Chapter 13

BIOMOLECULES

CARBOHYDRATES

The name "carbohydrates" was derived from their general formula $C_x (H_2O)_y$, which gives the impression that they are carbon compounds combined with water, resembling hydrates of carbon.

$$xCO_2 + yH_2O \xrightarrow{\text{Sunlight, chlorophyll}} \underset{\text{Carbohydrate}}{C_x(H_2O)_y} + xO_2$$

A polyhydroxy compound containing an aldehyde or ketone functional group, either in its free form or as a hemiacetal or acetal, is classified as a carbohydrate.

Carbohydrates are substances with the general formula $C_x (H_2O)_y$, and they were initially named "carbohydrates" because they were observed to have hydrogen and oxygen in the same proportion as in water. However, certain compounds have been identified that exhibit carbohydrate-like chemical behavior but do not adhere to the formula $C_x (H_2O)_y$.

For example, 2-deoxyribose has the molecular formula $C_5H_{10}O_4$.

It's essential to recognize that not all compounds conforming to the formula $C_x (H_2O)_y$, are carbohydrates; some examples include formaldehyde (CH_2O) and acetic acid ($C_2H_4O_2$). Carbohydrates are also commonly referred to as saccharides (derived from the Latin word "Saccharum," meaning sugar) because of the sweet taste exhibited by the simpler members of this class, namely sugars.

Classification of Carbohydrate

Carbohydrates are categorized into three main classes based on the number of individual sugar units present in their molecular structure.

1. **Monosaccharide**

   Monosaccharides are carbohydrates that cannot be further broken down into simpler compounds. Monosaccharides with six carbon atoms are classified as either aldohexoses or ketohexoses.

2. **Oligosaccharides**

   Oligosaccharides are carbohydrates that yield between two and ten monosaccharide units upon hydrolysis. They are further subdivided into categories such as disaccharides, trisaccharide's, tetra saccharides, and so on, depending on the number of monosaccharides they yield upon hydrolysis.

Disaccharides are the most common among them. In a disaccharide, the two monosaccharide units obtained upon hydrolysis can be either identical or different.
For example, sucrose, when hydrolyzed, yields one molecule each of glucose and fructose, while maltose produces two glucose molecules.

3. Polysaccharide

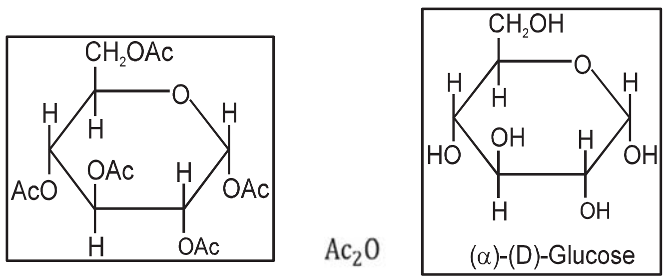
Polysaccharides are carbohydrates that can be hydrolyzed into numerous monosaccharide molecules. Examples of polysaccharides include starch, cellulose, and more.

4. Aldohexoses

Their structure has been clarified through the following steps:

I. Examination and determination of molecular weight reveal that the molecular formula of the aldohexoses is $C_6H_{12}O_6$.

II. When subjected to acetic anhydride, aldohexoses yield the penta-acetate, indicating the presence of five hydroxyl groups.



III. Aldohexoses form an oxime when treated with hydroxylamine, or add molecule of HCN to form Cyanohydrin and therefore contain a carbonyl group.

IV. When an aldohexose is oxidised with bromine-water or tolan's reagent or Fehling solution a pentahydroxy-acid of formula $C_6H_{12}O_7$ is obtained. This indicates that the carbonyl group present is an aldehydic group.

