

02 CARBOHYDRATES

Executive Summary

Carbohydrates are the most abundant biomolecules on Earth, serving as primary energy sources, structural components, and informational molecules in virtually all living organisms. Chemically defined as aldehydes or ketones with at least two hydroxyl groups, or substances that yield them upon hydrolysis, they range from simple sugars to complex polymers. The fundamental building blocks are **monosaccharides**, such as D-glucose, which can be linked together to form short chains called **oligosaccharides** (e.g., sucrose) or vast polymers known as **polysaccharides**.

The function of a polysaccharide is dictated entirely by its molecular architecture, specifically the type of monosaccharide units it contains and the nature of the chemical linkages, or **glycosidic bonds**, that connect them. This principle is best illustrated by comparing starch and cellulose. Both are polymers of D-glucose, yet they serve vastly different roles. Starch, linked by $\alpha(1\rightarrow4)$ bonds, forms a compact helix that is easily digestible, making it an ideal energy storage molecule. In contrast, cellulose, linked by $\beta(1\rightarrow4)$ bonds, forms straight, rigid fibers that are indigestible by most animals, providing structural integrity to plant cell walls. This simple difference in stereochemistry—alpha versus beta—is a masterclass in biochemical principles, demonstrating how a subtle change in molecular geometry creates a profound difference in biological function: one stores energy, the other builds worlds.

1. Introduction to Carbohydrates: The Molecules of Life

Understanding the vast world of carbohydrates begins with their basic chemical definition, their fundamental roles in biology, and the systematic way they are classified based on size. This classification—from single units to short chains to long polymers—provides a clear roadmap for exploring their increasing complexity and diverse functions in living systems, from providing metabolic fuel to encoding the language of cellular communication.

- **What is a Carbohydrate?** Carbohydrates are defined chemically as aldehydes or ketones with **at least two** hydroxyl groups, or substances that yield such compounds on **hydrolysis**. Many share the common empirical formula $(\text{CH}_2\text{O})_n$, which gives them their name ("hydrates of carbon").
 - **Monosaccharides** These are the simplest sugars, consisting of a single aldehyde or ketone unit. They are the fundamental building blocks of all complex carbohydrates. The most abundant example in nature is the six-carbon sugar, D-glucose.
 - **Oligosaccharides** These are short chains of monosaccharide units, or residues, joined by covalent linkages called glycosidic bonds. Disaccharides, which consist of two units, are the most common type; an everyday example is sucrose (table sugar), which is formed from D-glucose and D-fructose.
 - **Polysaccharides** Also known as glycans, these are long-chain polymers containing more than **ten** monosaccharide units, often numbering in the hundreds or thousands.
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They can be linear, like the structural polymer cellulose, or highly branched, like the energy-storage polymer glycogen.

The structure of these molecules, from the simplest monosaccharide to the most complex polysaccharide, is governed by a set of foundational principles that explain their stability, function, and biological recognition.

2. Foundational Principles of Carbohydrate Biochemistry

To fully appreciate the role of carbohydrates, it is crucial to understand the core biochemical principles that govern their structure and function. These principles provide a conceptual framework for why carbohydrates are structured the way they are and how they perform their diverse biological roles, from simple energy storage to complex cellular communication.

1. **Stereochemistry is Key** The precise three-dimensional arrangement of atoms (stereochemistry) is critical for biological function. Life almost exclusively uses sugars from the D-stereochemical series, and enzymes are highly specific for one stereoisomer over another.
2. **Monomers Build Polymers** A polysaccharide's biological function is determined by its specific monomeric subunits, the type of glycosidic linkages connecting them (e.g., α vs. β), and its overall branching pattern.
3. **Polymers Prevent Osmotic Stress** Storing fuel like glucose as a large polymer (glycogen in animals, starch in plants) prevents dangerously high intracellular concentrations. If stored as monomers, the resulting osmotic pressure would cause cells to swell and burst.
4. **Synthesis is Not Template-Based** Unlike proteins and nucleic acids, which are synthesized using a template (mRNA or DNA), polysaccharides are built by enzymes that add monomers one by one. This means their final length is often variable.
5. **Structure Follows Energy Minimization** Polysaccharides spontaneously fold into their most stable three-dimensional shapes, driven by weak interactions like hydrogen bonds. This is why starch forms stable helices and cellulose forms rigid, extended fibers.
6. **Molecular Complementarity Drives Recognition** The biological recognition of carbohydrates relies on a "lock-and-key" fit. Specialized proteins called **lectins** have binding sites that are precisely complementary to the shape and chemistry of specific oligosaccharide structures.
7. **Vast Structural Diversity from Simple Subunits** By varying the monosaccharide units, linkage types, and branching patterns, an immense variety of unique structures can be created from a small number of building blocks. This structural diversity allows carbohydrates to function as highly specific informational molecules.

