College of pharmacy

Biochemistry I third stage

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Lecture 5

Carbohydrates

Carbohydrates

Carbohydrates are widely distributed in plants and animals; they have important structural and metabolic roles. In plants, glucose is synthesized from carbon dioxide and water by photosynthesis and stored as starch or used to synthesize cellulose of the plant framework. Animals can synthesize carbohydrate from lipid glycerol and amino acids, but most animal carbohydrate is derived ultimately from plants and stored as glycogen.

Glucose is the most important carbohydrate; most dietary carbohydrate is absorbed into the blood stream as glucose, and other sugars are converted into glucose in the liver. Glucose is the major metabolic fuel of mammals and a universal fuel of the fetus. It is the precursor for synthesis of all the other carbohydrates in the body, including glycogen for storage; ribose and deoxyribose in nucleic acids; and galactose in lactose of milk, in glycolipids, and in combination with protein in glycoproteins and proteoglycans. Diseases associated with carbohydrate metabolism include diabetes mellitus, galactosemia, glycogen storage diseases, and lactose intolerance.

Classification of Carbohydrates

1. Monosaccharides are those carbohydrates that cannot be hydrolyzed into simpler carbohydrates. They may be **classified** as trioses, tetroses, pentoses, hexoses, or heptoses, depending upon the number of carbon atoms; and as aldoses or ketoses depending upon whether they have an aldehyde or ketone group.

2. Disaccharides are condensation products of two monosaccharide units. Examples are lactose, maltose and sucrose.

3. Oligosaccharides are condensation products of two to ten monosaccharides. Example maltotriose.

4. Polysaccharides are condensation products of more than ten monosaccharide units; examples are the starches and dextrins. Dextrins may be linear or branched polymers.

Classification of important sugars

|	Aldoses	Ketoses
Trioses ($C_3H_6O_3$)	Glycerose	Dihydroxyacetone
Tetroses ($C_4H_8O_4$)	Erythrose	Erythrulose
Pentoses ($C_5H_{10}O_5$)	Ribose	Ribulose
Hexoses ($C_6H_{12}O_6$)	Glucose	Fructose

Isomers and epimers of monosaccharides

Compounds that have the same chemical formula but have different structures are called **isomers**. For example, fructose, glucose, mannose, and galactose are all isomers of each other, having the same chemical formula, $C_6H_{12}O_6$.

Carbohydrate isomers that differ in configuration around **only one** specific carbon atom (with the exception of the carbonyl carbon) are defined as **epimers** of each other. For example, **glucose** and **galactose** are **C-4 epimers**-their structures differ only in the position of the OH group at carbon 4.

Note: The carbons in sugars are numbered beginning at the end that contains the **carbonyl carbon** that is, the **aldehyde** or **keto** group. **Glucose** and **mannose** are **C-2 epimers**.

However, galactose and mannose are not epimers, they differ in the position of OH groups at two carbons (2 and 4) and are, therefore, defined only as isomers.
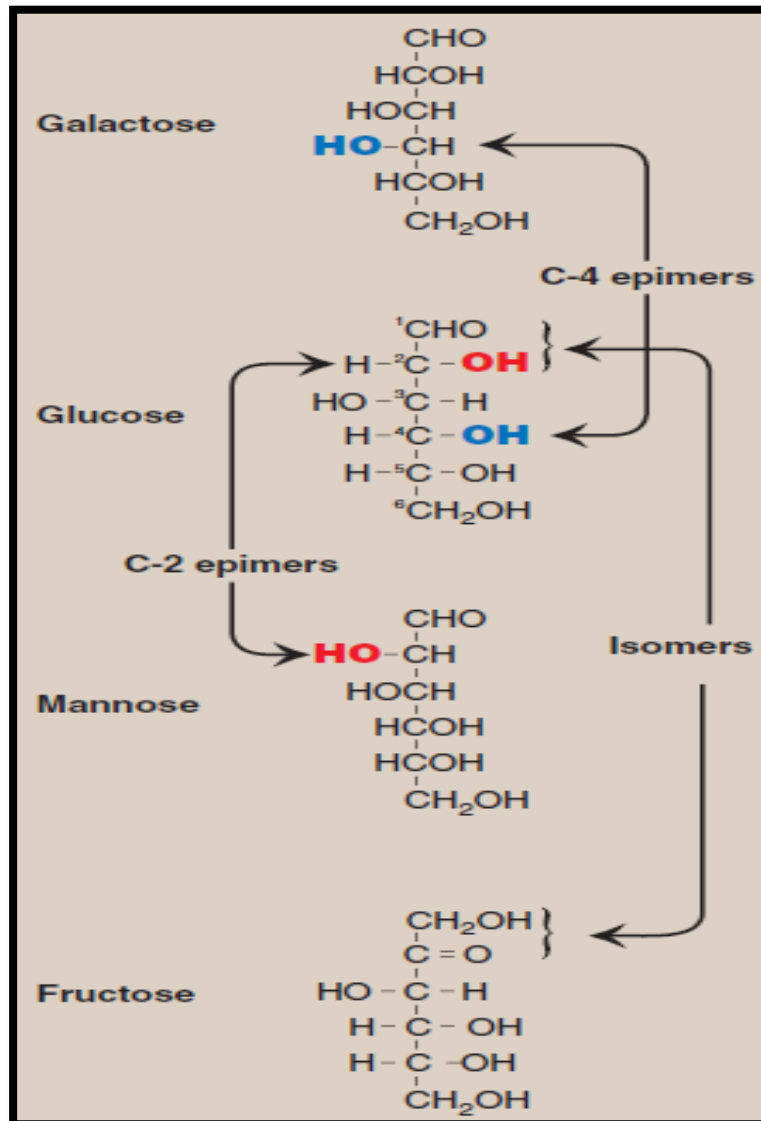
C-2 and C-4 epimers and an isomer of glucose

