

جامعة الملك سعود
King Saud University

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

King Saud University
College of Science
Department of Biochemistry

General Biochemistry (BCH 202)

Chapter 3
Carbohydrates


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| Topic | No of Weeks | Lectures |
|--|-------------|----------|
| Carbohydrates: function and classification: - Simple sugar, monosaccharides structure (Types and classification), - Functional groups - Stereochemistry and optical Activity, - Solubility, epimers, cyclic structure, anomers, - reducing vs nonreducing sugars - monosaccharide derivatives. - Functions of glucose, fructose and galactose - Reactions of simple sugars (oxidation-reduction, esterification and phosphorylation) - Amino derivatives | 1 | 2-4 |
| Glycosidic bonds (types and structure) - structure of disaccharides (e.g. maltose, lactose, sucrose), - structure of trisaccharides - oligosaccharides: - polysaccharides: classification, structure and Function. Storage polysaccharides: starch, glycogen Structural Polysaccharides: cellulose, chitin, | 1-33 | 5-8 |
| Functional polysaccharides: glycosaminoglycans and heparin. Glycoproteins and their functions: adhesion immunology, recognition Introduction to sugar metabolism | 1-33 | 9-12 |

CARBOHYDRATES

Carbohydrates are the most abundant biomolecules on Earth.

It is synthesized by plants through the process known as photosynthesis which converts more than 100 billion metric tons of CO₂ and H₂O per year into cellulose and other plant products.

Carbohydrates are polyhydroxy aldehydes or ketones, or substances that yield such compounds on hydrolysis. 

The simplest form is called monosaccharides.

Many, **but not all**, monosaccharides have the empirical formula (CH₂O)_n or C_n(H₂O)_n where $n \geq 3$; some also contain nitrogen, phosphorus, or sulfur.

Biological significance of carbohydrates

- 1- It represents 50-60% of most human food and 0.6% of his weight.
- 2- It is important rapid source of energy (4.2 Cal/g).
- 3- It can act as storage of energy in plants in the form of starch and less frequently in mammals as glycogen.
- 4- It can act as structural components of many organisms (supporting function in plants as cellulose).
- 5- It can be cell-membrane components mediating intercellular communication.
- 6- It can be cell-surface antigens (it participates in recognition and adhesion between cells).
- 7- It can be part of the body's extracellular ground substance (carbohydrate polymers lubricate skeletal joints).
- 8- It can be associated with other biological macromolecules like proteins and lipids to form glycoproteins and glycolipids, respectively.
- 9- It forms part of nucleic acids (ribose and deoxyribose in RNA and DNA, respect-)
- 10- It forms part of several coenzymes (like NAD⁺, NADP⁺, FAD, CoA).

There are three major size classes of carbohydrates:

- monosaccharides,
- oligosaccharides, and
- polysaccharides

(the word “saccharide” is derived from the Greek *sakcharon*, meaning “sugar”).

Monosaccharides, or simple sugars, consist of a single polyhydroxy aldehyde or ketone unit.

The most abundant monosaccharide in nature is the six-carbon sugar D-glucose, sometimes referred to as dextrose.

Monosaccharides of more than four carbons tend to have **cyclic structures**.

Examples of monosaccharides are glucose, fructose, mannose, ribose, etc.

Notice, all common monosaccharides end with the **suffix “-ose.”**

Oligosaccharides consist of short chains of monosaccharide units (2-20 units or residues), joined by characteristic linkages called **glycosidic bonds**.

The most abundant are the **disaccharides**, with two monosaccharide units.

Like monosaccharides, all disaccharides have names ending with the suffix “-ose.”

In cells, most oligosaccharides do not occur as free entities but are joined to nonsugar molecules (lipids or proteins) in glycol-conjugates.

Polysaccharides are sugar polymers containing more than 20 or so monosaccharide units, and some have hundreds or thousands of units.

Some polysaccharides, such as cellulose, are linear chains; others, such as glycogen and starch, are branched.

