Chapter 7

Carbohydrates

Overview

- **Carbohydrates** – main ingredient for energy production
  - Most abundant biomolecule in nature
  - Direct link between solar energy & chemical energy
  - Glucose – our main energy source
**Section 7.1: Monosaccharides**

- **Carbohydrate**: polyhydroxyaldehyde or polyhydroxyketone, most abundant biomolecules in nature, biological functions include:
  - Energy sources – glucose
  - Structural elements – cellulose & chitin in plants & insects
  - Cellular communication & identity
  - Precursors in production of other biomolecules

- **Monosaccharides** - simple sugars
  - **Aldoses** - aldehyde functional group
  - **Ketoses** - ketone functional group
  - Building blocks of all carbohydrates
  - General formula \( C_nH_{2n}O_n \) or \((CH_2O)_n\)
    where \( n \) varies from 3 – 8

- **Oligosaccharides** – 2-10 monosaccharides
- **Polysaccharides** - >10 monosaccharides

Section 7.1: Monosaccharides

- Carbohydrates are also classified by the number of carbon atoms they contain
  - Trioses, tetroses, pentoses, and hexoses
  - Most abundant in living cells are hexoses and pentoses
  - Class names often combine information about carbon number and functional group
- Glyceraldehyde contains a stereocenter on #2 C (chiral); exists as a pair of enantiomers
  - Chiral carbon – asymmetric carbon in molecule having mirror-image form
  - Enantiomers - Mirror-images stereoisomers

![Figure 7.2 Glyceraldehyde (an Aldotriose) and Dihydroxyacetone (a Ketotriose)](image-url)

Section 7.1: Monosaccharides

3-C sugars have 1 chiral C so only 2 enanitomers; more chiral C more possible stereoisomers

- **Diastereomers**: stereoisomers that are not mirror images
  - example: D-ribose (−OHs on right); L-ribose (−OHs on left)
  - example: D-arabinose and L-arabinose

- **Epimers**: diastereomers that differ from each other in configuration at only one chiral carbon

![Figure 7.4 The Optical Isomers D- and L- Ribose and D- and L- Arabinose](From McKeep and McKeep, Biochemistry, 5th Edition, © 2011 Oxford University Press)
Fischer projection: 2-D representation shows tetrahedral stereo-centers

- Carbons - numbered starting most highly oxidized C, top

- D- or L- configuration - determined by arrangement on C-5

- D-glucose, hydroxyl on right; L-glucose hydroxyl on left
Cyclic Structure of Monosaccharides

- Cyclization - interaction between functional groups on distant carbons
  - C1 to C5, to make a cyclic hemiacetal
  - Cyclization using C2 to C5 results in hemiketal formation.
- Carbonyl carbon is new chiral center and becomes an anomeric carbon

Figure 7.5 Formation of Hemiaceitals and Hemiketals
Section 7.1: Monosaccharides

Two possible diastereomers from cyclization are called **anomers**
- \(\alpha\)-D-glucose – OH on R; \(\beta\)-D-glucose – OH on L

5- and 6-membered hemiacetals are represented as planar pentagons or hexagons
- Commonly written with the anomeric carbon (C1) on right; hemiacetal oxygen to the back right

D-sugar form, when the anomeric hydroxyl is up it gives a \(\beta\)-anomeric form (right above) while down gives the \(\alpha\)-anomeric form (left)

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**Figure 7.6 Monosaccharide Structure**

**Figure 7.7 Haworth Structures of the Anomers of D-Glucose**

Section 7.1: Monosaccharides

- Five-membered rings are called **furanoses** and six-membered rings are **pyranoses**
- Cyclic form of fructose is fructofuranose, while glucose in the pyranose form is glucopyranose

Figure 7.8 Furan and Pyran

Figure 7.9 Fischer and Haworth Representations of D-Fructose
Section 7.1: Monosaccharides

**Conformational Structures**

- Furanoses are close to planar
  - Haworth projection adequately represent
- Pyranoses more accurately represented as strain-free chair conformation
  - α-D-Glucopyranose - OH on anomeric C down/back
  - β-D-Glucopyranose – OH on anomeric C on plane/right

Figure 7.10 α- and β-D-glucose

**Mutarotation**

- $\alpha$- and $\beta$-forms of monosaccharides are readily interconverted in aqueous environments.
- Spontaneous process produces an equilibrium mixture of $\alpha$- and $\beta$-forms in both furanose and pyranose ring structures.
- Open chain form can participate in redox reactions.