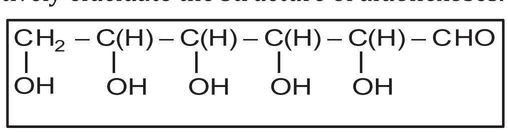
V. When reduced with concentrated hydroiodic acid and red phosphorus at 100°C, aldohexoses give n-hexane. This indicates that the six carbon atoms in an aldohexose are in a straight chain. The above reactions show that structure of aldohexoses is.

VI. Aldohexoses undergo oxime formation when exposed to hydroxylamine or react with HCN to create cyanohydrin, signifying the presence of a carbonyl group.

VII. Oxidizing an aldohexose with bromine-water, Tollen's reagent, or Fehling's solution results in the formation of a pentahydroxy-acid with the formula $C_6H_{12}O_7$, confirming the presence of an aldehydic group within the carbonyl group.

VIII. Reduction of aldohexoses with concentrated hydroiodic acid and red phosphorus at 100°C yields n-hexane, indicating that the six carbon atoms in an aldohexose are arranged in a straight chain.

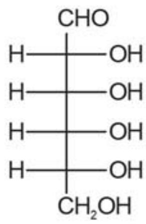
These reactions collectively elucidate the structure of aldohexoses.

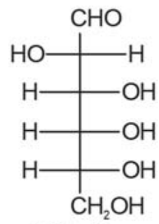


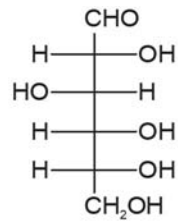
Due to four asymmetric carbon atoms, there are sixteen optical isomers.

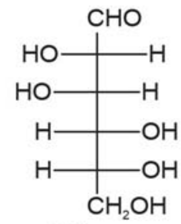
or Eight pairs of enantiomers. (8D-variety & 8L- variety).

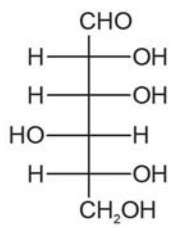
D-variety of them are as follows

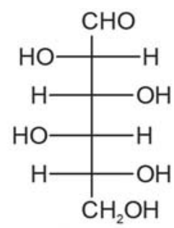

D(+)-allose
(VII)

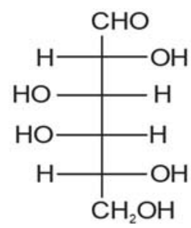

D(+)-altrose
(VIII)

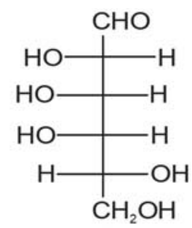

D(+)-glucose
(IX)


D(+)-mannose
(X)


D(–)-gulose
(XI)


D(–)-idose
(XII)


D(+)-galactose
(XIII)


D(+)-talose
(XIV)
(XII)

Note:

1. D-aldohexoses shown above have epimoric / diastereomeric relationship with each other
2. D-aldohexoses can be either dextro (+) or laevo (-)

Classification and Structure of Carbohydrates

Carbohydrates are compounds characterized by their polyhydroxy aldehyde and ketone nature, as well as their ability to break down into polyhydroxy aldehydes and ketones.

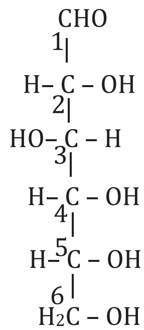
The most basic carbohydrates are referred to as sugars or saccharides, a term derived from the Latin word "Saccharum," meaning sugar. Carbohydrates can be categorized into three main groups: monosaccharides, oligosaccharides, and polysaccharides.

Glucose

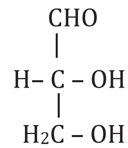
Glucose stands as the most prevalent monosaccharide and is often referred to as dextrose. This nomenclature is due to its primarily occurring in nature as optically active dextrorotatory isomers. Glucose functions as a potent reducing agent, capable of reducing both Fehling's solution and ammoniacal silver nitrate solution. Upon heating with sodium hydroxide, an aqueous glucose solution undergoes a browning reaction. This sugar, known as dextrose, is commonly found in natural sources such as grapes, honey, cane sugar, starch, and cellulose.

