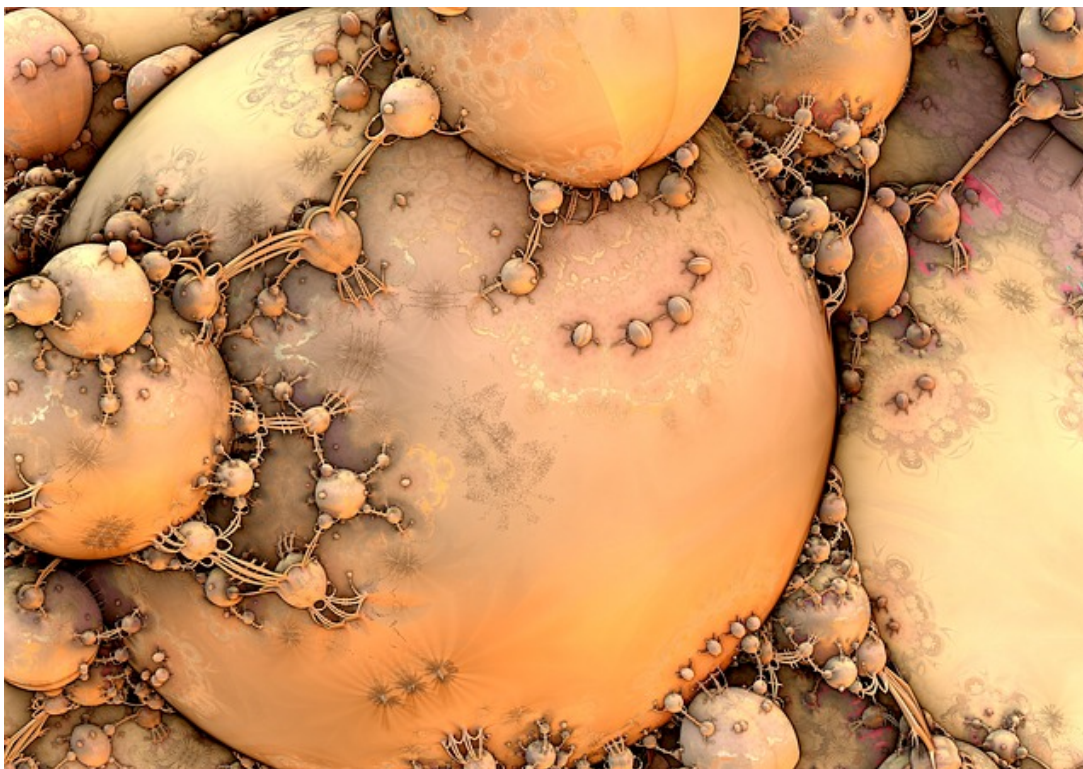


Biochemistry for Physicians: The Chemistry of Carbohydrates

[See online here](#)

Everywhere in biochemistry, there is mention of carbohydrates and carbohydrates; they are a fundamental part of almost all essential biochemical processes and, what's more, they form an extremely important part of medical exams, but what is it that makes carbohydrates so essential for biochemistry?



Structure and Function of Carbohydrates

Carbohydrates are the aldehydes or ketones of polyalcohols (alcohols with several carboxyl groups) with a carbon/water ratio of 1:1, which results in the chemical molecular formula of $C_n(H_2O)_n$. In case of a hexose with six carbon (C) atoms, the molecular formula would, therefore, be $C_6(H_2O)_6$.

The number of relevant carbohydrates that medical students must know, however, is very limited and, with a few tricks, students can study and understand them very quickly.

Note: The terms *carbohydrate*, *saccharide*, and *carbohydrate* are used as synonyms or interchangeably.

Monosaccharides (or simple carbohydrates) can be further classified by counting their carbon atoms. The most relevant monosaccharides for the metabolism (as well as for

medical exams) are **hexoses** (six C atoms) and **pentoses** (five C atoms).

Carbohydrates with more or fewer C atoms also play a role, but to a smaller extent—that is, glycerin aldehyde (three C atoms), erythrose (four C atoms), or sedoheptulose (seven C atoms), of which the last two represent an intermediate product in the hexose monophosphate pathway of glucose metabolism (see below). Aside from sedoheptulose, however, tetroses, trioses, or heptoses are not as relevant for medical students, which is why they are not discussed further here.

