shock absorber and lubricant.
15. Other types of glycosaminoglycans, all of which are composed of sulfated disaccharide units, include chondroitin sulfates, dermatan sulfate, keratin sulfate, and heparin. The last named substance is found in mast cells and inhibits blood clotting.

Glycoproteins

16. A large proportion of all proteins have covalently bound carbohydrates and are therefore glycoproteins. The polypeptide chains of glycoproteins are encoded by nucleic acids, whereas the attached oligosaccharide chains are products of enzymatic reactions. This is the source of microheterogeneity, the variability in composition of the carbohydrate component in a population of glycoprotein molecules that all have the same polypeptide chain.
17. Proteoglycans are found mainly in the extracellular matrix and are combinations of proteins and glycosaminoglycans that associate by both covalent and noncovalent bonds. These molecules have a bottlebrush-like structure (e.g., Figure 8-13) in which up to 100 core proteins with attached glycosaminoglycans and both *N*-linked and *O*-linked oligosaccharides are linked to hyaluronate. This assembly of protein and carbohydrate is a huge, space-filling macromolecule. Proteoglycans are highly hydrated, so that, in combination with collagen, they account for the high resilience of cartilage.
18. Bacteria possess rigid cell walls that are responsible in part for their virulence. In gram-positive bacteria, the cell wall consists of polysaccharide and polypeptide chains that are

covalently attached to form a baglike structure called peptidoglycan that completely envelops the cell. Gram-negative bacteria have a relatively thin peptidoglycan cell wall surrounded by a complex outer membrane.

19. The polysaccharide of some bacterial cell walls consists of alternating residues of $\beta(1\rightarrow4)$ -linked *N*-acetylmuramic acid and *N*-acetylglucosamine in which the *N*-acetylmuramic acid residues are linked via an amide bond to a tetrapeptide containing D-amino acids. A continuous meshlike framework is formed by cross-linking adjacent peptidoglycan chains through their tetrapeptide side chains (Figure 8-15). The enzyme lysozyme can degrade peptidoglycan by cleaving the glycosidic bond between *N*-acetylmuramic acid and *N*-acetylglucosamine. The antibiotic action of penicillin rests on its ability to inhibit the formation of cross-links in peptidoglycan.
20. Glycoproteins include nearly all membrane-bound and secreted eukaryotic proteins. The oligosaccharide chains are attached to the proteins by either *N*-glycosidic or *O*-glycosidic bonds. In an *N*-glycosidic bond, the amide group of an asparagine in the sequence Asn-X-Ser/Thr is linked to *N*-acetylglucosamine. *N*-glycosylation occurs in stages:
 - (a) An oligosaccharide rich in mannose and containing glucose and *N*-acetylglucosamine is attached cotranslationally, that is, while the polypeptide is being synthesized on ribosomes bound to the endoplasmic reticulum.
 - (b) The oligosaccharide undergoes trimming, the enzymatic removal of some sugars, as the glycoprotein moves from the endoplasmic reticulum to the Golgi apparatus.
 - (c) Further processing occurs in the Golgi apparatus, where monosaccharides such as *N*-acetylglucosamine, galactose, L-fucose, and *N*-acetylneuraminic acid are enzymatically added to the trimmed chain by glycosyltransferases. *N*-linked glycoproteins exhibit great diversity in their oligosaccharide chains due to differences in the extent of processing.
21. *O*-glycosidically linked oligosaccharide chains are covalently linked to a Ser or Thr side chain in a protein and vary considerably in structure. *O*-linked oligosaccharides are added to completed polypeptides in the Golgi apparatus and are built up by stepwise addition of monosaccharides in reactions catalyzed by glycosyltransferases.
22. The number and structure of *N*- and *O*-linked oligosaccharides attached to a given polypeptide chain can vary, giving rise to glycoprotein variants called glycoforms.
23. Particular functions can sometimes be attributed to the presence of oligosaccharides. Oligosaccharides attached to proteins may modulate the conformational freedom of the polypeptide. The hydrophilic oligosaccharide chains may take up considerable volume and thereby tend to protect the protein from enzymatic attack or modify its activity.
24. The enormous number of oligosaccharide structures suggests that they contain biological information and are important in molecular recognition. All cells carry a coat of glycoconjugates (a mixture of glycoproteins and glycolipids). Proteins called lectins specifically recognize and bind to individual monosaccharides or small oligosaccharides in

discrete glycosidic linkages at the cell surface. For example, the leukocyte selectins bind to cell-surface carbohydrates on endothelial cells, an interaction that helps direct leukocytes to a site of blood vessel injury.