Configuration of Glucose

Given that the structure described above contains four asymmetric carbon atoms, marked with asterisks, it can exist in a total of $2^4 = 16$ different optically active forms, which amounts to eight pairs of enantiomers. All of these forms are well-documented and correspond to the D- and L-isomers of glucose, mannose, galactose, allose, idose, and talose. The naturally occurring dextrorotatory glucose, denoted as (+)-glucose, represents just one of the 16 possible stereoisomers.



D (+) Glucose



(+)-Glyceraldehyde

The notations D- and L- to denote configuration were introduced by Rosan off. According to this convention, any compound with its lower asymmetric carbon atom configured similarly to dextrorotatory glyceraldehyde (as illustrated above, with the bottom carbon atom having -OH on the left and H on the right) is assigned the L-configuration. It's important to note that the symbols D- and L- are independent of the specific rotation value, meaning they are not linked to whether a compound is labeled as (+) or (-). For instance, natural (-) fructose falls under the D-series, specifically as D (-)-fructose.

Objections to Open-Chain Structure of Glucose

While the open-chain structure of (+) glucose accounts for many of its reactions, it falls short in explaining several key observations:

- Glucose does not result in the restoration of Schiff's reagent color.
- Glucose does not give rise to a basophile and aldehyde-ammonia compound.
- Glucose yields two isomeric penta-acetates, both of which exhibit no reactivity with carbonyl reagents.
- The existence of two isomeric forms of glucose and the phenomenon of mutarotation cannot be elucidated through an open-chain formula.
- Glucose, in the presence of dry HCl gas and methanol, forms two isomeric glucosides. Due to its reduced solubility in ethanol, it precipitates upon cooling the reaction mixture. Commercially, glucose is produced through the hydrolysis of starch, which is sourced from economical raw materials such as maize, potatoes, and rice.

Constitution of Glucose

Molecular Formula

By the usual analytical methods, the molecular formula glucose is found to be $C_6H_{12}O_6$.

Straight Chain of Six Carbon Atoms

1. The reduction of glucose with concentrated hydroiodic acid (HI) and phosphorus results in the formation of 2-iodohexane and n-hexane. This observation indicates that the six carbon atoms in glucose are arranged in a straight chain.

$$\underset{\text{Glucose}}{C_6H_{12}O_6} \xrightarrow[\text{Prolonged heating}]{\text{HIP}} \underset{\text{n-hexane}}{CH_3-(CH_2)_4-CH_3}$$

2. When glucose undergoes oxidation with bromine water, it forms gluconic acid. Subsequent reduction with an excess of HI leads to the formation of n-hexanoic acid, $CH_3.(CH_2)_4.COOH$, thus providing confirmation of the existence of a linear chain containing six carbon atoms in glucose.

Presence of Five Hydroxyl Groups

Upon treatment with acetic anhydride, glucose produces a penta-acetate, signifying the presence of five -OH groups. Given the stability of glucose, it is evident that these five -OH groups must be connected to five distinct carbon atoms.

$$\underset{\text{Glucose}}{C_6H_{12}O_6} \xrightarrow[C_6H_5N]{C_6H_5NHNH_2} \begin{array}{l} CHO \\ | \\ (CHOCOCH_3)_4 \\ | \\ CH_2OCOCH_3 \end{array}$$

Glucose pentaacetate

Presence of an Aldehydic Groups

1. Glucose yields a cyanohydrin when exposed to hydrogen cyanide and a mono-oxime when in contact with hydroxylamine, indicating the presence of a carbonyl group.

$$\underset{\text{Glucose}}{C_6H_{12}O_6} \xrightarrow{HCN} \begin{array}{l} CN \\ | \\ (CHOH)_5 \\ | \\ CH_2OH \end{array}$$

Glucose cyanohydrin

2. Glucose's ability to reduce Fehling's solution and Tollen's reagent is indicative of an aldehydic carbonyl group in its structure.
3. The presence of this aldehydic group is further substantiated by its oxidation to gluconic acid, which contains the same number of carbon atoms.

$$\underset{\text{Glucose}}{C_5H_{11}CHO + (O)} \xrightarrow{Br_2} \underset{\text{Gluconic acid}}{C_5H_{11}O_5.\,COOH}$$

Now since aldehydic group is monovalent, it must be present on the end of the chain.