Both glycogen and cellulose consist of repeated units of D-glucose, but they differ in the type of **glycosidic linkage** and consequently have strikingly different properties and biological roles.

Quiz

Q1: An unknown substance containing only C, H, and O was isolated from goose liver. A 0.423 g sample produced 0.620 g of CO₂ and 0.254 g of H₂O after complete combustion in excess oxygen. Is the empirical formula of this substance consistent with its being a carbohydrate? Explain.

Ans1: Yes, it could be carbohydrate

Explanation:

Calculate the g of C in 0.620 g CO₂

$$0.620 \times (12.011/44.010) = 0.1692 \text{ g C}$$

Calculate the g of H in 0.254 g of H₂O

$$0.254 \times (2.01588 / 18.01528) = 0.02842 \text{ g H}$$

Calculate the g of O by difference

$$0.423 \text{ g} - 0.1692 - 0.0284 = 0.225 \text{ g O}$$

Calculate moles ratios of C, H, and O

$$0.1692 \text{ g C} / 12.011 = 0.01409 \text{ mole C}$$

$$0.02842 \text{ g H} / 1.0079 = 0.02820 \text{ mole H}$$

$$0.225 \text{ g O} / 15.9994 = 0.01406 \text{ mole O}$$

Normalize to 1 mole of O

$$\text{C} = 0.01409 / 0.01406 = 1$$

$$\text{H} = 0.02820 / 0.01406 = 2$$

$$\text{O} = 0.01406 / 0.01406 = 1$$

The ration is 1:2:1 (C:H:O) So, CH₂O, it could be carbohydrate

Lehninger, Principles of Biochemistry, 4th ed.

Ask yourself

- هل بوسعي عمل الواجبات بالسرعة الواجبة حسب ما هو محدد في الاسئلة؟
- هل بوسعي حلّ الأسئلة المتعلقة بواجبات ومهام التعلّم الموكلة لي؟
- هل لديّ المقدرة على صياغة حلول لمشكلات تتعلّق بالمقرّر؟

Monosaccharides

Monosaccharides are colorless, crystalline solids that are freely soluble in water but insoluble in nonpolar solvents.

Most have a sweet taste.

Are they hydrophobic or hydrophilic?
Give reason.

The backbones of common monosaccharide molecules are **unbranched** carbon chains in which all the **carbon-carbon atoms are linked by single bonds**.

It can be found in open-chain form or in cyclic form

In the open-chain form,

- one of the carbon atoms is double-bonded to an oxygen atom to form a **carbonyl group**;
- each of the other carbon atoms has a hydroxyl group.

What is the structure of carbonyl group?

So, **monosaccharides can be found** in the form of aldehydes or ketones

If the carbonyl group is at an end of the carbon chain (that is, in an aldehyde form) the monosaccharide is called **aldose**;

If the carbonyl group is at any other position (in a ketone form) the monosaccharide is called **ketose**.

Monosaccharides (Cont.)

Monosaccharides are named by:

Prefix of the **Latin number** of the carbon atoms forming the sugar + the suffix **-ose**

| Arabic number | Latin | sugar | |
|---------------|--------------|--------------------|--------------------|
| 3 | Tri- | AldoTriose | KetoTriose |
| 4 | Tetr- | AldoTetrose | KetoTetrose |
| 5 | Pent- | AldoPentose | KetoPentose |
| 6 | Hex- | AldoHexose | KetoHexose |
| 7 | Hept- | AldoHeptose | KetoHeptose |
| 8 | Oct- | AldoOctose | KetoOctose |

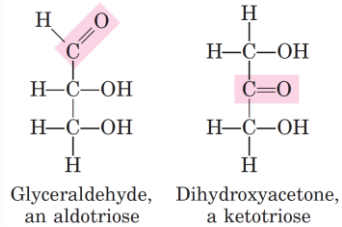
Notice, you can find two forms of monosaccharides having the same number of carbon atoms (aldose and ketose)

Monosaccharides (Cont.)