Enantiomers of monosaccharides

A special type of isomerism is found in the pairs of structures that are mirror images of each other. These mirror images are called **enantiomers**, and the two members of the pair are designated as a D- and an L-sugar. The majority of the sugars in humans are D-sugars. In the D isomeric form, the **OH group** on the asymmetric carbon (a carbon linked to four different atoms or groups) farthest from the carbonyl carbon is on the **right**, whereas in the L-isomer it is on the **left**. Enzymes known as racemases are able to interconvert D- and L-isomers.
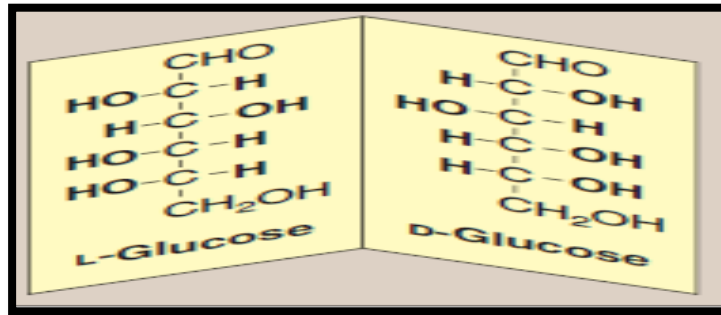
Enantiomers (mirror images) of glucose

Cyclization of monosaccharides

Less than 1% of each of the monosaccharides with five or more carbons exists in the open chain (acyclic) form. Rather, they are predominantly found in a ring (cyclic) form, in which the aldehyde (or keto) group has reacted with an alcohol group on the same sugar, making the carbonyl carbon (carbon 1 for an aldose or carbon 2 for a ketose) asymmetric.

 Note: **Pyranose** refers to a six-membered ring consisting of five carbons and one oxygen, for example, glucopyranose, whereas **furanose** denotes a five-membered ring with four carbons and one oxygen.

Anomeric carbon

Cyclization creates an anomeric carbon (the former carbonyl carbon), generating the **α** and **β** configurations of the sugar, for example, α-D-glucopyranose and β-D-glucopryanose. These two sugars are both glucose but are anomers of each other. Note: In the **α** configuration, the **OH** on the anomeric C projects to the same side as the ring in a modified Fischer projection formula, and is trans to the CH$_2$OH group in a Haworth projection formula.