Open Chain Structure

Considering the aforementioned observations, glucose's partial structure orientation can be described as follows: In the α anomer, the -OH group is positioned trans to the $-CH_2OH$ group, while in the β anomer, the -OH group is situated cis to the $-CH_2OH$ group.

Fructose

Also said to be fruit sugar

1. It exists both in a bound form and as a free compound.
2. Fructose is often referred to as "fruit sugar" because it is found freely in honey and many sweet fruits.
3. Being the sweetest monosaccharide, fructose is found in cane sugar and in the combined state within insulin.
4. It is also known as α-Laevulose, denoting that the naturally occurring form is levorotatory.

Preparation By Acid Hydrolysis of Cane Sugar

$$\underset{\text{Glucose}}{C_{12}H_{22}O_{11}} + H_2O \ C \xrightarrow{H^{\oplus}} {}_6H_{12}O_6 + \underset{\text{Fructose}}{C_6H_{12}O_6}$$

By enzymatic action of sucrose

$$\text{Sucrose } (C_{12}H_{22}O_{11}) \xrightarrow{\text{Invertase}} \underbrace{\text{Glucose + Fructose}}_{\text{Invert Sugar}}$$

(Disaccharide)

Note: Glucose and fructose, obtained through the acid hydrolysis of sucrose, can be isolated by subjecting them to treatment with Ca $(OH)_2$, resulting in the formation of calcium gluconate and calcium fructose. Notably, calcium fructose is water-insoluble, making it straightforward to separate from the mixture.

Properties

1. This substance exists as a colorless crystalline solid.
2. It readily dissolves in water but exhibits insolubility in ether, ketone, and benzene.
3. Being a pentahydroxy ketone, it displays mutarotation, similar to glucose.

Chemical Properties of Carbohydrates

Carbohydrates are a class of organic compounds composed of carbon, hydrogen, and oxygen atoms in the ratio of 1:2:1. They serve as a primary source of energy for living organisms and play essential structural roles in cells. The chemical properties of carbohydrates are diverse and depend on their molecular structure. Here are some key chemical properties:

- **Hydrolysis:** Carbohydrates can undergo hydrolysis, a chemical reaction where water is used to break chemical bonds. This reaction is commonly used to break down complex carbohydrates such as polysaccharides into simpler sugars. For example, the hydrolysis of starch yields glucose molecules.
- **Reduction:** Carbohydrates containing aldehyde or ketone functional groups can undergo reduction reactions, where they gain electrons. For instance, glucose can be reduced to sorbitol using reducing agents like sodium borohydride.
- **Oxidation:** Carbohydrates can be oxidized, especially those with aldehyde groups. For example, glucose can be oxidized to gluconic acid using mild oxidizing agents like Benedict's solution or Tollen's reagent.
- **Fermentation:** Some carbohydrates can undergo fermentation by microorganisms, producing various products such as alcohol and organic acids. For example, yeast can ferment glucose to produce ethanol and carbon dioxide.
- **Complex formation:** Carbohydrates can form complexes with other molecules, such as proteins and lipids. Glycoproteins, for example, are proteins that have carbohydrate molecules attached to them. These complexes often play crucial roles in cell recognition and signaling.
- **Isomerization:** Carbohydrates can undergo isomerization reactions, where the arrangement of atoms in the molecule changes, but the molecular formula remains the same. For example, glucose can be converted to fructose through an isomerization reaction.
- **Mutarotation:** Many carbohydrates exist in solution in equilibrium between different forms (e.g., alpha and beta anomers). This process, known as mutarotation, involves the interconversion of these forms in solution, often catalyzed by acids or bases.
- **Maillard reaction:** Carbohydrates can participate in the Maillard reaction, a chemical reaction between reducing sugars and amino acids or proteins. This reaction is responsible for the browning of food during cooking and contributes to flavor and aroma development.

