
Chapter 1.2

Properties of Carbohydrates

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1	Introduction to Monosaccharides, Oligosaccharides and Polysaccharides	53
2	Physical Properties	54
2.1	Solubility	54
2.2	Viscosity and Surface Activity	55
2.3	Crystallinity	55
2.4	Hygroscopicity	55
2.5	Stability	56
2.6	Optical Properties	57
3	Chemical Properties	57
3.1	Hydrolysis/Solvolysis	57
3.2	Oxidation/Reduction	57
3.3	Functional Groups	58
3.4	Chelation and Complexation	58
3	Biological Properties	59
4.1	Energy Storage	59
4.2	Structural Roles	59
4.3	Cell-Cell Interaction and Cellular Communication	59
5	Summary	60
	References	60

1

Introduction to Monosaccharides, Oligosaccharides and Polysaccharides

The physical, chemical, and biological properties of carbohydrates depend on their primary structures and, less frequently, on their higher-order structures. While monosaccharides are comprised of a single saccharide unit, oligosaccha-

rides are less clearly defined and may consist of from 2–10 glycosidically linked monosaccharide units. Because of the high level of conformational flexibility associated with monosaccharides and oligosaccharides, these molecules typically do not form stable secondary or higher order structures when dissolved in a solvent. Thus, the physical, chemical, and biological properties of monosaccharides and oligosaccharides are mainly attributable to their primary structures.

The dividing line between oligosaccharides and polysaccharides is not well demarcated. As analytical methods have improved, oligomers with 14 or more monosaccharide residues have been purified to homogeneity and their structures determined. More importantly, polysaccharides often form stable, higher-order structures in solution. The term polysaccharide has typically been used to describe mixtures of saccharide oligomers or polymers. These mixtures can result from both differences in saccharide chain length, called polydispersity, and/or sequence differences, called microheterogeneity. Polydispersity (P) is defined in Eq. (1), where M_w =weight averaged molecular weight and M_N =number averaged molecular weight.

$$P = \frac{\sum N_i M_i^2 / \sum N_i M_i}{\sum N_i M_i / \sum N_i} = \frac{M_w}{M_N} \quad (1)$$

A polysaccharide is polydisperse if $P > 1$ and monodisperse, i.e., of a single saccharide chain size or molecular weight, when $P = 1$. A microheterogeneous polysaccharide is defined as one in which the sequence of the saccharide units comprising it is variable. A polysaccharide can be polydisperse and microheterogeneous, polydisperse and non-microheterogeneous, or monodisperse and microheterogeneous.

2 Physical Properties

The physical properties of carbohydrates depend primarily on their micro-saccharide composition, glycosidic linkage, functional groups present, molecular size and branching [1]. In addition, chemical modification of the carbohydrate structure, such as functional group protection, can result in marked changes in the physical properties of these molecules [1].

2.1 Solubility

Unmodified monosaccharides, oligosaccharides and polysaccharides are generally readily soluble in aqueous solvents. Highly crystalline polysaccharides like cellulose [2], gelling polymers such as agarose [1] and highly branched or cross-linked polymers such as starch [3,4] are often insoluble in aqueous solvents. There are few organic solvents that can dissolve these unmodified carbohy-

drates. Polar solvents capable of hydrogen bonding interactions such as formamide, dimethylformamide, dimethyl sulfoxide, and pyridine are most commonly used to solubilize unmodified carbohydrates. Non-covalent derivatives of anionic carbohydrates such as the pyridinium, alkylammonium, or alkylphosphonium salts are often readily soluble in polar organic solvents. Covalent carbohydrate derivatives in which hydroxy groups have been esterified or etherified in organic carbohydrate synthesis are readily soluble in a variety of organic solvents.

2.2

Viscosity and Surface Activity

Polysaccharides are among the most viscous natural products, many being used in food industry as thickeners or gelation and high viscosity agents [5]. In biological systems, hyaluronic acid is a major component of synovial fluid and vitreous humor, making appropriate use of this highly viscous polysaccharide [4]. The viscosity of a polysaccharide increases with its chain length or molecular weight [1]. Polysaccharide molecular weight determination based on viscosity (MV) serves as a useful means of characterization [2]. While polysaccharides do not lower the surface tension of aqueous solutions, their affinity for the oil-water interface gives them great value as emulsifiers [1].

2.3

Crystallinity

Carbohydrates have a wide range of crystallinity. Sucrose, a disaccharide that is readily crystallized, may represent the natural product produced in the largest quantities as a pure crystalline material [6]. Similarly, cellulose, a highly crystalline polysaccharide, is probably the most widely distributed organic molecule found in nature [2]. With the exception of these notable examples, most carbohydrates are not easily crystallized and are often isolated or synthesized as amorphous solids, glasses, or syrups. Indeed, the structures of very few carbohydrates have been solved by X-ray crystallography [7]. The difficulty in crystallizing carbohydrates results from their conformational flexibility [1, 8, 9, 10] as well as the presence of multiple structural forms of reducing sugars, i.e., pyranose, furanose, acyclic, α - and β -configurations, resulting from mutarotation, and other dynamic equilibria [8].