Because the **α** and **β** forms are not mirror images, they are referred to as diastereomers. Enzymes are able to distinguish between these two structures and use one or the other differently. For example, **glycogen** is synthesized from α-D-glucopyranose, whereas **cellulose** is synthesized from β-D-glucopyranose. The

cyclic **α** and **β** <mark>anomers</mark> of a sugar can be interconverted in a process called mutarotation by enzyme named as mutase.
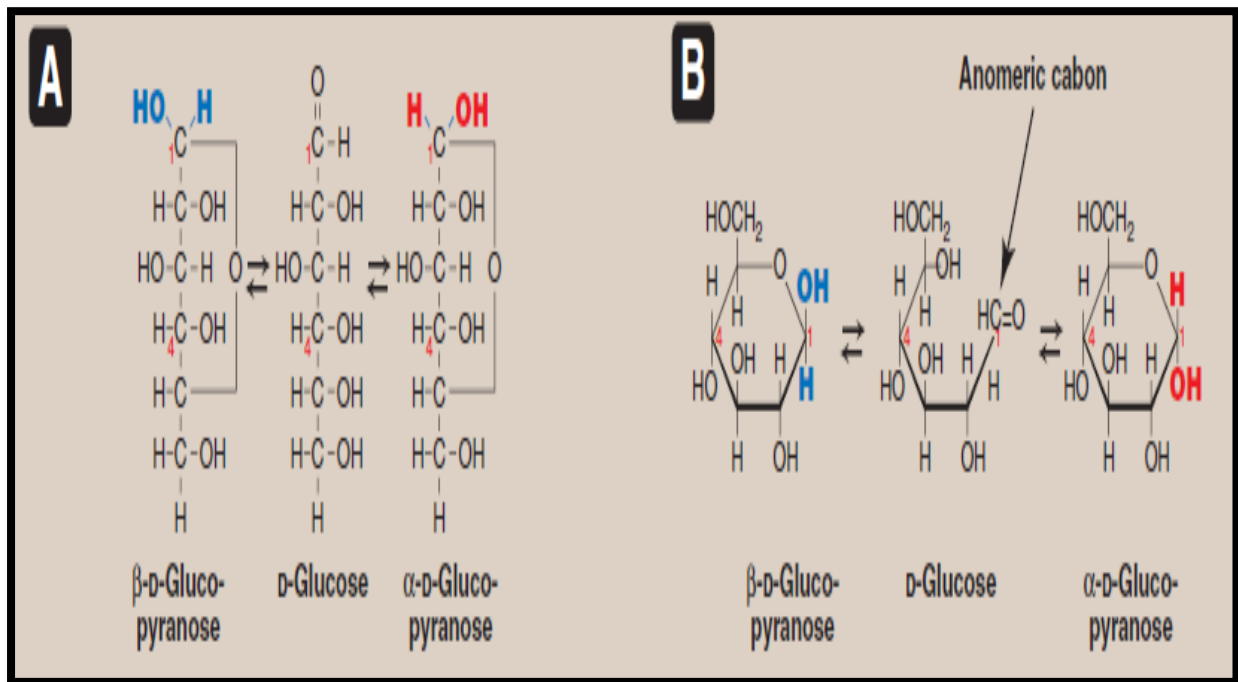
A. The interconversion (mutarotation) of the α and β anomeric forms of glucose shown as modified Fischer projection formulas. B. The interconversion shown as Haworth projection formulas. Carbon 1 is the anomeric carbon.

Reducing sugars

A reducing sugar is any sugar that is capable of acting as a reducing agent. If the hydroxyl group on the anomeric carbon of a cyclized sugar is not linked to another compound by a glycosidic bond, the ring can open. The sugar can act as a reducing agent, and is termed a reducing sugar. Such sugars can react with chromogenic agents (for example, Benedict's reagent or Fehling's solution) causing the reagent to be reduced and colored, with the aldehyde group of the acyclic sugar becoming oxidized. All monosaccharides are reducing sugars, along with some disaccharides (**non-reducing** disaccharides like **sucrose** while reducing disaccharides like lactose and maltose), some oligosaccharides, and some polysaccharides.

Joining of monosaccharides

Monosaccharides can be joined to form disaccharides, oligosaccharides, and polysaccharides. Important disaccharides include lactose (galactose + glucose), sucrose (glucose + fructose), and maltose (glucose + glucose). Important polysaccharides include **branched** **glycogen** (from animal sources) and **starch** (plant sources) and unbranched cellulose (plant sources); each is a polymer of glucose. The bonds that link sugars are called **glycosidic bonds**. These are formed by enzymes known as glycosyltransferases that use nucleotide sugars such as UDP-glucose as substrates.

Glycosidic bonds between sugars are **named** according to the numbers of the connected carbons, and with regard to the position of the anomeric hydroxyl group of the sugar involved in the bond. If this anomeric hydroxyl is in the α configuration, the linkage is an α-bond. If it is in the β configuration, the linkage is a β-bond. **Lactose**, for example, is synthesized by forming a glycosidic bond between carbon 1 of β-galactose and carbon 4 of glucose. The linkage is, therefore, a **β (1→4) glycosidic bond**.