Disaccharides and Polysaccharides

Disaccharides and polysaccharides are two categories of carbohydrates distinguished by their molecular structures and functions.

- Disaccharides are carbohydrates composed of two monosaccharide units joined together by a glycosidic bond.
- Examples of common disaccharides include
  - Sucrose: Composed of glucose and fructose, found in sugar cane, sugar beets, and many fruits.
  - Lactose: Composed of glucose and galactose, found in milk and dairy products.
  - Maltose: Composed of two glucose molecules, formed during the digestion of starch.
- Disaccharides are often used as energy sources in organisms and as sweetening agents in food due to their sweet taste.
- They can be broken down into their constituent monosaccharides through hydrolysis reactions, which involve the addition of water to break the glycosidic bond.

Polysaccharides

Polysaccharides are composed of monosaccharide polymers, and typical natural polysaccharides usually consist of approximately 100 to 3000 monosaccharide units. Interestingly, the three most prevalent natural polysaccharides—cellulose, starch, and glycogen—originate from the same monomer, namely glucose.

Starch

Starch is a polymer composed of glucose, with its molecular formula represented as $(C_6H_{10}O_5)_n$. The value of n can vary between 200 and 1000, depending on the source. It is the primary food reserve material or storage polysaccharide found in plants, predominantly in seeds, roots, and tubers. Rich sources of starch include wheat, rice, potatoes, corn, bananas, and more.

Starch is not a single compound but is rather a combination of two components: a water-soluble part known as amylose (comprising 20%) and a water-insoluble component referred to as amylopectin (constituting 80%). Both amylose and amylopectin are comprised of α-D glucose monomers.

Amylose represents a linear polymer of α-D glucose. It consists of approximately 200 glucose units linked to each other through α-linkages, involving C_1 of one glucose unit and C_4 of the adjacent unit.

In contrast, amylopectin is a highly branched polymer.

C1–C4 –linkage

Glucose – Glucose – Glucose

⟵ Cl–C6 α–linkage

Glucose – Glucose – Glucose

⟵ Cl–C6 α–linkage

Glucose – Glucose – Glucose

It is composed of numerous short chains, each containing 20-25 glucose units, which are interconnected through α-linkages, specifically C_1 of one glucose unit with C_4 of another. Additionally, the C_1 of the terminal glucose unit in each chain is further linked to C_6 of the adjacent glucose unit in the next chain, forming α-linkages between C_1 and C_6. This branching structure imparts amylopectin with its highly branched nature.

Hydrolysis

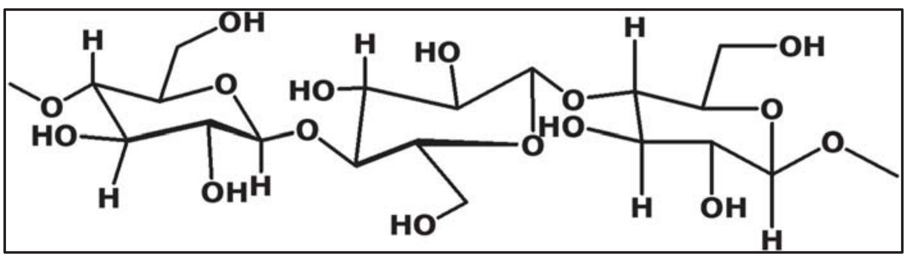
The breakdown of starch can be achieved through the hydrolysis of starch using hot dilute acids or enzymes, resulting in the formation of dextrin’s of different levels of complexity, maltose, and ultimately D-glucose. Notably, starch does not exhibit the ability to reduce Tollen's reagent and Fehling's solution.