25. Different oligosaccharide components of certain glycolipids distinguish the ABO blood group antigens.
26. Oligosaccharide chains mediate a variety of biological functions that depend on molecular recognition between proteins and carbohydrates. Among these are delivery of proteins to appropriate destinations within cells and the regulation of cell growth.

Guide to Study Exercises (text p. 218)

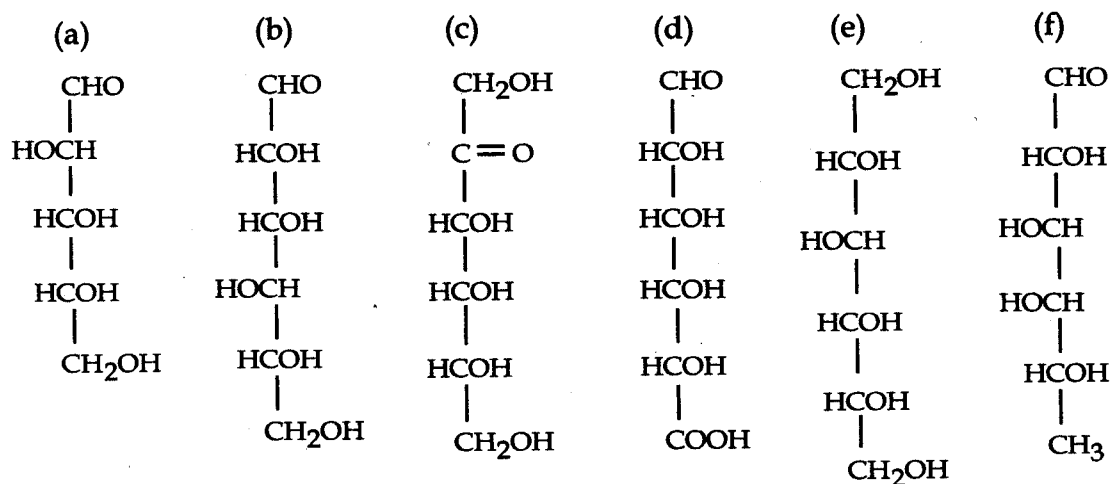
1. See Figure 8-3.
2. See Figure 8-3.
3. Cellulose, chitin, starch, and glycogen are similar in that all are polymers containing a single type of saccharide residue (either glucose or, in the case of chitin, a glucose derivative). Only glycogen and the amylopectin component of starch are branched; cellulose, chitin, and the α -amylose component of starch are linear polymers. The polymers differ in the glycosidic linkage between residues: A $\beta(1\rightarrow4)$ glycosidic bond links the glucose residues in cellulose and the *N*-acetylglucosamine residues in chitin, whereas an $\alpha(1\rightarrow4)$ linkage is the primary linkage in starch and glycogen, which also have $\alpha(1\rightarrow6)$ linkages at their branch points. Both cellulose and chitin are linear chains that assemble in stacked sheets. Starch and glycogen have an irregular helical structure such that they form globules in cells. Finally, the functions of the polymers differ: Cellulose provides structural support for plants, and chitin is a major component of the exoskeletons of arthropods and the cell walls of fungi and algae. In contrast, starch and glycogen are storage forms for the metabolic fuel glucose. Furthermore, the structural polymers, once formed, tend to be relatively permanent, whereas the storage polymers are readily synthesized and degraded. (Sections 8-2B and C)
4. Glycosaminoglycans are linear polymers of alternating uronic acid and hexosamine residues and are often sulfated. Their multiple negative charges cause them to assume an extended conformation and to be heavily hydrated. The large volume of bound water makes the glycosaminoglycans viscous and elastic. Furthermore, because of their long length, they exhibit shear-dependent viscosity, a property that suits their function as lubricants.
 Proteoglycans have similar properties due to their high content of glycosaminoglycans. These enormous molecules serve similar functions, for example, conferring resilience on cartilage. (Sections 8-2D and 8-3A)
5. *N*- and *O*-linked oligosaccharides differ in their structure and linkage to glycoproteins. *N*-linked oligosaccharides consist of a (mannose)₃(GlcNAc)₂ core whose terminal GlcNAc is β -linked to the amide nitrogen of an Asn side chain. A variety of other sugars may be added

