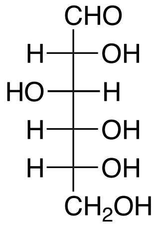
Carbohydrates (also known as sugars or saccharides) – See Handout

Approximately 0.02% of the sun's energy is used on this planet for photosynthesis in which organisms convert carbon dioxide (CO_2) and water (H_2O) to D-glucose ($C_6H_{12}O_6$) and oxygen (O_2). About 4×10^{11} metric tons of carbon dioxide are converted to glucose annually by plants, and glucose (as a subunit) is the most abundant organic compound on the planet. Learn the structure of D-glucose shown below.



Glucose (also called dextrose)

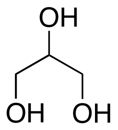
Carbohydrates occur in every living organism. The sugar in starch in food and the cellulose in wood, paper, and cotton, are carbohydrates. Modified carbohydrates form part of the coating in living cells, other carbohydrates are found in the DNA that carries genetic information, and still others are used in medicine.

The term carbohydrate is used to refer to a broad class of polyhydroxylated aldehydes and ketones commonly called sugars. Carbohydrates are also known as saccharides.

The general formula for a carbohydrate is approximated as $C_NH_{2N}O_N$. The number of carbons in the carbohydrate chain is also given special nomenclature.

3 carbons – Triose
4 carbons – Tetrose
5 carbons - pentose
6 carbons – hexose

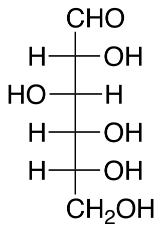
Example:



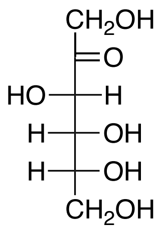
Glycerol

(a triose)

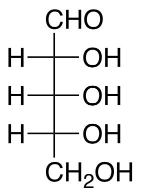
Carbohydrates can further be classified as either aldoses or ketoses. The –ose suffix is used to identify the carbohydrate, and the aldo- and keto- prefixes identify the nature of the carbonyl group. For example, glucose is an aldohexose, a six carbon aldehyde sugar; fructose is a ketohexose, a six carbon keto sugar; and ribose is an aldopentose, a five carbon aldehyde sugar. The most commonly occurring sugars are either aldopentoses or aldohexoses.



Glucose
(an aldohexose)



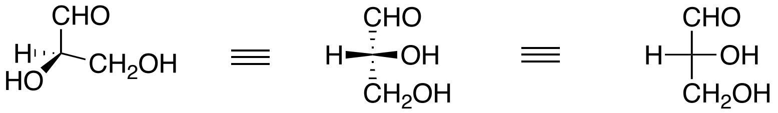
Fructose
(a ketohexose)



Ribose
(an aldopentose)

Configuration of Sugars: Fischer Projections

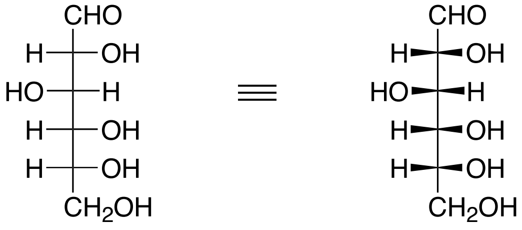
Fischer projections depict the stereogenic centers on a flat page surface. A Fischer projection is represented by two crossed lines, in which the horizontal line represents bonds coming out of the page, and the vertical lines represent bonds going into the page. By convention, the carbonyl is placed at or near the top of the Fischer projection. Shown below is the Fischer projection of (R)-glyceraldehyde.



(R)-glyceraldehyde

Fischer projection of
(R)-glyceraldehyde

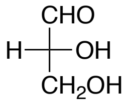
Another example is the Fischer projection of glucose. Glucose has four stereogenic centers stacked on top of one another, with the carbonyl placed near the top.



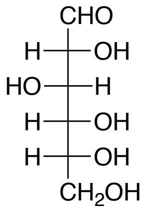
Fischer projection of Glucose

D,L Configuration of Sugars

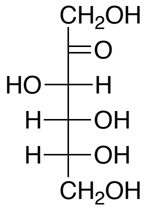
Glyceraldehyde has only one stereogenic center and therefore has two enantiomers (mirror image) forms. A D-sugar is defined as one that has R configuration at the stereogenic center with the highest number. L-sugars are those that have S-configuration at the stereogenic center with the highest number (see handout).