Note: Because the anomeric end of the glucose residue in lactose is not involved in the glycosidic linkage, therefore it remains a reducing sugar.
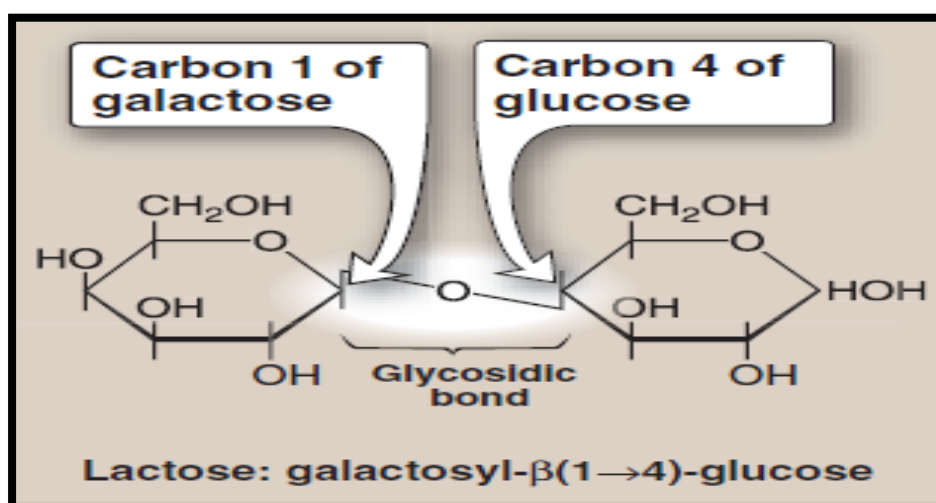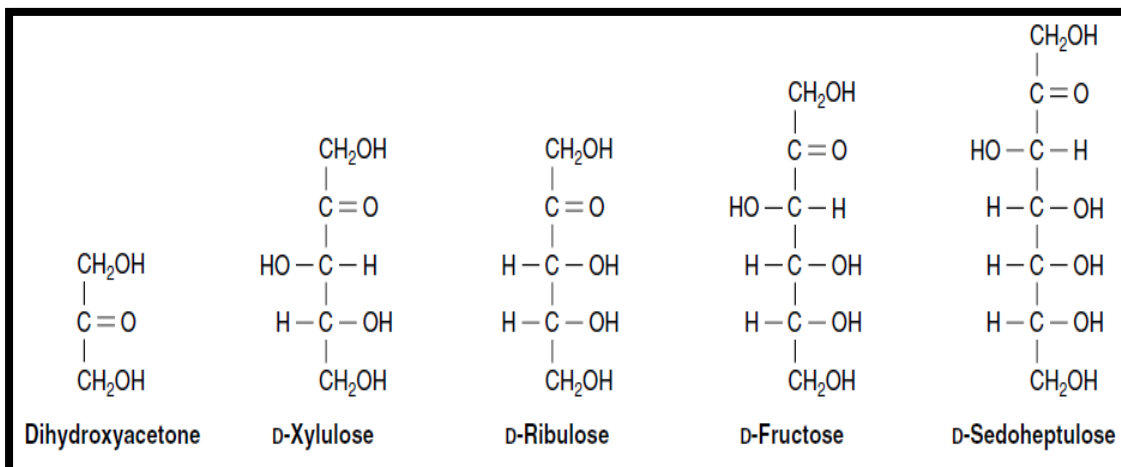

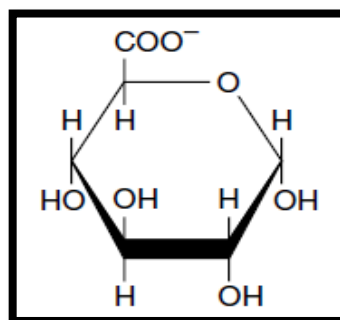**A glycosidic bond between two hexoses producing a disaccharide.**