2.4

Hygroscopicity

Many carbohydrates are hygroscopic, often containing substantial amounts (2–10%) of water even after extensive efforts at drying. Alginic acid, a polysaccharide found in seaweed, for example, functions as an anti-desiccant maintaining the viability of seaweed washed ashore on hot beaches [4].

2.5 Stability

Carbohydrates are generally fairly stable molecules. However, reducing sugars contain an aldehyde or hemiacetal (masked aldehyde) function, and are therefore sensitive to oxidation. This chemical instability is often used for assays in which Cu^{2+} is used to oxidize the sugar aldehyde and the resultant Cu^+ is determined [4]. Reducing sugars are also frequently base-sensitive, undergoing enolization [8] and eliminative breakdown called peeling, in which one monosaccharide at a time is removed from the reducing end of the molecule [8, 11]. Oligosaccharides and polysaccharides also contain acid-sensitive glycosidic linkages [8, 11]. The ease of acid catalyzed hydrolysis of these linkages is dependent on the type of the saccharide unit, the linkage position (i.e., 1→4, 1→6, etc.), and linkage configuration [6, 8, 11, 12].

Many polysaccharides can form stable secondary structures (Fig. 1), such as helices, in solution [1]. Stable secondary structures can often be disrupted by elevating the temperature, changing the pH, or through the addition of denaturants [12, 13]. Transitions [13], such as melting a helix to a random coil, most often represent completely reversible denaturation processes [1]. Some polysaccharides can also form stable, higher order structures in solution [14]. Higher order structures such as a triple helix [15], fibers [16], or gels [12] can also be denatured but this process is not always reversible. Finally, the stability of many higher order structures in polysaccharides can be influenced through either covalent or non-covalent cross-linking of the polysaccharide chains. Non-covalent cross-linking includes both favorable or unfavorable hydrogen bonding, ionic (often mediated by bridging ions such as Ca^{2+}), or steric interactions between the polysaccharide backbone or branch structures [12].

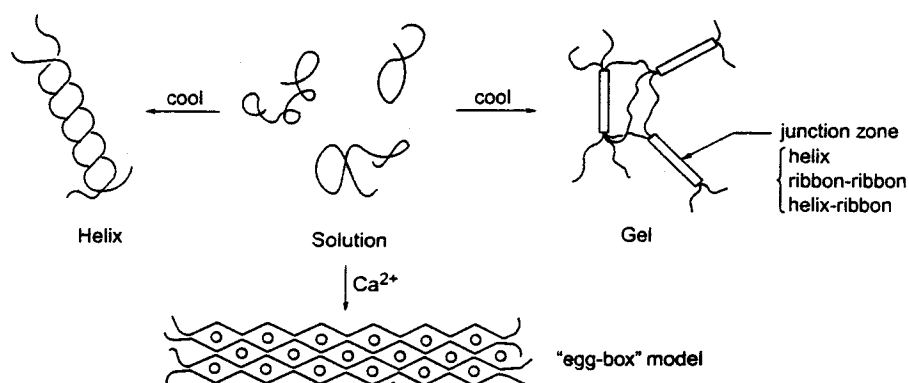


Fig. 1. A polysaccharide, such as alginate, in warm aqueous solution can form either a helix or a gel on cooling and in the presence of Ca^{2+}

2.6 Optical Properties

Most carbohydrates absorb very little light in the ultraviolet and visible spectral regions. Any functional groups present, either natural or chemically introduced, can act as chromophores or fluorophores [1]. Virtually all carbohydrates contain multiple chiral centers and are, thus, optically active. Many carbohydrates are either enantiomers, i.e., D- and L-glucose, or diastereomers, i.e., D-glucose and D-mannose, and are characterized by a specific optical rotation [7]. Most reducing sugars exhibit mutarotation when dissolved in water [8]. Circular dichroism (CD), optical rotary dispersion (ORD), and infrared (IR) spectroscopy have been used to study the conformations of carbohydrates [1, 4, 7, 8].

3 Chemical Properties

The chemical properties of carbohydrates depend on the monosaccharide residues present, their functional groups, the linkage position(s) and configuration(s). In spite of the unique properties of each molecular entity, some general chemical properties can be ascribed to carbohydrates.

3.1 Hydrolysis/Solvolysis

The most frequently used chemical transformation of oligosaccharides and polysaccharides is the acid-catalyzed hydrolysis to cleave the glycosidic linkages [6, 8, 11, 12]. The conditions required for hydrolysis range from very mild, such as the autohydrolysis of aqueous solutions of polysialic acid at room temperature and neutral pH, to the harsh conditions of 1 M mineral acid at >100 °C required for the hydrolysis of crystalline cellulose. Branching sugars glycosidically linked to a linear core structure can usually be preferentially cleaved under mild hydrolysis conditions. Oligosaccharides and polysaccharides can be solvolyzed in methanolic hydrogen chloride to afford methyl glycoside products [12].