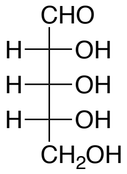
D-Glyceraldehyde



D-Glucose



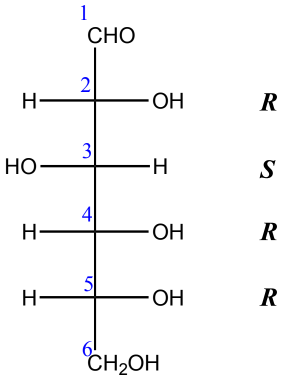
D-Fructose



D-Ribose

For example:

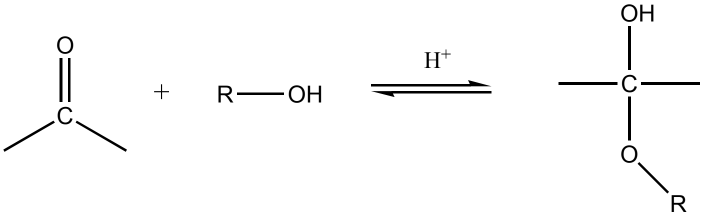
D-glucose has the structure shown below (you must know its structure). It is an aldohexose (“aldo” since it contains aldehyde functionality and “hexose” since it is a six carbon sugar, numbered on structure).



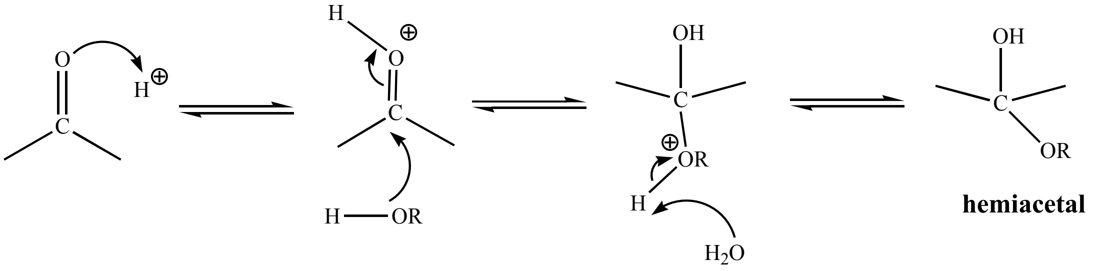
It contains 4 stereogenic carbons (C2, C3, C4 and C5). The highest numbered stereogenic center tells you whether it is a D (if it is R configuration at that stereogenic center) or an L (if it’s S configuration at that stereogenic center) sugar. For glucose, the highest numbered stereogenic center is C5. It has an R configuration. By convention, it is designated as a “D” sugar. Configurations of other stereogenic centers are also shown next to the structure.

Carbohydrates- Hemiacetal Formation

You know from previous lectures that carbonyl compounds react with all kinds of nucleophiles. Hydration and hemiacetal formation are typical examples.



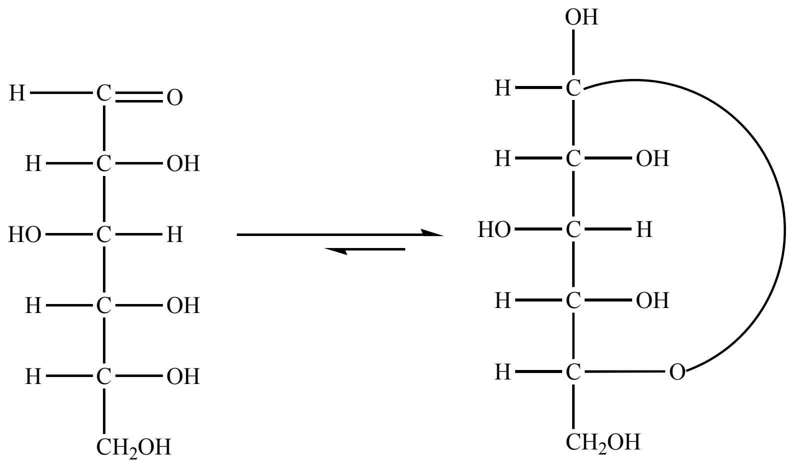
Mechanism (this should be a review from previous lecture):



In nature, formations of 5- and 6-membered rings are favored, and if possible, a molecule will form such a ring when it can.