- The simplest monosaccharides is trioses having 3 carbons.

Two trioses are present; glyceraldehyde and dihydroxyacetone.

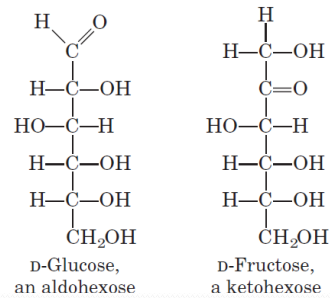
Notice, Both can be written $C_3H_6O_3$ or $(CH_2O)_3$
One is aldotriose and the other is ketotriose.



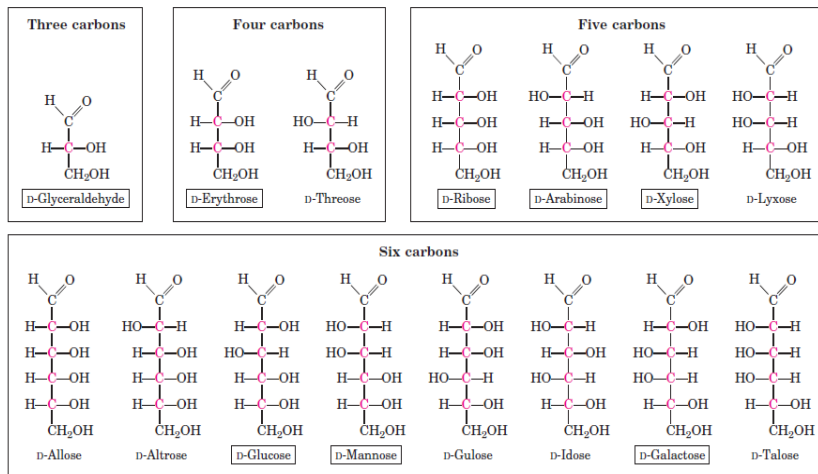
- Monosaccharides having 6 carbons are glucose and fructose.

Notice, Both can be written $C_6H_{12}O_6$ or $(CH_2O)_6$
One is aldohexose and the other is ketohexose.

Notice, Many other aldohexoses and ketohexoses are present



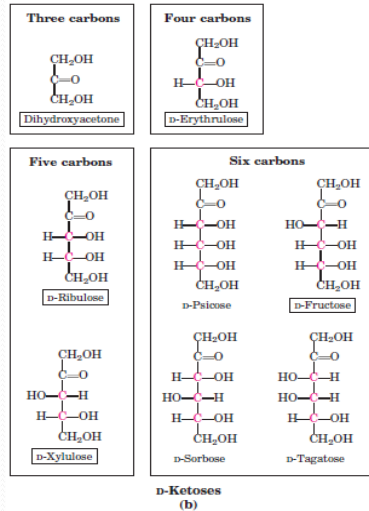
Monosaccharides, Aldoses, opened form (Cont.)



D-Aldoses
(a)

Lehninger, Principles of Biochemistry, 4th ed.

Monosaccharides, *Ketoses opened form (Cont.)*



Write short note about tagatose.

Lehninger, Principles of Biochemistry, 4th ed.

ISOMERISM

Isomers

Compounds with the same molecular formula but having different structures or different orientation.

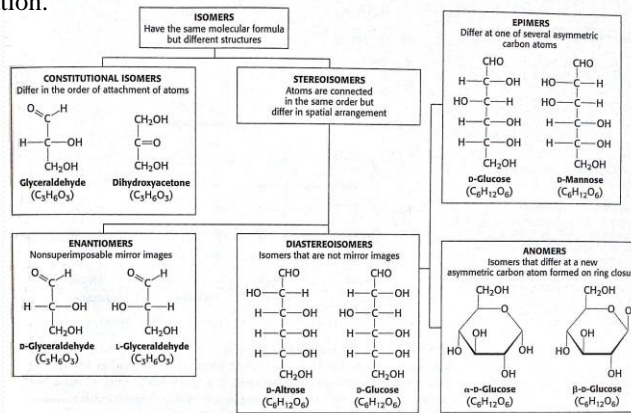


FIGURE 11.1 Isomeric forms of carbohydrates.