Uses

Starch finds application as a food ingredient and is a common part of our daily diet, present in foods like potatoes, bread, cakes, and rice. It serves a purpose in coating and sizing paper to enhance its writing properties. Additionally, starch is employed in the treatment of textile fibers before they are woven into fabric, ensuring they can be woven without rupturing. Starch plays a role in the production of various products including dextrin’s, glucose, and ethyl alcohol. Notably, starch is also utilized in the manufacturing of starch nitrate, which serves as an explosive material.

Cellulose

Cellulose serves as the primary constituent of wood and plant fibers. For example, cotton consists almost entirely of cellulose. It exhibits insolubility in water, has a neutral taste, and qualifies as a non-reducing carbohydrate. These characteristics are, at least in part, attributed to its exceptionally high molecular weight.



Cellulose

Cellulose possesses the chemical formula ($C_6H_{10}O_5$) n. When subjected to complete acid hydrolysis, it yields D (+)-glucose as the resulting monosaccharide. Full methylation of cellulose leads to the production of a substantial amount of 2, 3, 6-tri-O-methyl-D-glucose. Hence, like starch, cellulose is comprised of chains composed of D-glucose units. These units are interconnected through glycoside linkages at C-4 of the subsequent glucose unit.

However, cellulose distinguishes itself from starch through the configuration of its glycoside linkage. When treated with acetic anhydride and sulfuric acid, cellulose forms octa-O-acetyl cellobiose, which suggests that all the glycoside linkages in cellulose, similar to the one in (+) cellobiose, are beta linkages.

Physically determined molecular weights for cellulose range from 250,000 to over 1,000,000, with an estimated minimum of approximately 1,500 glucose units per molecule. End group analysis through both methylation and periodic acid oxidation indicates a chain length of 1,000 glucose units or more. X-ray analysis and electron microscopy reveal that these lengthy chains lie closely together in bundles, firmly bound by hydrogen bonds formed between the numerous neighboring -OH groups. These bundles are twisted together to create a rope-like structure, and these structures, in turn, combine to form the fibers visible to the naked eye. In wood, these cellulose "ropes" are embedded in lignin, creating a structure akin to reinforced concrete.

Properties of Cellulose

We have observed that the glycoside linkages within cellulose can be cleaved through the action of acids, yielding numerous molecules of D (+)-glucose from each cellulose molecule. Now, let's briefly examine reactions of cellulose in which the polymer chain remains predominantly intact. In cellulose, each glucose unit contains three available -OH groups, which serve as sites for various reactions.

These cellulose reactions, conducted to modify the characteristics of an easily accessible and cost-effective polymer, hold immense industrial significance.

Similar to other alcohols, cellulose can form esters. When treated with a combination of nitric and sulfuric acid, cellulose is transformed into cellulose nitrate. The properties and applications of the resulting product are contingent on the degree of nitration. Guncotton, which finds use in the production of smokeless powder, is nearly completely nitrated cellulose and is sometimes referred to as cellulose trinitrate, signifying the presence of three nitrate groups per glucose unit. Pyroxylin is a less heavily nitrated material, containing between two and three nitrate groups per glucose unit. It is utilized in the manufacturing of items such as celluloid, collodion, photographic film, and lacquers. It should be noted that pyroxylin is flammable and emits highly toxic nitrogen oxides when burned.

In industrial applications, cellulose is alkylated to form ethers by employing alkyl chlorides (which are more cost-effective than sulfates) in the presence of alkali. It is important to acknowledge that these reactions unavoidably result in some degree of chain degradation. Methyl, ethyl, and benzyl ethers of cellulose play a crucial role in the production of textiles, films, and a variety of plastic items.