Chirality and Isomerism of Monosaccharides

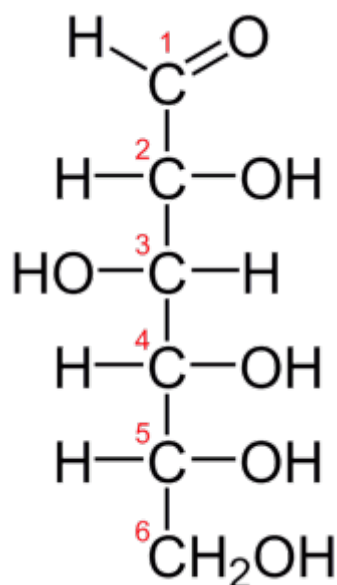


Image: D-glucose. By Ben; Yikrazuul,
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Essential for the detection of isomerism is the ability to identify **chiral centers** in a molecule. An atom is always chiral if it has four different binding partners. Therefore, if this is applied to an aldohexose, i.e. D-glucose, one realizes that it possesses four chiral centers (C2–C5). Pentoses are one carbon atom smaller than hexoses, so they only possess three chiral centers (C2–C4).

The D- and L-nomenclature of carbohydrates always refer to the position of the OH group at the C5 atom in the Fischer projection (i.e. the second carbon atom from the bottom). If the OH group is to the left, it is an L-carbohydrate; if it is to the right, it is a D-carbohydrate ('D' from Latin *dexter* = right). **All carbohydrates in the human body are D-carbohydrates.**

Three of the four most important hexoses for the body are **isomers**, and they are therefore very similar to each other. On one hand, this quality makes them easy to learn. On the other hand, however, special caution is warranted to avoid mistaking one for the other.

Excursus: Stereochemistry and Isomerism Relationships of the Most Important Carbohydrates

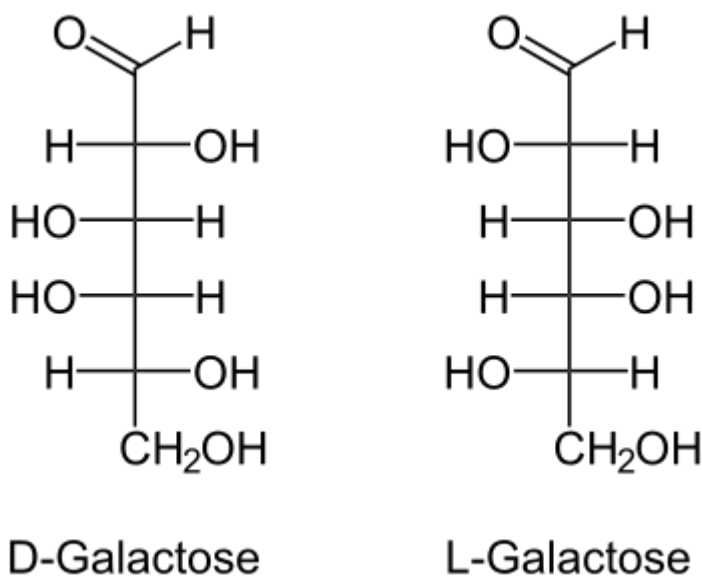
With this flow chart, all isomerisms—not only those of carbohydrates—in organic

chemistry can be identified.

Definition:

- **Constitutional isomers = structural isomers** (same molecular formula, different bonding pattern)
- **Stereoisomers** (same molecular formula, same bonding pattern, different spatial arrangement)
- **Conformers** (they can be converted into each other via rotation of the substituents to C-C mono binding (tub shape/chair shape))
- **Configurational isomers** (same bonding pattern, a different arrangement of the substituents around a center)
- **Cis/trans isomers** (cannot be converted into each other via rotation of the substituents but rather face each other (trans) or they are on the same side (cis), which is often the case in double bonds)
- **Chirality** (C atom is asymmetrically substituted—from the Greek word for hand ('cheir'), chirality is the geometric property displayed by any object that is not superimposable on its mirror image)
- **Enantiomers** (not superimposable mirror-image molecules)
- **Diastereomers** (not (entirely) mirror-image molecules)

The most important hexose is **glucose**. All other hexoses can be synthesized from glucose. In addition, the breakdown (glycolysis) of glucose meets 50% of a human's daily energy needs. When trying to remember the molecular structure of glucose, one can use the sound of a German fire engine as a mnemonic. '**Ta Tü Ta Ta**' is the code for glucose molecules if one remembers that starting at the first chiral C atom, 'tü' stands for an OH group to the left and 'ta' for an OH group to the right.