**Figure 7.11 Equilibrium Mixture of D-Glucose**

Section 7.1: Monosaccharides

- **Oxidation**—undergo several oxidation reactions in presence of metal ions or certain enzymes
  - Oxidation of aldehyde group yields **aldonic acid**
  - Oxidation of terminal CH₂OH group yields **uronic acid**
  - Oxidation of both groups yields **aldaric acid**
  - **Lactone** - produced if the carbonyl groups of aldonic or uronic acids react with an OH group in the same molecule
    - Readily produced in nature - **L-ascorbic acid** (vitamin C)
    - Vitamin C is a powerful reducing agent, protects cells from reactive oxygen and nitrogen species

- Ascorbic acid

- d-Gluconic acid

- d-Glucuronic acid

- d-Glucaric acid
Section 7.1: Monosaccharides

Reduction – aldehyde and ketone groups yields sugar alcohols, **alditols**

- **Reducing sugars** - reduced by weak, oxidizing agents such as Benedict’s reagent
  - Needs open chain - all aldoses are reducing sugars
  - ketoses (fructose) are reducing sugars also, due to isomerization

![Reaction of Glucose with Benedict’s Reagent](image)

**Figure 7.14 Reaction of Glucose with Benedict’s Reagent**

- **Alditols** - used in commercial food processing and in pharmaceuticals (e.g., sorbitol can be used to prevent moisture loss)
Isomerization - undergo several types of isomerization
- D-glucose incubated in an alkaline solution for several hours produces two isomers: D-mannose and D-fructose
- Both involve an enediol intermediate
- Transformation of glucose to fructose is an aldose-ketose interconversion.
- Transformation of glucose to mannose is referred to as epimerization.

Figure 7.16 Isomerization of D-Glucose to Form D-Mannose and D-Fructose

Section 7.1: Monosaccharides

- **Esterification** - free OH groups of carbohydrates can be converted to esters by reactions with acids
  - Can dramatically change a sugar’s chemical and physical properties
- Phosphate and sulfate esters most common in nature
  - Phosphate esters are formed during reactions with ATP
  - Sulfate esters – found predominantly in the proteoglycan components of connective tissue
  - Participate in forming of salt bridges between carbohydrate chains

**Section 7.1: Monosaccharides**

**Glycoside Formation**—hemiacetals and hemiketals react with alcohols to form the corresponding acetal and ketal

- Cyclic hemiacetal or hemiketal form reacts with an alcohol a glycosidic linkage is formed, compound a glycoside
  - Chemically an ether, ROR’
  - Naming of glycosides specifies the sugar component – glucose and fructose are glucoside and fructoside

**Disaccharide** – acetal linkage between hemiacetal hydroxyl of 1 monosaccharide & hydroxyl of another

**Polysaccharides** – many monosaccharides linked together

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*Figure 7.17 Formation of Acetals and Ketals*

Glycosylation Reactions attach sugars or glycans (sugar polymers) to proteins or lipids

- Catalyzed by glycosyl transferases
  - Glycosidic bonds are formed between anomeric carbons in certain glycans and oxygen or nitrogen of other types of molecules, resulting in N- or O-glycosidic bonds

Glycation is reaction of reducing sugars with nucleophilic nitrogen atoms in a nonenzymatic reaction

- Most researched is the nonenzymatic glycation of protein (Maillard reaction)
  - Schiff base that forms rearranges to a stable ketoamine, called Amadori product
  - Can further react to form advanced glycation end products (AGEs)
    - Promote inflammatory processes and involved in age-related diseases