to the core oligosaccharide to produce a branched structure. *O*-linked oligosaccharides have a more variable size and structure but most commonly have GalNAc linked to the OH group of a Ser or Thr side chain. (Section 8-3C)

Questions

Monosaccharides

1. Indicate which of the following is an aldose, a ketose, a pentose, a hexose, a uronic acid, an alditol, a deoxy sugar, or a reducing sugar.



2. Draw the following monosaccharides as Haworth projections:
- α anomer of D-ribose
 - β anomer of D-glucose
 - β anomer of D-fructose
 - methyl- β -D-galactose.

Which of these compounds contains a glycosidic bond?

3. An equilibrium mixture of D-glucose contains approximately 63% β -D-glucopyranose and 36% α -D-glucopyranose. There are trace amounts of three other forms. What are they?
4. Although β -D-glucopyranose is the predominant form of glucose in solution, crystalline glucose consists almost exclusively of α -D-glucopyranose. What accounts for this difference?
5. Draw the most stable chair conformation of α -D-galactose.

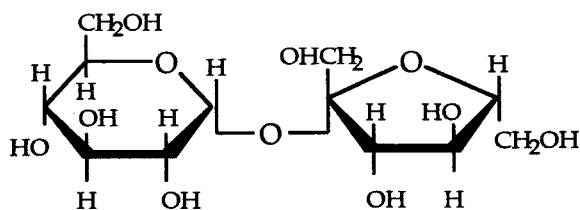
Polysaccharides

6. Match each term with its definition.

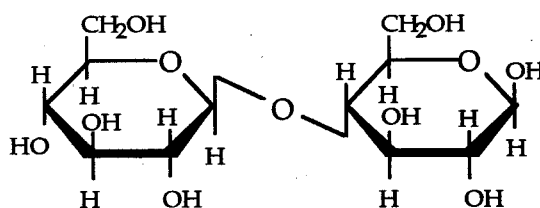
- | | | |
|--------------|-------|--|
| A. Alditol | _____ | Differs in configuration at the anomeric carbon |
| B. Epimer | _____ | Polyhydroxy alcohol |
| C. Glycan | _____ | Product of condensation of anomeric carbon with an alcohol |
| D. Anomer | _____ | Differs in configuration at one carbon atom. |
| E. Glycoside | _____ | Polymer of monosaccharides |