[Image](#): Structure of galactose. By NEUROtiker. License: [Public Domain](#).

Galactose is an epimer of glucose and only differs from it in one chiral center (C4). If the OH groups are connected, the result is a 'galactic fighter plane,' a type of spacecraft.

Mannose is an epimer of glucose as well and only differs in the second C atom. Here, one can remember '**the second man is epimer**,' meaning that mannose is a C-2 epimer of glucose.

The final most important carbohydrate for the body is **fructose**, which differs from glucose because its carbonyl group is attached to the second carbon atom, making it a **ketose**. As a ring form, fructose forms a furanose, in contrast to the other three hexoses, which form a pyranose.

Caution: The ring formation that creates a pyranose/furanose generates a new chiral center!

The ring formation creating a **pyranose** in aldoses is generated through a reaction between the functioning aldehyde group at C1 and the OH group at C5. The molecule thus formed is also called **hemiacetal**. The newly created carboxyl group in the new chiral center is highly reactive because it lends the carbohydrate its reducing capabilities—it even has its own name: the glycosidic OH group.

Hemiketal (i.e. fructose) is created when the keto group at C2 of a ketose reacts with the hydroxyl group at C5, thereby forming a pyranose instead of a **furanose**.

Pyranoses or furanoses are mostly written using the **Haworth formula**, meaning another nomenclature rule is added. This is, however, just as simple as the D-/L- nomenclature.

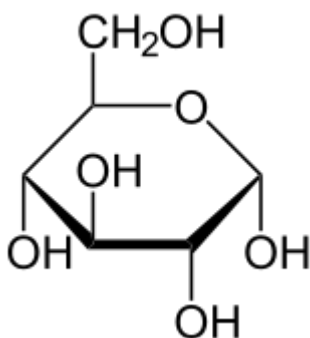


Image: Structure of alpha-D-glucopyranose. By NEUROtiker. License: [Public Domain](#).

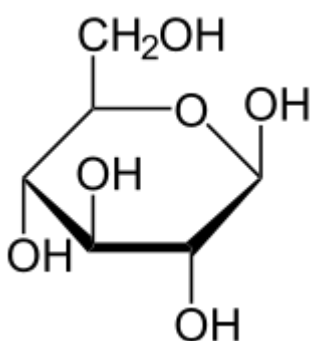


Image: Structure of beta-D-glucopyranose. By NEUROtiker. License: [Public Domain](#).

When the OH group is the first C atom from the bottom, it is an α -molecule; if it is at the top, it is a β -molecule.

For the process of converting the carbohydrate from the Fischer projection to the Haworth formula and vice versa, the 'FLOH' rule is helpful: **'What's left at Fischer's is at the top at Haworth's.'**

α - and β -glucose are **anomers** and can be converted into each other via the open-chain

form. However, because the OH groups in α -glucose at the C1 and C2 atoms are closer together than in β -glucose and nature ensures that conditions are as low energy as possible, the balance shifts to the side of β -glucose.

In the **chair conformation**, the cis/trans isomerism, as well as the spatial structure of molecules, are best recognized.

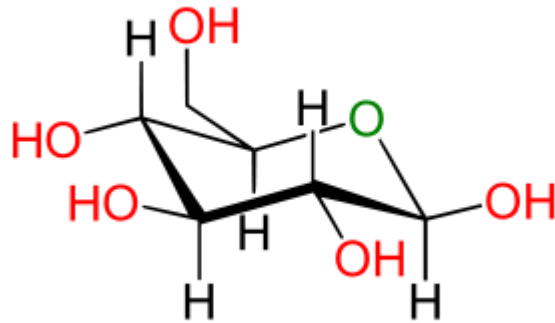


Image: β -glucoses. By Lecturio.

Thereby, the question frequently asked is which OH groups are in the axial position and which are in the equatorial position. Here, the hydroxy groups are positioned equatorially. An axial position can always be recognized by the vertical binding line (in this case, hydrogen atoms).

Caution: In α -D-glucose in chair form, the carbonyl group is positioned axially on C1. The same OH group (C1) is positioned downward in the Haworth formula!