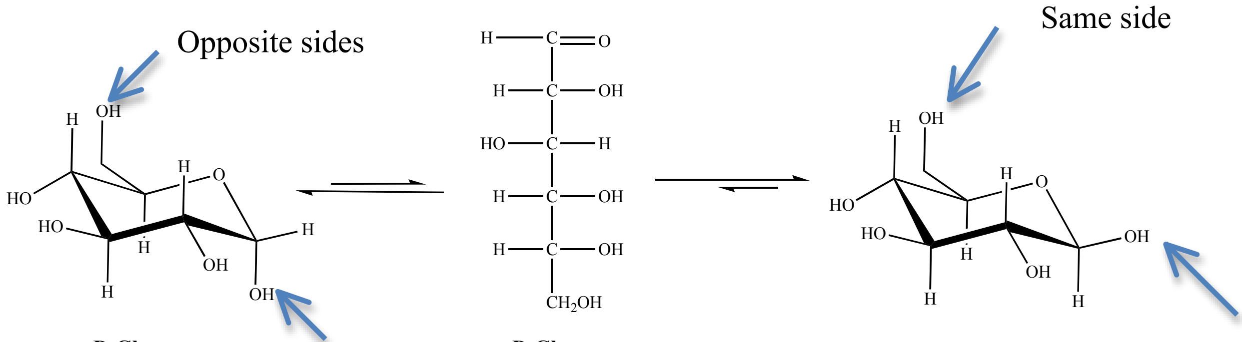
In sugars, the cyclic forms with 5-membered rings are called furanoses, and 6-member rings are called pyranoses. For most aldohexoses, the five membered furanose and six-membered pyranose can be formed. However, with D-glucose the six-membered pyranose usually predominates.

For example, glucose can react internally to form a hemiacetal (an intramolecular cyclization).



D-Glucose **hemiacetal**

The molecule exists predominantly in the cyclic form; however, it is still in equilibrium with a small amount of the acyclic form. The cyclic 6-membered rings exist in energy minimum chair forms (shown in figure below). This is also depicted in the handouts given.



α-D-Glucopyranose **D-Glucose** **β-D-Glucopyranose**

The cyclic forms are indicated in the name by combining the simple name of the sugar with "furanose" or "pyranose" to indicate the size of the ring. Therefore, glucose in its 6-membered ring form is called glucopyranose.

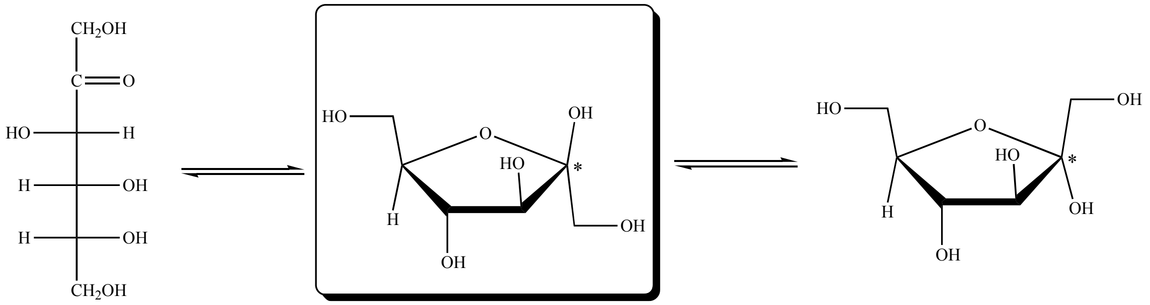
The intramolecular cyclization reaction creates a new stereogenic carbon that can be either R or S configuration, with OH group in equatorial or axial position. The terms ***α*** and ***β*** refer to position of OH at C1 relative to CH_2OH group of C6.

When the OH group attached to C1 is down relative to the CH_2OH group that is up (they are *trans* to each other), The configuration is ***α***. When they are on the same side (both are up), the configuration is ***β***.

The two stereoisomers are interconverting structural isomers called **anomers**. They differ only in stereochemistry at C1 position, which is known as the **anomeric carbon**.

The ***α*** and ***β*** anomers can equilibrate through the linear form.

Formation of a 5-membered ring is possible for D-glucose, but it exists predominantly as the 6-membered ring. Fructose, on the other hand, exists predominantly as 5-membered ring.