Monosaccharides

The biochemically important monosaccharides includes aldoses, ketoses and carboxylic acid derivatives of glucose including D-glucuronate are shown in following figures:
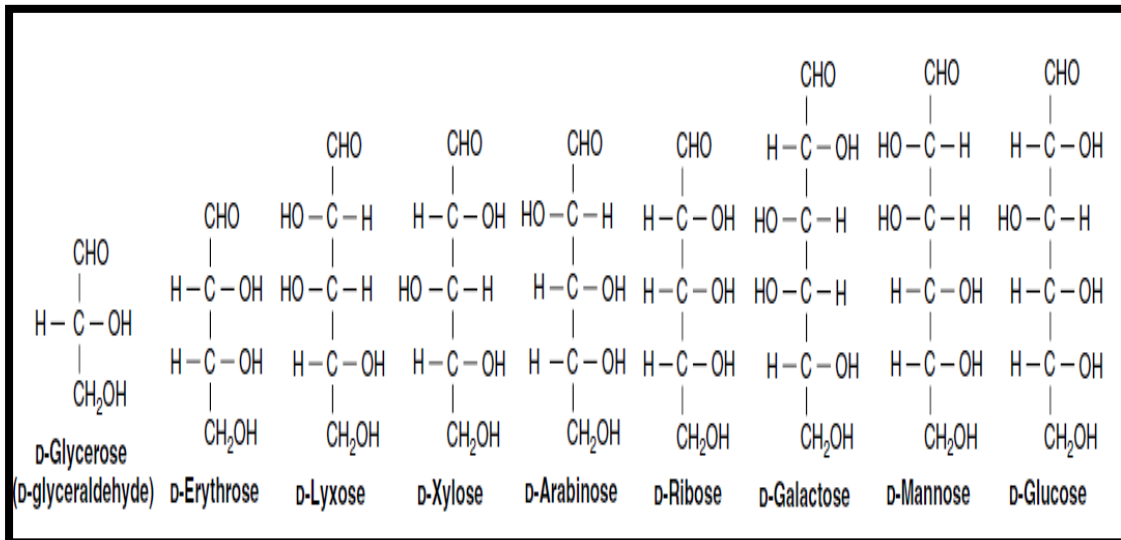
Examples of aldoses of physiologic significance

Examples of ketoses of physiologic significance

α-D-Glucuronate

Disaccharides

Disaccharides are formed from two monosaccharides and can be classified as either reducing or non-reducing. **Reducing** disaccharides like lactose and maltose have only one of their two anomeric carbons involved in the glycosidic bond, while the other is free and can convert to an open-chain form with an aldehyde group. **Nonreducing** disaccharides like sucrose have glycosidic bonds between their anomeric carbons and thus cannot convert to an open-chain form with an aldehyde group; they are stuck in the cyclic form.
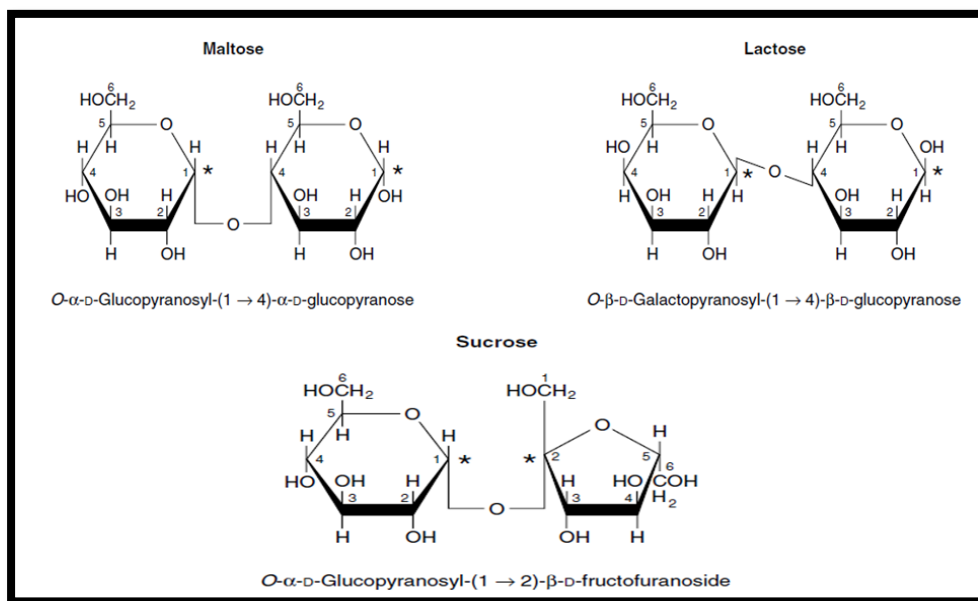