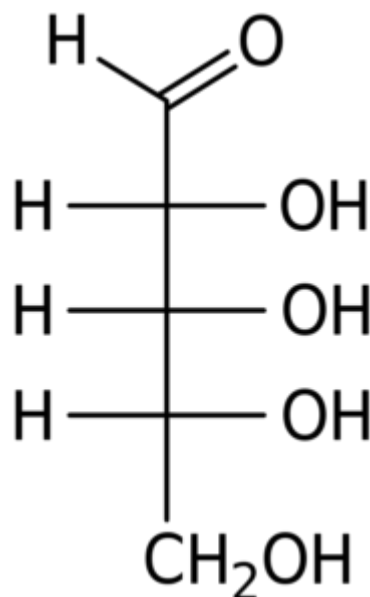


Image: The Fischer projection of the aldopentose monosaccharide, D-ribose. By Christopher King. License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/).

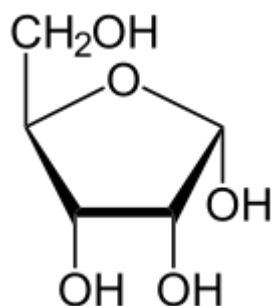


Image: Structure of alpha-D-ribofuranose. By NEUROtiker.
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The most important pentose overall is the D-ribose on whose exact origin the pentose phosphate pathway provides more detailed information. Pentoses are essential components of ribonucleic acids.

Bond Structures of Carbohydrates

Carbohydrates can form a **glycosidic bond** with each other, as well as with other molecules, whereby one differentiates between an O-glycosidic bond and an N-glycosidic bond.

An **O-glycosidic** bond exists when the anomeric C atoms of two molecules react. The nomenclature of these bonds again consists of the α - or β -conformation, as well as the indication of the numbers of the particular anomeric centers.

The α - β -conformation refers to the position 'top' (β) or 'bottom' (α), just like with the monosaccharides.

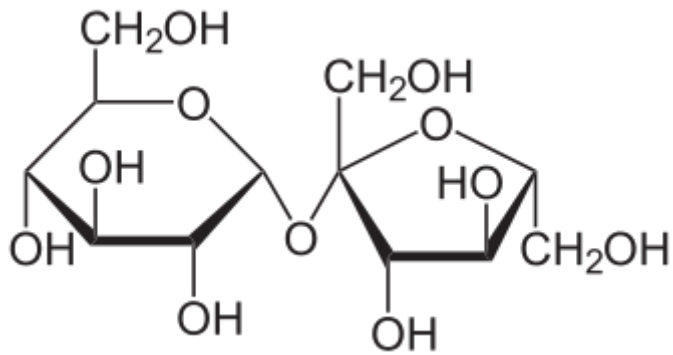
The **N-glycosidic** bond describes the binding of carbohydrate, not with another OH group, but rather with an NH group of another molecule. The most frequent occurrence of this type of bond is with asparagine, but the binding of a DNA-ribose, with bases such as adenine, should be remembered under the term 'n-glycosidic bindings' as well.

Classification of Carbohydrates

Disaccharides

Even though there are incredibly large amounts of disaccharides, only three of them are applicable for a medical student, including their structural formula and all of their characteristics such as splitting and bond structure.

1. Sucrose (fructose + glucose)
2. Lactose (galactose + glucose)
3. Maltose (glucose + glucose)

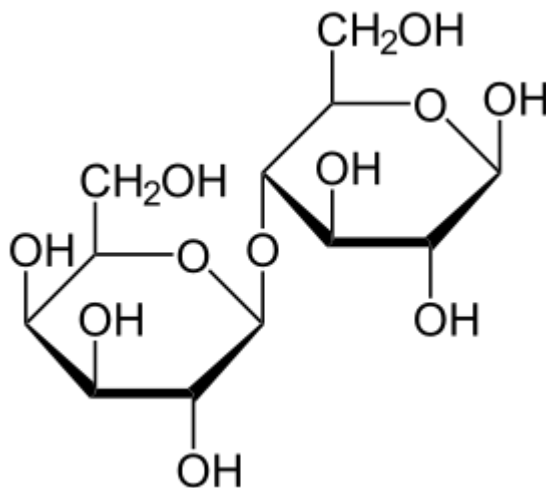


[Image](#): Structure of sucrose (saccharose). By NEUROtiker. License: [Public domain](#).