Having established these guiding principles, we can now apply them by examining the fundamental building blocks of all carbohydrates: the monosaccharides.

3. Monosaccharides: The Simple Sugar Building Blocks

A deep understanding of complex carbohydrates is impossible without first mastering the structure and chemistry of their fundamental units, the monosaccharides. These simple sugars are the foundation upon which all larger carbohydrate structures are built. This

section covers their basic classification, three-dimensional structure, and key chemical properties.

3.1. Aldoses and Ketoses: The Two Families

Monosaccharides are classified into two main families based on the location of their carbonyl group:

- **Aldoses:** The carbonyl group is at the end of the carbon chain, forming an **aldehyde**. The simplest example is the three-carbon sugar glyceraldehyde.
- **Ketoses:** The carbonyl group is at any other position, forming a **ketone**. The simplest example is the three-carbon sugar dihydroxyacetone.

3.2. The Importance of Stereochemistry

Most monosaccharides have multiple chiral centers—carbon atoms bonded to four different groups—which gives rise to a variety of stereoisomers. These are molecules with the same chemical formula but different spatial arrangements, and this structural difference is biologically critical. **Enantiomers** are stereoisomers that are non-superimposable mirror images of each other, like a left and right hand (e.g., D-glucose vs. L-glucose). More subtle, but equally important, are **epimers**: stereoisomers that differ in configuration at only *one* of several chiral centers. For example, D-galactose is the C-4 epimer of D-glucose, and D-mannose is the C-2 epimer of D-glucose. Pay close attention to this distinction, as it explains a key feature of biochemistry: enzymes that act on sugars are strictly stereospecific, typically preferring one stereoisomer to another by three or more orders of magnitude. Trying to fit the wrong stereoisomer into an enzyme's binding site is as difficult as putting a left glove on your right hand; the shapes simply do not match.

3.3. Cyclic Structures in Solution

In aqueous solution, monosaccharides with five or more carbons do not exist as linear chains but as more stable ring structures. This cyclization is an *intramolecular* reaction that occurs when the carbonyl group reacts with an internal hydroxyl group on the same molecule.

- **Hemiacetal/Hemiketal:** The cyclic structure formed when an aldehyde (in an aldose) or a ketone (in a ketose) reacts with an internal alcohol.
- **Anomeric Carbon:** The carbon atom that was formerly the carbonyl carbon becomes a new chiral center in the ring structure.
- **Anomers (α and β):** The two possible stereoisomers that form at the anomeric carbon are called anomers. These can freely interconvert in solution through a process called **mutarotation**.
- **Pyranose vs. Furanose:** These terms refer to the size of the ring. A six-membered ring is a pyranose, and a five-membered ring is a furanose.

3.4. Key Derivatives and Properties

Monosaccharides are often chemically modified to serve specific biological functions.

- **Sugar Phosphates:** The addition of a phosphate group (e.g., glucose 6-phosphate) traps the sugar inside the cell (as there are no transporters for phosphorylated sugars) and "**activates**" it for metabolism by raising its energy level, priming it for subsequent chemical transformation.
- **Reducing Sugars:** A reducing sugar is any sugar with a free anomeric carbon. Because the ring can open to expose a reactive aldehyde group, these sugars can reduce other compounds, such as Cu^{2+} ions. All monosaccharides are reducing sugars.

These individual monosaccharide units are joined together to form the vast polymers that are central to biology.

4. Polysaccharides: Structure Dictates Function

Linking individual monosaccharides creates vast polymers whose biological functions are directly determined by their underlying molecular architecture. As we build these large structures, recall from our foundational principles that unlike proteins, polysaccharides are synthesized without a template, resulting in polymers that are variable in size. By contrasting the structures of polysaccharides used for energy storage with those used for structural support, a core principle of biochemistry is revealed: minor changes in chemical linkage lead to major differences in form and function.

4.1. The Glycosidic Bond: Linking Sugars Together

The **O-glycosidic bond** is the covalent bond that links the anomeric carbon of one sugar to a hydroxyl group on another sugar. Simple examples of this linkage are found in common disaccharides:

- **Maltose:** Two D-glucose units linked $\alpha(1\rightarrow4)$.
- **Lactose:** D-galactose linked to D-glucose, specified as $\text{Gal}(\beta1\rightarrow4)\text{Glc}$.
- **Sucrose:** D-glucose linked to D-fructose, specified as $\text{Glc}(\alpha1\rightarrow2\beta)\text{Fru}$.

Notably, sucrose is a **non-reducing sugar** because the anomeric carbons of *both* of its monosaccharide units are involved in the glycosidic bond, leaving no free anomeric carbon to open into a reactive aldehyde.