7. Which of the following di- and trisaccharides contains fructose, contains an α anomeric bond, or is a reducing sugar?

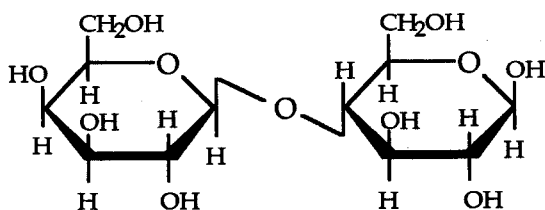
(a) sucrose



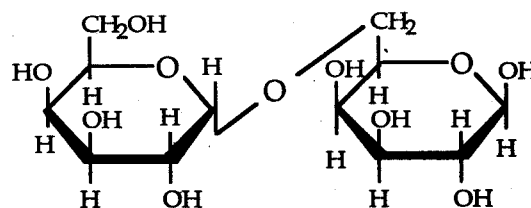
(b) cellulubiose



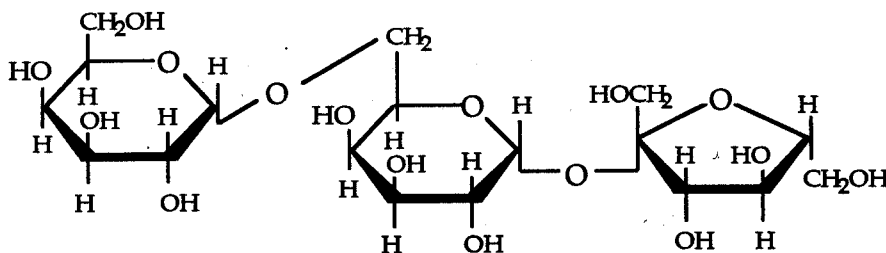
(c) lactose



(d) melibiose



(e) raffinose



8. An unknown trisaccharide was treated with methanol in HCl (to methylate its free OH groups) then subjected to acid hydrolysis (to break glycosidic bonds). The products were 2,3,4,6-tetra-*O*-methylgalactose, 2,3,4-tri-*O*-methylglucose, and 2,3,6-tri-*O*-methylglucose. Treatment of the intact trisaccharide with $\beta(1\rightarrow6)$ -galactosidase yielded D-galactose and a disaccharide. Treatment of this disaccharide with $\alpha(1\rightarrow4)$ -glucosidase yielded D-glucose. Draw the structure of this trisaccharide and give its systematic name.
9. How do the chemical differences between starch and cellulose result in their very different polymeric structures?
10. Glycogen and starch are extensively branched high-molecular-weight polymers. Give two reasons why such a structure is advantageous for a fuel-storage molecule.

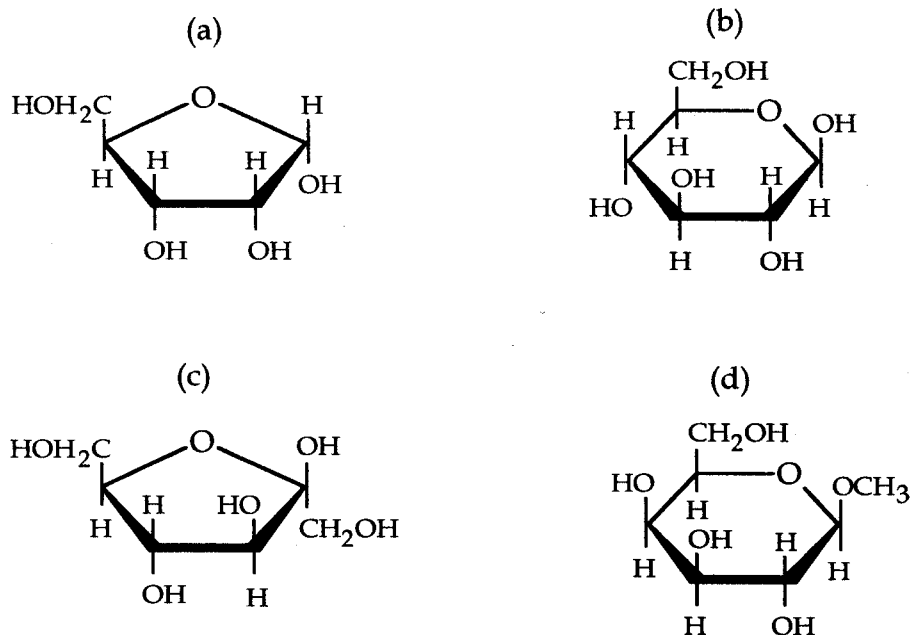
Glycoproteins

11. How could lectins be used to purify polysaccharides and glycoproteins?
12. Figure 8-16 presents structures of typical *N*-linked oligosaccharides. (a) Which sugars make up the core oligosaccharide? (b) What other sugars are typically found at the termini of branched oligosaccharides?
13. A major protein of saliva contains several hundred identical covalently attached disaccharides containing *N*-acetylneuraminic acid in $\alpha(2\rightarrow6)$ linkage to *N*-acetylgalactosamine that is linked to a Ser residue. Solutions of the intact protein are extremely viscous. However, when the protein is treated with sialidase, the viscosity decreases markedly. What features of the glycoprotein structure give rise to the high viscosity and why does sialidase treatment bring about the observed change?
14. Explain why a type AB individual can receive a transfusion of type A or type B blood, but a type A or type B individual cannot receive a transfusion of type AB blood.

