Number 7

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Carbohydrates (saccharides) can be classified into these main categories:

1. **Monosaccharides**, they are simple sugars (the simplest units), such as glucose, galactose and fructose. They can be classified according to:
   - **Number of carbon atoms they contain**:
     - Trioses (3 carbons), Tetroses (4 carbons), Pentoses (5 carbons), Hexoses (6 carbons), Heptoses (7 carbons), Nonoses (9 carbons)
   - **Type of carbonyl group they contain**:
     - Aldoses: with an aldehyde as their carbonyl group.
     - Ketoses: with a ketone group as their carbonyl group.

2. **Disaccharides**
   - Sucrose = glucose + fructose (heterodisaccharide)
   - Lactose = galactose + glucose (heterodisaccharide)
   - Maltose = glucose + glucose (homodisaccharide) – 2 glucose residues.

The formation of disaccharides requires the formation of glycosidic bonds by dehydration, the synthesizing enzymes are glycosyltransferases.

✓ **Notes**: How to recognise disaccharides?

   a. Indicate the 2 specific sugar monomers (residues) involved and their stereoconfigurations (D- or L-)
   b. The carbons involved in the linkage (Is it C-1 with C-4, or C-2 with C-6 ...)
   c. The order of the two monomer units, if they are heterosaccharides (example: galactose followed by glucose) the first one is the one on the left, the second one is on the right.
   d. Indicate the **anomeric** carbon for both residues (α or β)

*But how to determine the bond’s form?*

It can be determined by the position of the anomeric hydroxyl group of the sugar involved in the bond. If it’s below the ring then it’s alpha, and if it’s above the ring then it’s beta.

Figure 7.00 shows you that this anomeric carbon is in the \( \beta \) configuration, the linkage is a \( \beta \)-bond.
3. **Oligosaccharides**, they are formed when a few **monosaccharides** (residues) are linked. *From 3 to 10 monosaccharides*

4. **Polysaccharides**, they are formed when many monosaccharides are bonded together, such as starch and glycogen. *More than 10 monosaccharides*

   See the definition of residues, at the end of this sheet.

✓ **Notes:**

- D- sugars, rather than L-sugars, are physiological sugars in our bodies, we cannot metabolise L-sugars.
- D-sugars are mainly found in the nature except in some organisms such as some bacteria
- D-sugar (D-glucose), clinically, is called Dextrose.

**How could we decide if a ring sugar is a D- or an L- sugar?**  **not important**

   Answer: As previously mentioned, D-sugars are predominant, all the rings we are going to study are D- sugars. But, the main difference between D- and L- sugars’ rings is that carbon-6 of the L-sugar is found bellow the ring, but the 6 carbon of a D- sugar ring is found above the ring.
Monosaccharides are found in two forms:-

1. Open-chain (acyclic) form. Only 1% exist in this form because it is unstable.
2. Ring (cyclic) form. Most sugars exist in this form.

We have 2 types of rings; they are:

A. Pyranose: a sugar with a six-membered ring (5C + 1O), such as glucose and galactose.
B. Furanose: a sugar with a five-membered ring (4C + O) such as fructose.

✓ Note:

Once the ring is formed, hydroxyl groups’ positions are fixed, they don’t interconvert or change position, this is true for (C-2, C-3, C-4 of glucose) but the hydroxyl group that is attached to the anomeric carbon (C-1 of glucose), it interconverts in a process called mutarotation to form either an alpha (when the hydroxyl group is below the ring) or a beta sugar (when the hydroxyl group is above the ring) – go to the end of the sheet for anomeric carbon definition.

Figure 7.1 - The circled carbon is the anomeric carbon, the hydroxyl group is not fixed, it can interconvert to give either alpha or beta sugar (REMEMBER: beta & alpha sugars are both anomers)

β configuration is more stable than α

✓ Note:

Anomers differ in the position of the hydroxyl group on the anomeric carbon, but if the hydroxyl group changed position on other carbons (carbon-3, carbon-4 ...), the result would be totally different sugars (other isomers such as epimers.) - Go to the last page for a definition e.g.:

- Glucose and Mannose are carbon-2 epimers.
- Glucose and Galactose are carbon-4 epimers
How can we determine the position of the anomeric carbon?

The oxygen atom in the ring can be our guide to indicate the position of the anomeric carbon, you should take the following points into account,

a. The sugar type.

b. The position of the oxygen atom (sometimes the ring is flipped) – look at Figure 7.2.

c. Start numbering.

Figure 7.2: Although the hydroxyl group is below the ring, we consider this a beta sugar, because the ring is flipped.

**From an open chain to a ring form sugar and vice versa:**

When cyclising a sugar, you should change the positions of hydroxyl groups as follows:

- Any hydroxyl group to the right of the carbon in the open chain (Fischer Projection), has a downward direction in the ring form (Haworth Projection).

- Any group that is written to the left of the carbon, it has an upward direction in the ring.

Go to the last page to see the definition of the cyclisation process.