Section 7.1: Important Monosaccharides

- **Glucose (D-Glucose)** — originally called dextrose, it is found in large quantities throughout the natural world
  - Primary fuel for living cells
  - Preferred energy source for brain cells and cells without mitochondria (erythrocytes)
  - Dietary sources: plant starch, disaccharides lactose, maltose, sucrose

- **Fructose (D-Fructose)** - fruit sugar, because of its high content in fruit
  - Per-gram basis, it is twice as sweet as sucrose; often used as a sweetening agent in processed food
  - Sperm use fructose as an energy source

- **Galactose** is necessary to synthesize a variety of important biomolecules
  - Important biomolecules - lactose, glycolipids, phospholipids, proetoglycan, glycoproteins
  - **Galactosemia** is a genetic disorder resulting from a missing enzyme in galactose metabolism
Section 7.1: Monosaccharide Derivatives

- **Uronic Acid** - $\alpha$-D-glucuronate (7.24a) and its epimer $\beta$-L-iduronate (7.24b) are important in animals
  - D-Glucuronic acid is used in the liver to improve water solubility to remove waste molecules

- **Amino Sugars** - a hydroxyl group (usually on carbon 2) is replaced with an amine group
  - D-Glucosamine (a) and D-galactosamine (b) are most common and often attached to proteins or lipids

- **Deoxy Sugars** - have an $-\text{OH}$ replaced by an $-\text{H}$ or $-\text{CH}_3$
  - 2-deoxy-D-ribose (7.25b) is pentose sugar of DNA; fucose (7.25a) part of ABO blood group determinants
Section 7.2: Disaccharides

- **Lactose** (*milk sugar*) - reducing sugar, found in milk
  - Galactose linked to glucose (β(1,4) linkage)
  - Lactose intolerance results from lactase deficiency
    - Inability to break down lactose to galactose & glucose
- **Maltose** (*malt sugar*) – intermediate of starch hydrolysis
  - α(1,4) linkage between two molecules of glucose
  - Does not exist freely in nature
- **Cellobiose** is a degradation product of cellulose
  - Two molecules of glucose linked with a β(1,4) glycosidic bond
  - Does not exist freely in nature
- **Sucrose** – cane or beet sugar; nonreducing sugar
  - Glucose linked to fructose by an α,β(1,2) glycosidic bond
  - Glycosidic bond occurs between both anomeric carbons

Section 7.2: Disaccharides

α-Lactose

β-Lactose

α-Maltose

β-Maltose

β-Cellobiose

Sucrose
Polysaccharides (glycans) - large numbers of monosaccharides connected by glycosidic linkages

- Can be linear or branched
- Two classes: homoglycans and heteroglycans
- Smaller glycans - 2 to 10 monomers called oligosaccharides
- Most often attached to polypeptides as glycoproteins
  - N-linked by N-glycosidic bond with asparagine R amide nitrogen
  - O-linked through serine or threonine R group hydroxyl

Homoglycans

- Found in starch, glycogen, cellulose, and chitin (glucose monomer)
- **Starch** and **glycogen** are energy storage molecules while chitin and cellulose are structural
- **Chitin** is part of the cell wall of fungi and arthropod exoskeleton
- **Cellulose** is the primary component of plant cell walls
  - Most abundant organic substance on earth
- No fixed molecular weight - size is a reflection of the metabolic state of the cell producing them
Section 7.3: Polysaccharides

- **Starch** - energy reservoir of plant cells; significant source of carbohydrate in the human diet
- **Amylose** - long, unbranched chains of D-glucose with $\alpha(1,4)$ linkages
  - Contains thousands of glucose monomers - molecular weight from 150,000 to 600,000 Da
- **Amylopectin** - branched polymer containing both $\alpha(1,6)$ and $\alpha(1,4)$ linkages
  - Branch points occur every 20 to 25 residues; $\alpha1,6$ linkages

Glycogen - carbohydrate storage molecule in animals; greatest abundance in liver and muscle cells