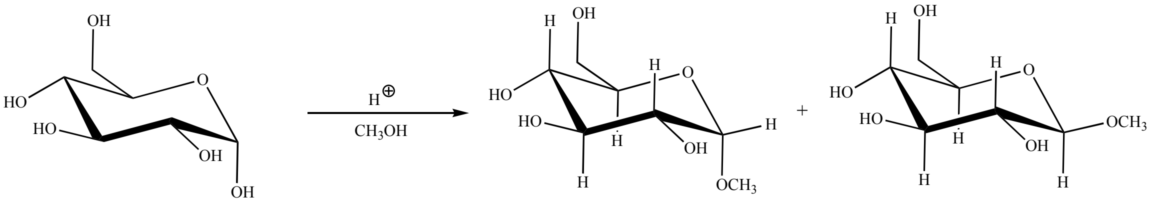
D-Fructose **D-β-Fructofuranose** **D-α-Fructofuranose**

D-fructose is a ketohexose ("keto" since it contains ketone). Its cyclized form, D-fructofuranose is a hemiacetal since the anomeric carbon (marked by asterisk) has a free OH group and a OR group attached. An easy way to find the anomeric carbon is to find a carbon with 2 oxygen atoms attached directly.

*Is the fructofuranose highlighted in box an **α** or **β** sugar?*

Answer: It is ***β***. The rule is to find the CH_2OH group (not on the anomeric carbon) and the OH substituent of the anomeric carbon, and see of they are on the same or opposite side. Since the OH group and the CH_2OH group are on the **same** side as each other, the ring is ***β***.

Acetal formation

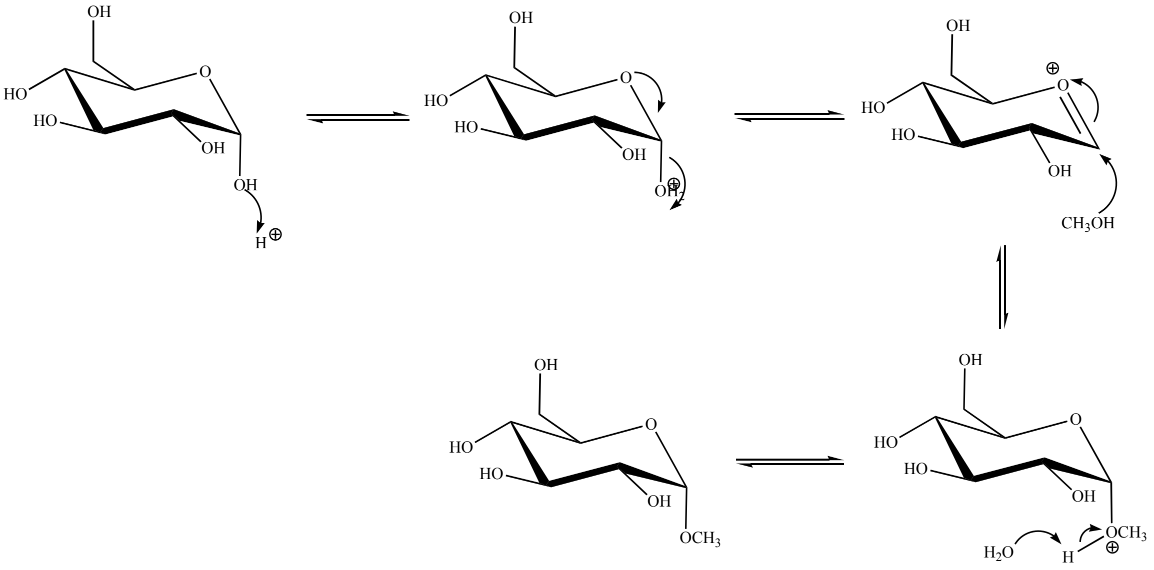


α-D-Glucopyranose **α-D-Glucopyranoside (favored)** **β-D-Glucopyranoside (minor)**

Treatment with dilute acid and alcohol converts only the OH at the anomeric position into an acetal called a glycoside. Specific glycosides are named by replacing the "ose" of the simple sugar's name with "oside". When glucopyranose is reacted, its product is called glucopyranoside.

The ***α*** anomer with the methoxy group in axial position is favored due to the anomeric effect (details about the anomeric effect is beyond the scope of this class).

Mechanism:



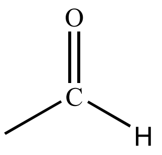
Reducing or non-reducing sugars

We can perform chemical reactions on a sugar to find out if it's a reducing or non-reducing sugar, such as the silver mirror reaction. Silver nitrate in aqueous ammonia is allowed to react with sugar. If a silver mirror is observed, then the sugar is reducing.