Biochemistry, Berg, et al., 8th Ed. (Stryer)

ISOMERISM (cont.)

a- Structure (constitutional) isomers

it can be divided into: functional group isomers and positional isomers

- Functional group isomers

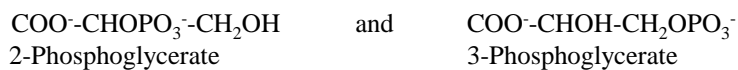
with different functional groups

e.g. glyceraldehyde and dihydroxyacetone (aldehyde and ketone)

- Positional isomers

with substituent groups on different C-atoms

e.g. 2-Phosphoglycerate and 3-Phosphoglycerate



ISOMERISM (cont.)

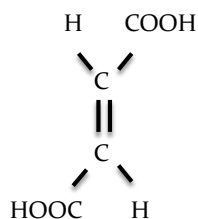
b- Stereoisomers

Compounds with the same molecular formula, functional groups, and position of functional groups but have different conformations.

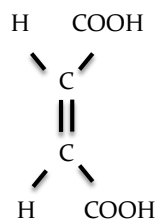
It can be divided into: cis-trans isomers and optical isomers

- cis-trans isomers

Compounds with different conformation around double bonds



Fumaric acid (*trans*)



Maleic acid (*cis*)

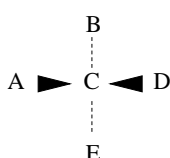
Notice, compounds of this example are not sugar

ISOMERISM (cont).

b- Stereoisomers

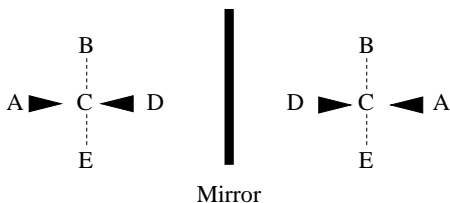
- optical isomers

Compounds with different conformation around chiral or asymmetric carbon atoms



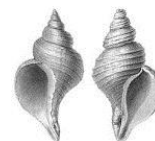
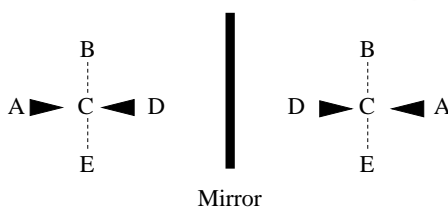
The carbon C is asymmetric if A, B, D, and E are different groups

The four different groups A, B, D, and E can be arranged in space around the C-atom in two different ways to generate two different compounds



The mirror image isomers constitute an *enantiomeric pair*; one member of the pair is said to be the *enantiomer* of the other. The mirror images can't be superimposed on each other, i.e. they are different

ISOMERISM (cont).



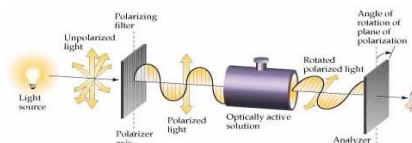
One member of an *enantiomeric pair* will rotate a plane of polarized light in a clockwise direction. It is said to be *dextrorotatory* which is labelled (+)

The other member of the pair will rotate the light in a counterclockwise direction. It is said to be *levorotatory* which is labelled (-).

Remember

Compound with optical activity means it has chiral carbon and it can rotate the plane of polarized light as it travels through it to either right, *dextrorotatory* (clockwise) or to the left, *levorotatory* (anticlockwise)

Do you know the meaning of polarized light and optical activity?



In general, a molecule with n chiral centers can have 2^n stereoisomers.