3.2 Oxidation/Reduction

Carbohydrates are highly oxidized molecules (Fig. 2) and thus, except for specific functional groups, are relatively insensitive to oxidation. The aldehyde group present in reducing sugars can be oxidized to an aldonic acid under relatively mild conditions [7]. Stronger oxidants are required to oxidize primary hydroxy groups to carboxylic acids [1, 7], and secondary hydroxy groups require even stronger reagents, such as chromic acid [7]. In the Smith degradation, sugars are cleaved with periodate, and the resulting aldehyde(s) are reduced with sodium borohydride. The glycosidic linkages of the ring-opened sugar fragments can

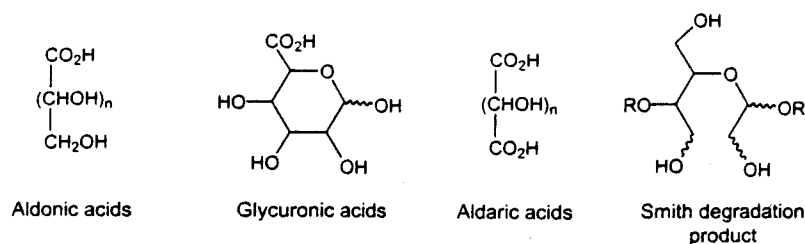


Fig. 2. Oxidized forms of carbohydrates

then be hydrolyzed under very mild conditions [7, 12]. Reaction of the reducing-sugar aldehyde with an amine results in the formation of the corresponding Schiff base that can be subsequently reduced with sodium cyanoborohydride (reductive amination) to afford an amine derivatized carbohydrate [7].

3.3

Functional Groups

Carbohydrates can possess a number of different functional groups in addition to the commonly found aldehydes, primary and secondary hydroxy groups. The free amino group in amino sugars can be acylated, sulfonated, or phosphorylated. Oxidative treatment of 2-amino sugars with nitrous acid can result in deaminative ring contraction resulting in hydrolysis of the adjacent glycosidic linkage [7]. Carboxy sugars can be esterified [1] (as an ester or lactone) or amidated [7]. Base treatment of uronic acids and esters containing an adjacent 4-glycosidic linkage can result in β -eliminative cleavage of the glycoside affording a Δ^4 -uronate product [7]. Hydroxy groups substituted as *O*-acyl, *O*-sulfo and *O*-phospho esters are typically hydrolyzed under basic conditions.

3.4

Chelation and Complexation

Many native glycans and their derivatives display affinities towards various classes of metal ions [1]. Anionic groups such as carboxylate, *O*-sulfo, and *O*-phospho, are often capable of chelating metal ions. Divalent ions such as Ca²⁺ have been used to ionically cross-link acidic polysaccharides such as alginate (polycarboxylate) and carageenan (polysulfate) to form gels [1]. Copper can readily chelate polysulfated polysaccharides such as heparin and dermatan sulfate, thus affecting their solubility and their detection [17]. Linear and cyclic glucose oligomers (cyclodextrins) and polymers also form complexes with a wide range of molecules [1, 18].

4 Biological Properties

Carbohydrates have a number of important biological roles [1, 19, 20], which fall into three major functions: namely, 1) energy storage, 2) structural, and 3) cellular interaction and communication. Each of these biological properties is related to the physical and chemical properties of the carbohydrate.

4.1 Energy Storage

The first of these roles, energy storage, is the major function of starch in plants and glycogen in animals [1, 4]. These highly branched, glucose-based polysaccharides serve as efficient means in the high density storage of energy for rapid utilization through enzymatic hydrolysis to the monosaccharide, glucose, when required to maintain the energy balance of cell function.

4.2 Structural Roles

Linear polysaccharides that contain highly ordered secondary structures are important in making up structural components in both plant and animal tissues [1, 21]. Cellulose and pectins are the major structural components of plant tissue [2] while the glycosaminoglycan chains of proteoglycan molecules, the major component of the extracellular matrix (the scaffolding on which tissue is built), serve a similar role in animal tissue [21].

4.3 Cell-Cell Interaction and Cellular Communication

Carbohydrates in cell-cell interaction and communication include both oligosaccharides and polysaccharides having unique and often very complicated primary structures i.e., the presence of unusual sugars, linkages, or functional groups. These oligosaccharides are often found as glycoconjugates, covalently linked to proteins (i.e., glycoproteins and proteoglycans) or lipids (i.e., glycolipids). These glycoconjugates are often localized on the cell surface or in the extracellular spaces. The role of these glycoconjugates is to function in cell-cell interaction, communication, and regulation [22]. These carbohydrates typically perform these functions through their interaction with protein receptors and ligands [23]. These carbohydrate-interacting proteins include lectins, receptors (sweetness receptor in the taste buds [24]), growth factors, cytokines, and adhesion proteins. In addition to their normal functions in cellular communication, these glycans also are important in pathological processes as they can be tumor antigens or receptors for bacteria and virus particles promoting the localization of these pathogens to cell surfaces [25].

5 Summary

In summary, the physical, chemical, and biological properties are all intimately related to the carbohydrate structure. The great diversity in the number of possible carbohydrate structures, based on their high degree of chirality and functionalization, makes the full understanding of the properties of these molecules a challenging undertaking.

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