Sucrose

With regard to sucrose, it is important to note that it is **not a reducing carbohydrate** because all anomeric carboxyl groups are involved in the bond.

Lactose, the milk carbohydrate

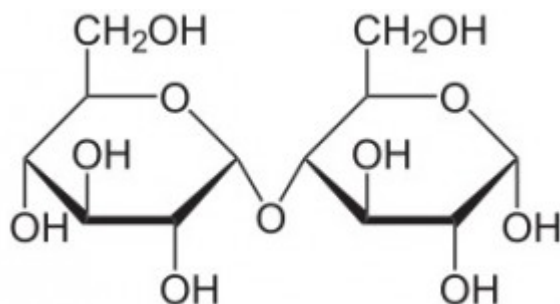


[Image](#): Structure of lactose. By NEUROtiker. License: [Public domain](#).

The splitting of the clinically significant lactose is an exception for the human body. The **β -glycosidic** bond of lactose is the only β -glycosidic bond that can be split by a human being.

In cases of the metabolic defect **lactose intolerance**, this splitting of the β -glycosidic bond is no longer possible. The typical symptoms, such as diarrhea and pain in the abdomen, occur because lactose remains in the intestinal lumen and causes osmotic absorption of water and osmotic diarrhea.

Maltose, the carbohydrate in beer



[Image](#): Balance between the cyclic and open form of maltose. By NEUROtiker. License: [Public domain](#).

Maltose (as well as isomaltose $\text{Glc } \alpha 1 \rightarrow 6 \text{ Glc}$) is created, among others, by splitting starch with α -amylase. Maltose is a reducing carbohydrate.

Reducing and non-reducing carbohydrates can easily be distinguished by the fact that non-reducing disaccharides have **two Greek letters** in their names (sucrose: α -D-glucose(1.2)- β -fructose) and reducing ones only have one (maltose: α -glucose (1.4)-glucose)

Oligosaccharides

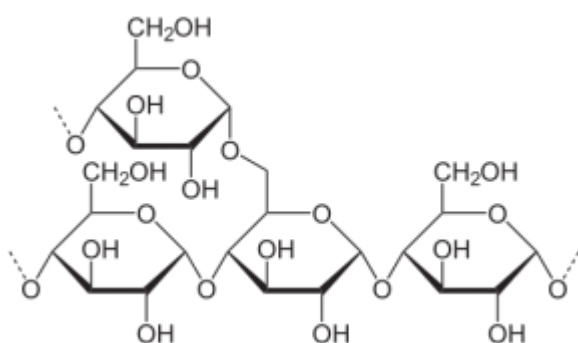
Oligosaccharides are combinations consisting of 3–20 carbohydrates. They play a role in metabolism as glycoproteins.

Polysaccharides

Polysaccharides are carbohydrates that come to mind first due to diets, bodybuilding, and alternative lifestyles that are broadcast by the media. **Starch**, enemy number one in the 'low-carbohydrate diet,' is a polysaccharide, for instance.

With regard to the general structure of polysaccharides, one should know that there are hetero- and homo-polysaccharides. **Hetero-polysaccharides** consist of several different monosaccharides, while **homo-polysaccharides** are a sequence of several of the same monosaccharides.

The most important homo-polysaccharides are cellulose, glycogen, and starch. All of them consist of several glucose molecules.



[Image](#): Section of an amylopectin polymer. By NEUROtiker. License: [Public domain](#).

Starch is the carbohydrate stored in plants, as opposed to **glycogen** in which animals (as well as humans) store carbohydrates.

Starch consists of amylose (α -(1.4) Glc) as well as amylopectin (α -(1.4) Glc and sometimes α -(1.6) Glc) branched out due to its bonds α -(1.6). Glycogen consists of α -(1.4) Glc and α -(1.6) Glc glycosidic bonds between glucose molecules, as well. It does, however, have more α -(1.6) bonds, which is why it is more branched out than amylopectin.

Cellulose does not play a role in human metabolism, but it is an important **fiber** and promotes the proper functioning of the intestines.

Hetero-polysaccharides: Complex structure, easy to understand

Heteropolysaccharides are polysaccharides consisting of at least two different monosaccharides.