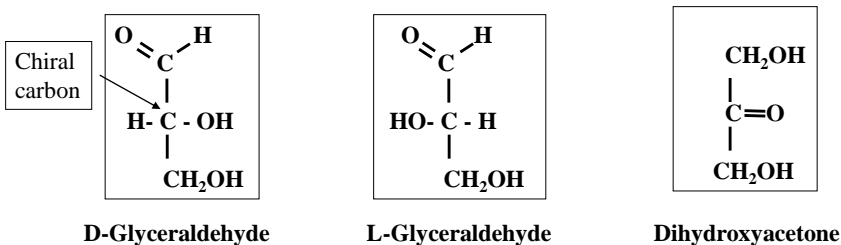
e.g. Glyceraldehyde has $2^1 = 2$;

Aldohexoses, with four chiral centers, have $2^4 = 16$ stereoisomers.

| Number of carbon atoms | Number of | | Number of optical isomers (2^n) |
|------------------------|---------------|-----------------------|-------------------------------------|
| | Aldose/Ketose | asymmetric carbon (n) | |
| 3 | Aldose | 1 | 2 |
| 4 | Aldose | 2 | 4 |
| 5 | Aldose | 3 | 8 |
| 6 | Aldose | 4 | 16 |
| | | | |
| 3 | Ketose | 0 | -- |
| 4 | Ketose | 1 | 2 |
| 5 | Ketose | 2 | 4 |
| 6 | Ketose | 3 | 8 |

- Glyceraldehyde is used as a reference for optical isomers because it is the simplest monosaccharide with an asymmetric carbon.

Q1



D-Glyceraldehyde is the isomer that has the hydroxyl group on the **RIGHT** when the aldehyde group is at the top in a Fischer projection formula.

It is also dextrorotatory, so it is also **D(+)-Glyceraldehyde**

L-Glyceraldehyde is the isomer that has the hydroxyl group on the **LEFT** when the aldehyde group is at the top in a Fischer projection formula.

It is also levorotatory, so it is also **L(-)-Glyceraldehyde**

Dihydroxyacetone has only one form. **It does not have D nor L form .**

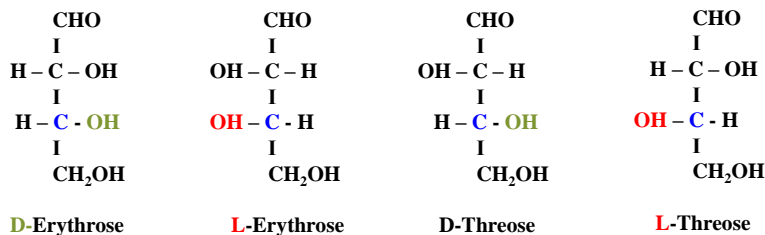
Explain why?

Q2

enantiomers

D & L designate absolute configuration of the asymmetric carbon atom **farthest** from the aldehyde or ketone group.

Notice: enantiomers are two isomers of the same sugar



The 6-C aldoses have 4 asymmetric centers. Thus there are **16 stereoisomers** (8 D-sugars and 8 L-sugars).

Most naturally occurring sugars are D isomers.

Calculate the number of stereoisomers of glucose and name them?

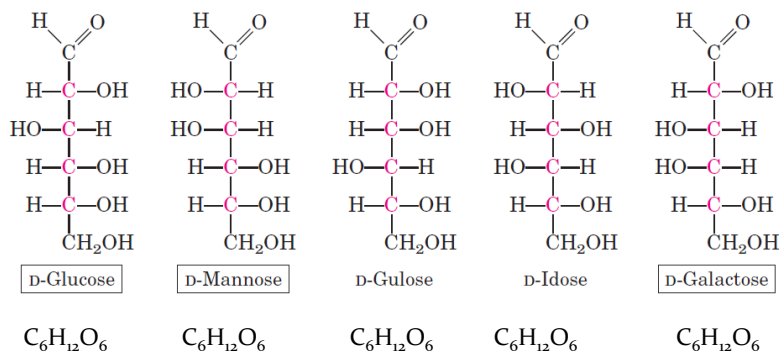
Ask yourself

- هل تساعد التسهيلات المتوافرة في بيئة التعلّم على إنجاز أنشطة التعلّم؟
- هل أستمتع بالتعلّم مع زملائي في هذا المقرّر؟
- هل أشعر بالرضا عن مصادر التعلّم (مواد المقرّر، الكتب، مساعدات التعلّم، إلخ ...) المتوفرة لدعم نشاطاتي في التعلّم؟