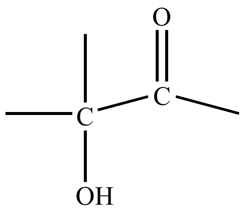
$$\mathrm{Ag(NH_3)_2OH} \xrightarrow{\text{Sugar}} \mathrm{Ag}^{\bullet}$$

silver nitrate **silver mirror**

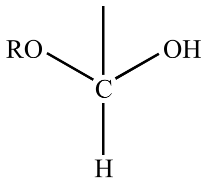
Usually, reducing sugars contain one of the three functional groups:



aldehyde

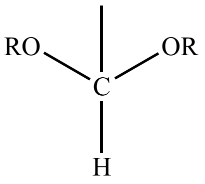


α-hydroxyketone



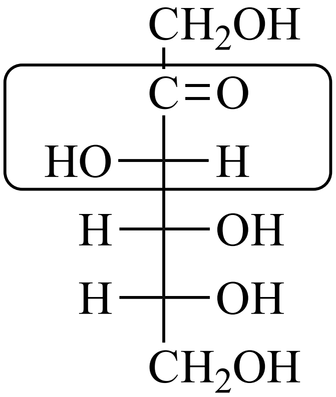
hemiacetal

The non-reducing sugars do NOT contain the above functionality, but may contain acetal functionality:



acetal

Example:

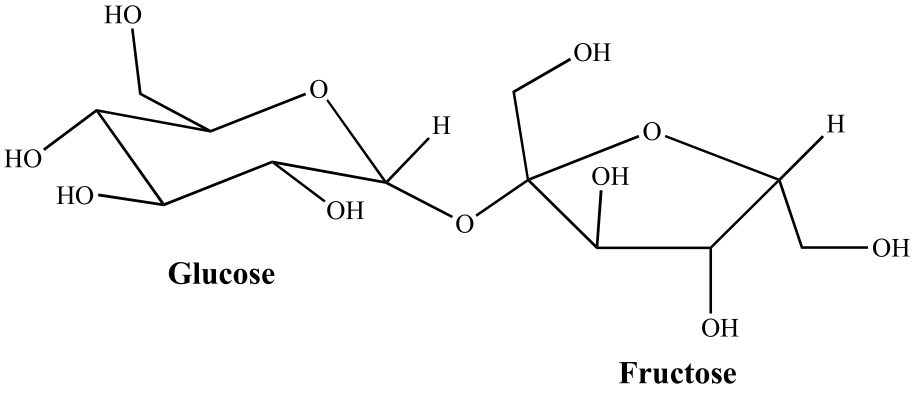


D-Fructose

Fructose is the sweetest sugar of all (sweetness index 180)

Is it a reducing or non-reducing sugar?
It is reducing since it contains a α-hydroxyl ketone group in open form and the cyclized form is a hemiacetal at anomeric position.

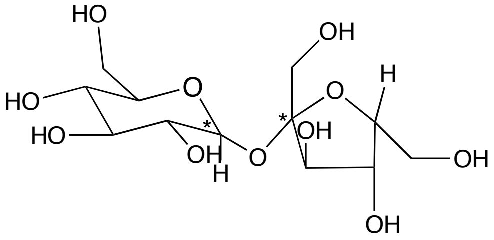
Example: a disaccharide



The structure shown is sucrose (table sugar). It is made up of a glucose and a fructose molecule (sweetness index 100)

Does this molecule have anomeric carbon?
Yes.

Identify the anomeric carbon.
They are highlighted with asterisks.

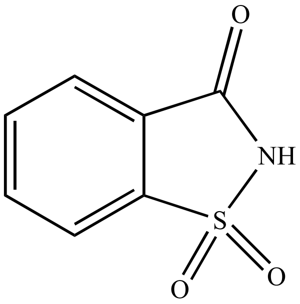


Glucose Fructose

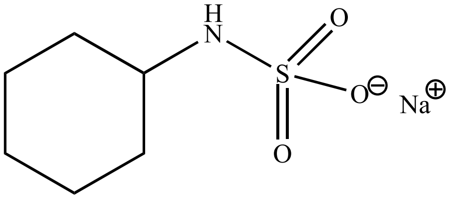
Are they acetals or hemiacetals?
They are acetals. In both cases, the carbon has two OR group attached. There is no free OH group.