4.2. Storage Polysaccharides: Starch and Glycogen

Starch (in plants) and glycogen (in animals) are the primary storage forms of glucose, with structures optimized for dense, accessible energy storage.

- **Structure:** Both are polymers of D-glucose linked primarily by **$\alpha(1\rightarrow4)$ glycosidic bonds**, with branches formed by **$\alpha(1\rightarrow6)$ linkages**. Glycogen is more highly branched than starch.
- **Function:** Here we see two critical principles in action. First, the α -linkages cause the polymer chains to adopt a compact, helical conformation. This helical coil is the polymer's lowest-energy conformation, stabilized by extensive intrachain hydrogen bonds, perfectly illustrating the principle of **structure following energy minimization**. Second, this polymeric storage is vital for preventing osmotic stress. For example, liver cells store glycogen equivalent to a glucose concentration of 0.4 M. If this were stored

as free glucose, the osmotic pressure would rupture the cell. Instead, the actual concentration of glycogen particles is about 0.01 μM , posing no osmotic threat.

4.3. Structural Polysaccharides: Cellulose and Chitin

Cellulose (in plants) and chitin (in arthropods) are structural polymers designed for rigidity and strength.

- **Structure:** Cellulose is an unbranched polymer of D-glucose units joined by **$\beta(1\rightarrow4)$ glycosidic bonds**.
- **Function:** The β -linkage is the critical feature. It causes **each glucose unit to be turned 180° relative to its neighbors**, yielding a straight, extended chain rather than a helix. These straight chains align side-by-side to form an extensive network of **interchain hydrogen bonds**. This arrangement maximizes stabilizing interactions, creating rigid, water-insoluble fibers of immense tensile strength—another direct consequence of **energy minimization**. Chitin, the principal component of insect exoskeletons, is structurally similar but is a polymer of N-acetylglucosamine.

Beyond energy and structure, carbohydrates also serve as sophisticated informational molecules when attached to other biomolecules.

5. Glycoconjugates: Carbohydrates as Informational Molecules

Beyond their roles in energy metabolism and structural support, carbohydrates play a sophisticated role in cellular communication. By forming complex, information-rich oligosaccharide chains attached to proteins and lipids on cell surfaces, they create a "sugar code." This code mediates critical biological events, including cell-cell recognition, immune responses, and pathogen binding.

5.1. Introducing the Glycoconjugates

Glycoconjugates are hybrid molecules where carbohydrates are covalently attached to proteins or lipids.

Glycoconjugate Type	Brief Description
Glycoproteins	Proteins with one or more covalently attached oligosaccharides. Found on the cell surface, in the extracellular matrix (ECM), and as secreted proteins.
Proteoglycans	Macromolecules consisting of a core protein with one or more long, sulfated glycosaminoglycan chains attached. Major components of the ECM and cell surfaces.
Glycolipids	Membrane lipids where the hydrophilic head groups are oligosaccharides. They are exclusively on the outer face of the plasma membrane and are important for cell recognition.

5.2. Decoding the "Sugar Code" with Lectins

The concept of the "sugar code" arises from the immense structural diversity of oligosaccharides. Variations in monomers, linkage types (α/β , 1 \rightarrow 4, 1 \rightarrow 6, etc.), and branching patterns allow even short oligosaccharide chains to act as unique biological signals or recognition markers.

Lectins are proteins that are specialized to "read" this sugar code. They bind to specific oligosaccharide structures with high affinity and specificity, translating the structural information of the "code" into a biological response. While individual binding interactions can be modest, the presence of multiple binding sites on lectins (**multivalency**) leads to very strong and specific overall attachment (**high avidity**) to cell surfaces, which are dense with oligosaccharides.

5.3. A Biological Example: Cell Recognition

A clear example of the sugar code in action is the movement of immune cells to sites of infection, which occurs in a carefully orchestrated two-step process:

1. **Initial Tethering and Rolling: Selectins**, a family of lectins on the surface of endothelial cells lining blood vessels, recognize and weakly bind to specific oligosaccharides on circulating leukocytes (immune cells). This initial interaction is just strong enough to slow the fast-moving leukocytes, causing them to "roll" along the blood vessel wall near the site of infection.
2. **Firm Adhesion and Migration:** This slowing allows for a second, much stronger interaction to occur between **integrin** molecules on the leukocyte and adhesion proteins on the endothelial cell surface. This firm adhesion stops the leukocyte completely, allowing it to migrate out of the capillary and into the infected tissue to fight the pathogen.

In this process, the selectin lectin effectively reads the sugar code on the leukocyte surface to initiate a targeted immune response, perfectly illustrating the immense versatility of carbohydrates—from simple fuels to the complex language of the cell.