7.3- cyclising a glucose molecule
For Glucose + Galactose:

See the two carbons that are attached to the oxygen atom (\(-O-\)), and give number one to the carbon that has a hydroxyl group pointed above or below the ring (NOT the one which is attached to a carbon group projected above or below ring) This number one carbon C-1 is the anomeric carbon.

For Fructose

See the two carbons that are attached to the oxygen atom, you can see that one of them is attached to a hydroxyl group, this would be the anomeric carbon, give it number two (because it is originally a ketone group).

Figure 7.4 - REMEMBER, the anomeric carbon is attached to four different groups, this is why it is chiral, so the cyclization process gives rise to another chiral center in addition to the ones already present in the sugar molecule.

Reducing sugars and Non-reducing sugars:

- If the hydroxyl group on the anomeric carbon of a cyclized sugar is not linked to another compound by a glycosidic bond (free anomeric carbon), the ring can open. - See the definition of glycosidic bond at the end of the sheet - The sugar can act as a reducing agent (reducing sugar) - See the definition at the end of this sheet -

- Benedict’s test is used to detect monosaccharides by oxidising them, The copper (II) ions in the Benedict’s solution are reduced to form a precipitate, which causes the color change:

7.5 As the concentration of reducing sugar increases, more reduction of cupper (the greater the precipitate formed) and the nearer the final colour is to brick-red and.
There are some reagents are used to detect the presence of reducing sugars:

A. Tollen’s reagent, which uses the silver ammonia complex ion Ag(NH3)2+ as the oxidising agent. If a reducing sugar is present, a silver mirror is deposited, as a result of reduction of Ag+ to free silver metal. **REMEMBER:** Tollen’s test used to distinguish between an aldehyde and a ketone.

B. Glucose Oxidase Enzyme, a method used for detection of glucose (not other reducing sugars)

C. Benedicts test can be also used to detect monosaccharides which are reducing sugars.

All **monosaccharides are reducing sugars**, monosaccharides (whether ketoses or aldoses) can cyclize to produce an anomeric carbon, if Hydroxyl group is not attached to another molecule then ring opens and the carbonyl group gets oxidised.

**Not all disaccharides** are reducing sugars.

**Some Monosaccharides:**

[Images of glucose, galactose, and fructose structures]
7.6 The green dot represents the anomeric carbon, we notice that when this carbon is attached to a hydroxyl group (-OH), the sugar is considered as a reducing sugar.

Some dissaccharides

7.8 When it comes to disaccharides, some rings (such as maltose and lactose) can open from the side which is not linked to the glycosidic bond (-O-), but other rings (such as sucrose) cannot open because as you can notice the green dot is not directly attached to a hydroxyl group.

In other words, once the glycosidic bond is formed, the anomeric carbon gets occupied, it is no longer free. That is why reducing disaccharides have one occupied anomeric carbon and another free one, but non-reducing sugars have both anomeric carbons occupied.
- Glycosidic bonds are very **stable**, in addition to attaching carbohydrates together, they also connect carbohydrates with non-carbohydrates to form glycosides.

- We are going to talk about it in details, in the modified sugars.

**Modified Sugars**

There are many reactions that can modify sugars, here are some:

I. **Oxidation**

- We know from organic chemistry:
  - Aldehyde groups can be oxidized to give the carboxyl group.
  - Hydroxyl groups can be oxidised to give aldehydes. And further oxidation can give rise to carboxyl groups. (Double Oxidation) or ketones.

  Thus, **in an open chain**, oxidation of a monosaccharide produces sugar acids.

- **Aldoses:**
  - Such as glucose.

Examples on Glucose Oxidation:

- In the presence of specific **enzymes** in biological systems, oxidation of the hydroxyl group on carbon 6 of glucose gets oxidized to produce **Glucuronic acids/ Glucuronate**.
- When using a **weak oxidizing agent** with a glucose molecule, the carbonyl group on carbon 1 of glucose, produces **Gluconic acid/ Gluconate**. (double oxidation)
- When using strong oxidizing agents such as KMnO4 or Cr2O3, each functional group on carbon 1 & carbon 6 gets oxidized into a carboxyl group, the product is **galactaric acid- dicarboxylic**. **Refer to the slides to see the previously mentioned reactions.**

*What is the difference between gluconate and gluconic acid:*

- Gluconate: a deprotonated form (_COO-)  
- Gluconic acid: a protonated form (_COOH)

The difference between **Glucuronate and Glucuronic acid** is the same.
Notes
- Gluconate is formed when the hydroxyl group on carbon number 1 of glucose gets oxidised
- Glucuronate is formed when the hydroxyl group on carbon number 6 of glucose, gets oxidized.

Ketoses

A carboxyl group cannot be produced by directly oxidizing the ketone.

Although oxidation of ketoses to sugar acids does not occur naturally, ketoses such as fructose undergo isomerisation to become reducing sugars such as glucose, and thus can oxidize.

In the cyclic form, the compound produced by oxidation of an aldose is a lactone.

A lactone: a cyclic ester linking the carboxyl group and one of the sugar alcohols, one important example is Vitamin C (ascorbic acid).