- Up to 8–10% of the wet weight of liver cells and 2–3% in muscle cells
- Similar in structure to amylopectin, with more branch points
- More compact and easily mobilized than other polysaccharides
Figure 7.34 (a) Amylopectin and (b) Glycogen

Section 7.3: Polysaccharides

- **Cellulose** - D-glucopyranosides linked by $\beta(1,4)$ glycosidic bonds
  - Most important structural polysaccharide of plants (most abundant organic substance on earth)
  - Pairs of unbranched cellulose molecules (12,000 glucose units each) are held together by hydrogen bonding to form sheetlike strips, or **microfibrils**
    - Each microfibril bundle is tough and inflexible with a tensile strength comparable to that of steel wire
    - Important for dietary fiber, wood, paper, and textiles

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**Heteroglycans** – high molecular weight; consisting of more than 1 type of monosaccharide; linkages to proteins

- N-linked (N-glycans) are linked via a β-glycosidic bond
- O-linked (O-glycans) have a disaccharide core of galactosyl-β-(1,3)-N-acetylgalactosamine linked via an α-glycosidic bond to the hydroxyl of serine or threonine residues

**Glycosaminoglycans (GAGs)** – linear polymers with repeating disaccharide units

- Five classes: hyaluronic acid, chondroitin sulfate, dermatan sulfate, heparin & heparin sulfate, keratin
Section 7.4: Glycoconjugates

- **Glycoconjugates** — carbohydrates linked to proteins and lipids

- **Proteoglycans**
  - Distinguished by their high carbohydrate content (about 95%)  
  - Occur on cell surfaces or are secreted to the extracellular matrix

Figure 7.37 Proteoglycan Aggregate
Proteoglycans

All contain GAG chains that are linked to core proteins by N- and O-glycosidic bonds

Aggrecan is an example of a type of proteoglycan that is found in abundance in cartilage

- A core protein linked to over 100 chondroitin sulfate and 40 keratin sulfate chains
- Up to 100 aggrecans are in turn attached to hyaluronic acid to form a proteoglycan aggregate

Roles in organizing extracellular matrix and are involved in signal transduction

Metabolism involved in many genetic disorders

- Hurler’s syndrome – enzyme deficiency
**Glycoproteins**

- Defined as proteins covalently linked to carbohydrates through N- and O-linkages
  - Several addition reactions in the lumen of the endoplasmic reticulum and Golgi complex are responsible for final N-linked oligosaccharide structure
  - O-glycan synthesis occurs later, probably initiating in the Golgi complex
- Carbohydrate could be 1%–85% of total weight
  - Usually linked to serine, threonine or asparagine

**Glycoprotein Functions**

- Metal-transport proteins transferrin & ceruloplasmin
- Blood-clotting factors
- Proteins involved in cell destruction during immune reactions
- Hormones - signaling
Section 7.5: The Sugar Code

- Living organisms require large coding capacities for information transfer
  - Profound complexity of functioning systems
  - To succeed as a coding mechanism, a class of molecules must have a large capacity for variation
  - Glycosylation is the most important posttranslational modification in terms of coding capacity
  - More possibilities with hexasaccharides than hexapeptides
  - In addition to their immense combinatorial possibilities; relatively inflexible, perfect for precise ligand binding

- Lectins
  - Lectins, or carbohydrate-binding proteins, are involved in translating the sugar code
  - Bind specifically to carbohydrates via hydrogen bonding, van der Waals forces, and hydrophobic interactions

Lectins Continued

- Biological processes include binding to microorganisms, binding to toxins, and involved in leukocyte rolling.

Figure 7.39 Role of Oligosaccharides in Biological Recognition

Section 7.5: The Sugar Code

- **The Glycome**
  - Total set of sugars and glycans in a cell or organism
  - Constantly in flux depending on the cell’s response to environment
  - There is no template for glycan biosynthesis; it is done in a stepwise process
  - **Glycoforms** can result based upon slight variations in glycan composition of each glycoprotein