**Structures of important disaccharides**

Polysaccharides

Polysaccharides include the following:

Starch: is a homopolymer of glucose forming an α-glucosidic chain. It is the most abundant dietary carbohydrate in cereals, potatoes, and other vegetables. The two main constituents are amylose (15-20%), which has a nonbranching helical structure; and amylopectin (80-85%), which consists of branched chains composed of 24-30 glucose residues united by 1→4 linkages in the chains and by 1→6 linkages at the branch points.
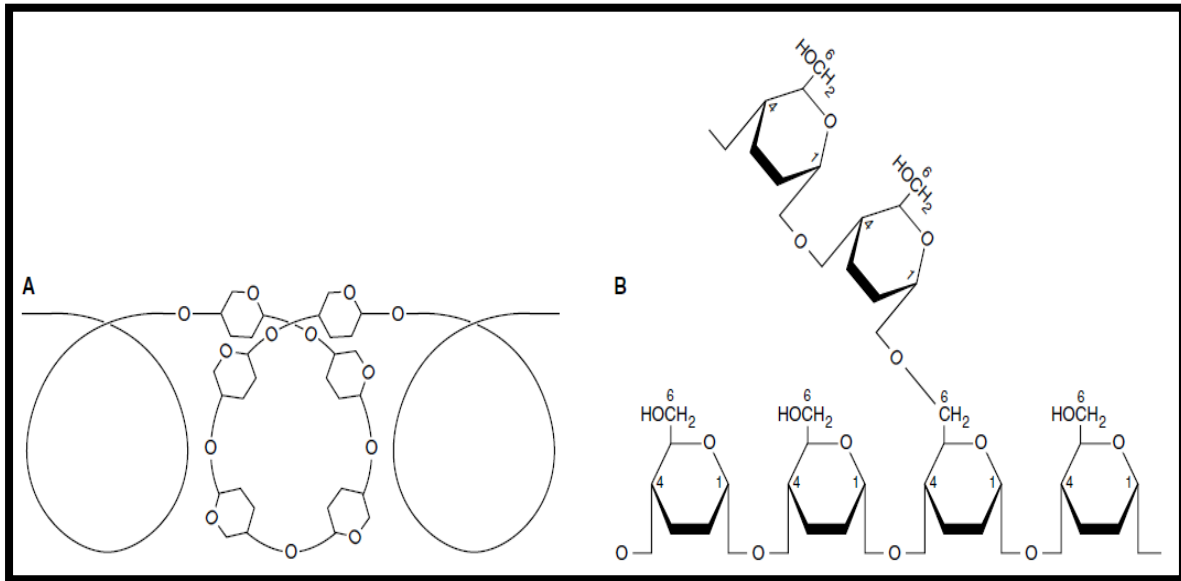
Structure of starch. A: Amylose, showing helical coil structure. B: Amylopectin, showing 1→6 branch point.

Glycogen: is the storage polysaccharide in animals. It is a more highly branched structure than amylopectin, with chains of 12-14 α-D-glucopyranose residues (in α (1→4)-glucosidic linkage), with branching by means of α (1→6)-glucosidic bonds.
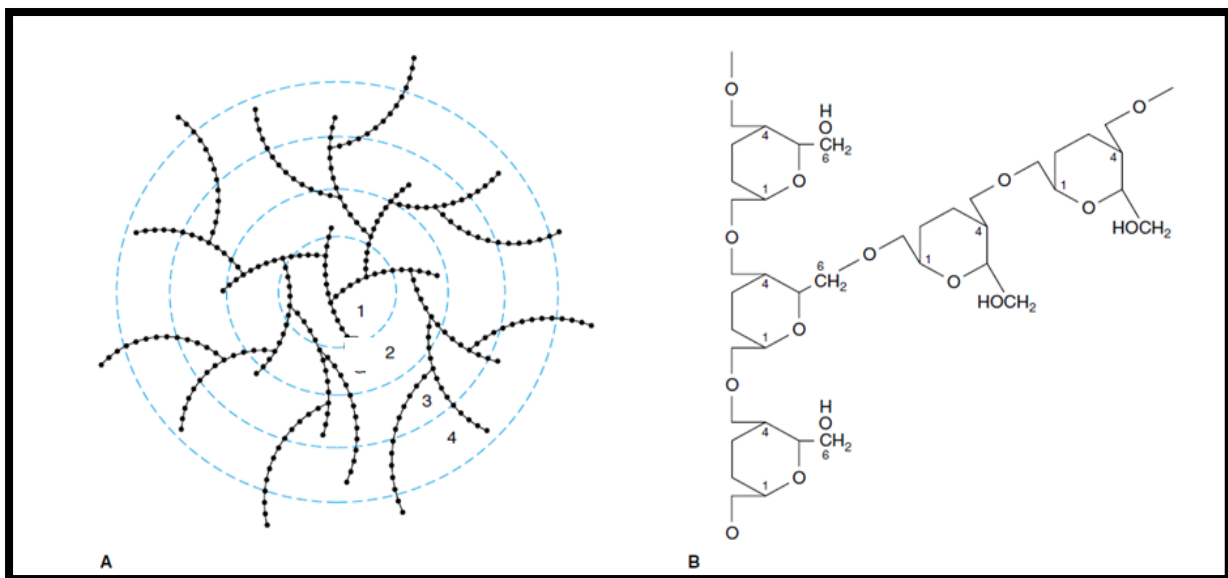
The glycogen molecule. A: General structure. B: Enlargement of structure at a branch point.