They are further categorized as follows:

1. Mucopolysaccharides
2. Proteoglycans
3. Glycoprotein

Mucopolysaccharides (glycosaminoglycans)

These polysaccharides occur mainly in the extracellular matrix and support it through their extraordinary water-binding capacity. **Hyaluronic acid**, used by the cosmetics industry, is such a mucopolysaccharide and is supposed to fill in wrinkles with its water-binding characteristics and thereby smooth the skin.

Proteoglycans

Proteoglycans are basically glycosaminoglycans that are covalently bound to a protein (**core protein**), thereby organizing the saccharide chains and preventing them from scattering about without any structure in the extracellular matrix. The proportion of saccharides is higher in relation to the proteins.

Glycoproteins

Glycoproteins are saccharides bound to proteins. Their proportion is smaller in relation to the proteins. The attachment of the oligosaccharides to a protein is called glycosylation, which is a post-translational modification mainly taking place in the Golgi apparatus. Almost all blood cells are glycosylated, except for albumin. Therefore, glycoproteins have different tasks such as immune defense in the form of immunoglobulins.

Glycolipids

In addition to bonds between individual carbohydrates, carbohydrates can also form bonds with other biomolecules. *Glycolipid* means a carbohydrate that has been attached to a lipid; this lipid is designated beneath the carbohydrate. For example, in a molecule such as the one in the figure on the right, on the top, there is glucose, drawn in the axial equatorial form and that glucose is linked in the alpha position to a molecule that is a diacylglycerol.

Diacylglycerol is related to fat. Normally, if this were fat, this would have a glycerol

backbone that would be the three carbons and each carbon would be attached to a fatty acid. Such a molecule could exist, for example, in the membrane of a cell.

Glycoglycerolipids exist, but they are not very common. A much more common glycolipid is that of the sphingolipid.

Sphingolipids

Sphingolipids are related in structure to glycoglycerolipids, but they are not the same: the glycoglycerolipid has a glycerol backbone that consists of three carbons. The sphingolipid has a backbone that is a bit different: On the right side of the molecule, part of this backbone includes the N, the carbon that is bonded above it, and then the CH₂, which is bonded to the glucose at the very top.

This backbone is common to sphingolipids. In contrast to the glycerolipid diacylglycerol, these sphingolipids have only one fatty acid and another molecule attached to that. This looks like a fatty acid known as sphingosine.

In the third position at the very top is glucose, a combination of glucose and sphingolipid that creates cerebroside. Cerebroside is a very common component of the nerve tissue that was discovered in the brain. Whenever a simple carbohydrate such as glucose, in this case, is attached, a cerebroside is formed.

However, if a more complex carbohydrate is attached at the very top, you get a ganglioside.

Peptidoglycans

Another interesting group of modified saccharides is peptidoglycans. Peptidoglycans, as the name suggests, are long polymers of carbohydrate residues; they are modified carbohydrates that are presented with a repeating disaccharide. These components are linked to short peptides, in the case of the bacterial cell wall. The peptides are linked to only contain four amino acids.

The other repeating disaccharide is N-acetylglucosamine. When laying it out, the linkage makes a mesh or a network. There are long polymers running diagonally from the upper left to the lower right; those polymers and those diagonals contain the repeating glycan structure of N-acetylglucosamine and N-acetylmuramic acid. Perpendicular to those are the tetrapeptides that are interacting with each other.

Those tetrapeptides are interesting for two reasons: One is that the tetrapeptides contain within them at least one amino acid in the D configuration, which almost never happens in nature or by accident. The other reason is that this is an example of how bacteria have used chemistry to their advantage.

Proteases are enzymes that break down proteins; enzymes that would break down peptides will not work on D amino acids. They are designed to work on L amino acids. So this is a defense mechanism that has evolved over the years to protect the bacteria's cell walls from being degraded.

Bacteria do not get the last word in this overall scheme, though, and the reason for this relates to the antibiotic penicillin. Penicillin kills bacteria for a very important reason: It stops the bacterial cell wall from being assembled. Bacteria that cannot make a cell wall go on to divide and bacteria that cannot divide are doomed to die.

Easy distinction in exams

Proteoglycans: more carbohydrates than proteins; no branched-out chain

Glycoproteins: fewer carbohydrates than proteins; branched-out chain

This basic information establishes the foundation to understand the metabolism of carbohydrates.

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Notes