How vitamin C is related to sugars?
1) vitamin C (ascorbic acid) which is unsaturated lactone.
2) Air oxidation of it, followed by hydrolysis of the ester bond, leads to loss of activity as a vitamin
3) A lack of fresh food can cause vitamin C deficiencies which in turn can cause diseases, such as Scurvy.

ii. Reduction
- We know from organic chemistry:
  - Aldehyde groups can be reduced to give primary alcohol.
  - Ketone groups can be oxidised to give secondary alcohols.

Thus, sugars when reduced, can either form:-
• **Sugar alcohols:** When the carbonyl group of a sugar is reduced to a hydroxyl group. The resulting compound is sugar alcohols. They are very important in industry, they have commercial importance as sweeteners in chewing gums and candies.

  E.g.: Sorbitol (a reduced glucose), Manitol, Xylitol

• **Deoxy sugars (reduced):** In addition to oxidised sugars; there are reduced sugars. In Deoxy Sugars, one or more hydroxyl groups are replaced by hydrogen atoms. One important example on such sugar is the sugar found in DNA

![Sugar Alcohols](image)

**iii. Esterification** (forming esters),

-To form sugar esters, carbons involved are 1 or 6.

1. **Phosphorylation**

An important reaction that takes place inside our cells, it is the process of adding a phosphate group to the sugar molecule (Esterification)

Adding phosphate group to a carbon, increases its activity (high energy molecule, less stability). **This is why it is the first step of glucose metabolism**, to enable the sugar to continue the metabolism by providing energy.

**iv. glycosides**

- See the definition at the end of this sheet-

  - **O-glycosides:** a sugar molecule bonded to an oxygen atom of another molecule.

  - e.g.:
- If the group on the non-carbohydrate molecule to which the sugar is attached is an -OH group, the structure is an O-glycoside (linked by O glycosidic bond).

  - Sugar-sugar glycosidic bonds are O-type linkages.

Figure 7.8, O-glycosidic bond in disaccharides-

A hemiacetal carbon (anomeric) can react with an alcohol such as a methyl alcohol to give a full acetal (2 ether groups) or glycoside.

- **N-glycosides**, a sugar molecule bonded to a nitrogen atom of another molecule.

  - e.g.: If the group on the non-carbohydrate molecule to which the sugar is attached, is an -NH2 group.

✓ **Note:**

*Amino-sugar (sugar amine)*, sugar molecule bonded to a nitrogen atom of another molecule.

**What is the difference between N-glycosides and amino-sugar?**

- In N-glycoside- the addition of amino group is to the anomeric carbon.

- Amino sugar involves the addition of amino group to any other carbon (mainly at carbon number 2, further modifications can occur such as acetylation).
Definitions:

**Anomeric carbon**: is originally the carbonyl group (the former carbonyl group), it is the asymmetric carbon that is formed when a sugar cyclizes, so its aldehyde (or keto) group reacts with a hydroxyl group (OH) on the same sugar, making the carbonyl carbon (carbon 1 for an aldose, carbon 2 for ketoses) asymmetric.

It is called anomeric carbon because it can form anomers (α or β).

**Cyclisation of a sugar**: is an interaction between functional groups in a sugar to turn it from the form of open chain to a cyclic (ring) form, the cyclization process involves the attack of the carbonyl group by a hydroxyl group to form a ring. This leads to giving rise to another chiral center in addition to the ones already present in the sugar molecule.

**Epimers**: isomers that differ in configuration around one specific carbon atom (with the exception of carbonyl atom).

**Glycosidic linkages**: it is a bond between an anomeric carbon in a carbohydrate molecule with another carbohydrate molecule or a noncarbohydrate one, its formation involves the loss of water molecule - H2O-, these linkages are responsible for the bonding of monosaccharides to form oligosaccharides and polysaccharides. They can also link carbohydrates to non-carbohydrate structures, (all sugar-sugar glycosidic bonds are O-type linkages).

**Hemiacetal**: it is produced when an aldehyde reacts with alcohol. When more alcohol involves in the reaction, an acetal is produced.

**Hemiketal**: it is produced when a ketone reacts with alcohol. When more alcohol involves in the reaction, a ketal is produced.

**Non-reducing sugar**: is any sugar that does not carry reduction reactions.

**Reducing sugar**: is any sugar that is capable of acting as a reducing agent, it is a chemical term for a sugar that acts as a reducing agent and can donate electrons to another molecule, it carries reduction reactions and its carbonyl group gets oxidised.

**Residue** refers to a specific monomer/subunit within the polymeric chain of a polysaccharide, protein or nucleic acid. One might say, "This protein consists of 118 amino acid residues".

**Mutarotation**: is the change in position (flipping) of hydroxyl group in a cyclic sugar.
1. What is the name of the ring of the fructose molecule that is shown here?
   - Furan

2. What is the number of the anomeric carbon of fructose?
   - number2

3. Why lactose and maltose are reducing sugars?
   - Because the anomeric end of the glucose residue is not involved in the glycosidic bond. (Free anomeric carbon)

“I’VE LEARNED THAT I STILL HAVE A LOT TO LEARN.”