Inulin: is a polysaccharide of fructose found in tubers and roots of plants. It is readily soluble in water and is used to determine the glomerular filtration rate.

Dextrins: are intermediates in the hydrolysis of starch.

Cellulose: is the chief constituent of the framework of plants. It is insoluble and consists of β-D-glucopyranose units linked by β (1→4) bonds to form long, straight chains strengthened by cross-linked hydrogen bonds. Cellulose **cannot** be digested by mammals because of the absence of an enzyme that hydrolyzes the β linkage. It is an important source of "bulk" in the diet.

Digestion of carbohydrates

The principal sites of dietary carbohydrate digestion are the **mouth** and **intestinal lumen**. This digestion is rapid and is catalyzed by enzymes known as glycosidases that hydrolyze glycosidic bonds. The majority of carbohydrate in diets are disaccharides, oligosaccharides and polysaccharides with little monosaccharide present in diets. The final products of carbohydrate digestion are into monosaccharides, glucose, galactose and fructose, which are absorbed by cells of the small intestine.

A. Digestion of carbohydrates by mouth

The major dietary polysaccharides are of plant (starch) and animal (glycogen) origin. During mastication, salivary α-amylase acts briefly on **dietary starch** and **glycogen**, hydrolyzing random **α (1→4) bonds**. There are both **α (1→4)-** and **β (1→4)-glucosidases** in nature, but humans do not produce the latter. Therefore, we are unable to digest cellulose a carbohydrate of plant origin containing **β (1→4)** glycosidic bonds between glucose residues. Because branched amylopectin and glycogen also contain **α (1→6)** bonds, which α-amylase cannot hydrolyze, the digest resulting from its action contains a mixture of short, branched and unbranched oligosaccharides known as dextrins. Disaccharides are also present as

they, too, are resistant to amylase. Carbohydrate digestion **stops** temporarily in the **stomach**, because the high acidity **inactivates** salivary α-amylase.

B. Digestion of carbohydrates by pancreatic enzymes

When the acidic stomach contents reach the small intestine, they are neutralized by bicarbonate secreted by the pancreas, and pancreatic α-amylase continues the process of starch digestion.

C. Digestion of carbohydrates by intestinal mucosal cells

The final digestive processes occur primarily at the mucosal lining of the upper jejunum, and include the action of several disaccharidases. For example, isomaltase cleaves the α (1→6) bond in isomaltose and maltase cleaves maltose and maltotriose, each producing glucose, sucrase cleaves sucrose producing glucose and fructose, and lactase (β-galactosidase) cleaves lactose producing galactose and glucose.

D. Absorption of monosaccharides by intestinal cells

The duodenum and upper jejunum absorb the bulk of the dietary sugars. However, different sugars have different mechanisms of absorption. For example, **glucose** and **galactose** are transported into the mucosal cells by an active, energy-requiring process that requires a concurrent uptake of sodium ions; the transport protein is the sodium dependent glucose cotransporter 1 (**SGLT-1**). **Fructose** uptake requires a sodium independent monosaccharide transporter (**GLUT-5**) for its absorption. **All three monosaccharides** are transported from the intestinal mucosal cell into the portal circulation by yet another transporter, **GLUT-2**.