Answers to Questions

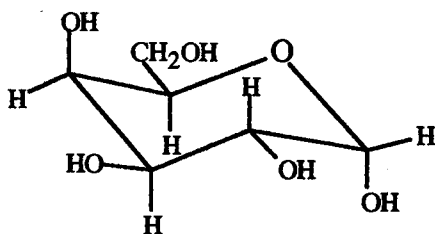
1. (a) aldose, pentose, reducing sugar
(b) aldose, hexose, reducing sugar
(c) ketose, hexose, reducing sugar
(d) aldose, hexose, uronic acid, reducing sugar
(e) hexose, alditol
(f) aldose, hexose, deoxy sugar, reducing sugar

2.



Only methyl- β -D-galactose (d) contains a glycosidic bond.

3. The three other forms are the open chain form of glucose, α -D-glucofuranose and β -D-glucofuranose.
4. The α anomer of glucose is less soluble than the β anomer and therefore comes out of solution more readily. As it crystallizes, the β -glucose remaining in solution interconverts with α -glucose in order to maintain the 36% α -63% β equilibrium ratio. Thus, the α anomer is continually generated and deposited in the crystal.
- 5.



The most stable conformation has its bulky CH_2OH group and two OH groups in equatorial positions, which minimizes their steric interference.

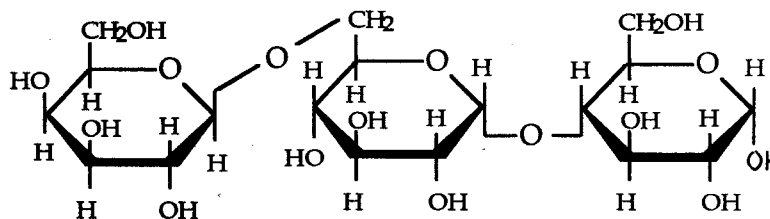
6.

- D Differs in configuration at the anomeric carbon
A Polyhydroxy alcohol
E Product of condensation of anomeric carbon with an alcohol

- B Differs in configuration at one carbon atom.
C Polymer of monosaccharides

7. (a) Contains fructose, contains an α anomeric bond.
 (b) Is a reducing sugar.
 (c) Is a reducing sugar.
 (d) Contains an α anomeric bond, is a reducing sugar.
 (e) Contains fructose, contains an α anomeric bond.

8.



β -D-galactopyranosyl-(1 \rightarrow 6)- α -D-glucopyranosyl-(1 \rightarrow 4)-D-glucopyranose

9. The $\beta(1\rightarrow4)$ glycosidic bonds that join glucose groups in cellulose give rise to extended polymers that line up in parallel and are stabilized by extensive intrachain and interchain hydrogen bonds. This gives cellulose fibers unusual strength and renders them water insoluble. In contrast, the $\alpha(1\rightarrow4)$ glycosidic bonds linking glucose residues in starch give rise to a totally different structure, namely a linear chain that assumes a relatively open helical conformation.
10. Two advantages are (1) the reduction in osmotic pressure in a cell when many residues are combined into a single polymeric molecule, and (2) the rapid mobilization of glucose when it is removed from the ends of many branches simultaneously.
11. Lectins are proteins that bind specific sugars with high affinity. Thus, a lectin attached to an immobile support can be used to selectively adsorb polysaccharides or glycoproteins via affinity chromatography. The adsorbed molecules can then be eluted by applying a solution containing an excess of the free sugar to which the lectin preferentially binds.
12. (a) The core oligosaccharide is (mannose)₃(GlcNAc)₂.
 (b) Typical terminal sugars are galactose, *N*-acetylneuraminic acid (sialic acid), and fucose.
13. Each disaccharide unit bears a negative charge (from the ionized COOH group of *N*-acetylneuraminic acid). Because of the strong repulsion between charged groups, the protein assumes a rigid elongated shape, thereby accounting for the high viscosity of the solution. Removal of the *N*-acetylneuraminic acid residues by sialidase abolishes the large net negative