Is this sugar reducing or non-reducing?
Non-reducing since the anomeric carbons has acetal groups.

Some artificial sweeteners are shown below:

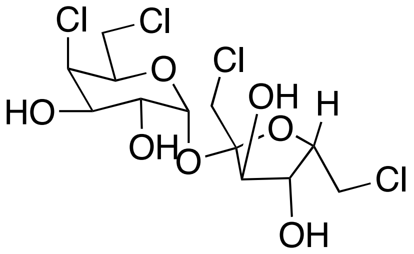


saccharin



sodium cyclamate

Although a small amount tastes a lot sweeter than sugars, these are suggested to be carcinogenic in very large doses.

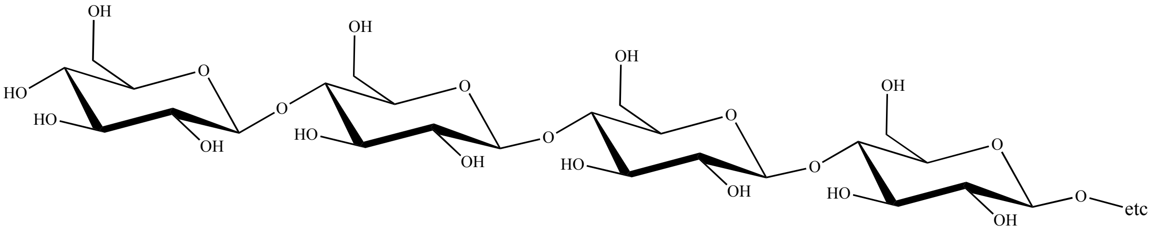


Splenda (sucralose)

Polysaccharides = polymers of sugars

Disaccharides = 2 sugar linked
Trisaccharides = 3 sugar linked
Tetrasaccharides = 4 sugar linked
.
Oligosaccharides = Polysaccharides

Example: Cellulose; β-(1,4) linked D-glucose polymer

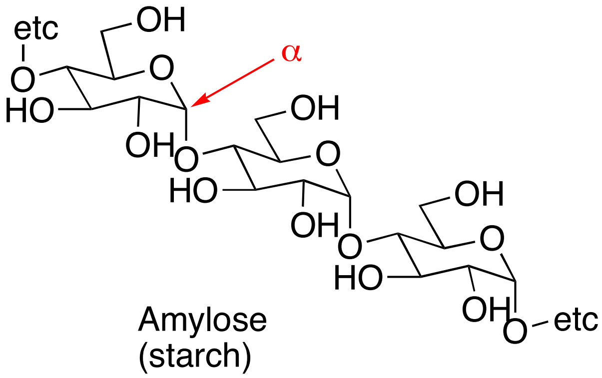


Cellulose is a polymer of simple repeating monosaccharide units (D-glucose).

Polysaccharides

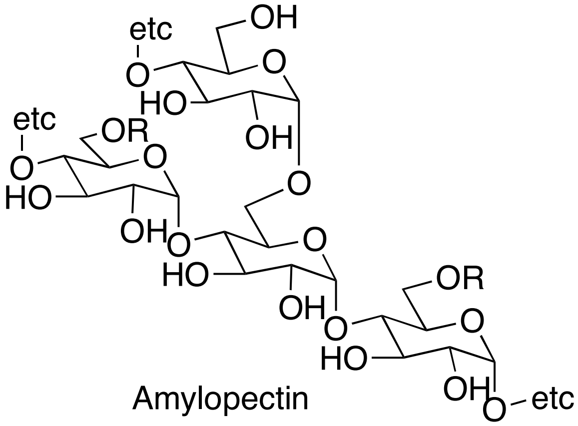
Many mammals cannot digest cellulose directly. Ruminants such as cows or goats have bacteria in their stomach to break it down to its simpler unit. The bacteria have a cellulose hydrolysis enzyme called cellulase which we do not have. Humans cannot metabolize β linkages.

Example: Amylose; α-(1,4) linked D-glucose polymer



In contrast, amylose is a polysaccharide with α linkage between each monosaccharide units. Humans can digest amylose. Starch is comprised of approximately 20% amylose.

Example: Amylopectin



Amylopectin

Amylopectin is the other component in starch (~ 80%), which is similar to glycogen.