Enantiomers vs diastereomers

Optical isomers that are not enantiomers are *diastereomers*

Diastereomers are pairs of stereoisomers that are **not** mirror images of each other.



Lehninger, Principles of Biochemistry, 4th ed.

Diastereomers vs Epimers

Epimers are types of diastereomers that differ by their configuration on a single asymmetric carbon.

Ex. D-glucose and D-mannose, are epimers differ only in the stereochemistry at C-2.

Ex. D-glucose and D-galactose are also epimers at C-4

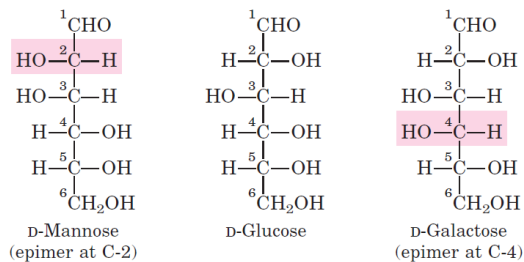
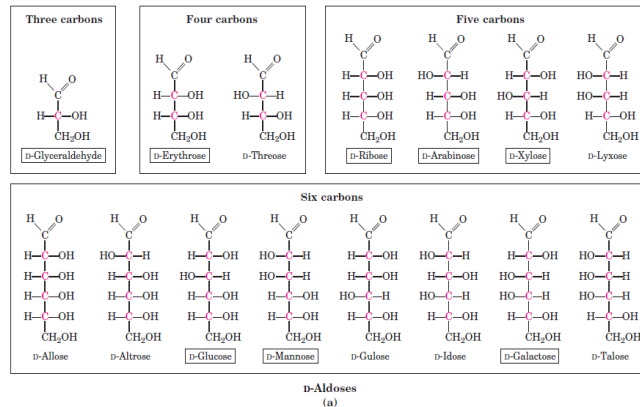


FIGURE 7-4 Epimers. D-Glucose and two of its epimers are shown as projection formulas. Each epimer differs from D-glucose in the configuration at one chiral center (shaded red).

Lehninger, Principles of Biochemistry, 4th ed.

Quiz

- Q2: Explain the meaning of epimer and identify the epimers of (a) D-allose, (b) D-gulose, and (c) D-ribose at C-2, C-3, and C-4 in the Fig.



- Ans: Epimers differ by the configuration about only one carbon.
- (a) D-altrose (C-2), D-glucose (C-3), D-gulose (C-4)
- (b) D-idose (C-2), D-galactose (C-3), D-allose (C-4)
- (c) D-arabinose (C-2), D-xylose (C-3)

ISOMERISM (cont.)

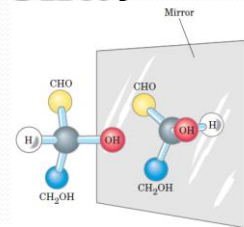
Three ways to represent the two stereoisomers of glyceraldehyde.

- **Ball and stick models** show the actual configuration of molecules.

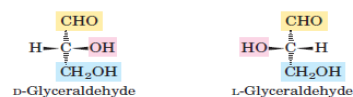
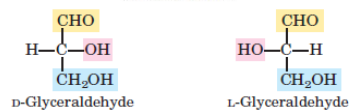
- **Fischer projection formulas**, horizontal bonds project out of the plane of the paper, toward the reader; vertical bonds project behind the plane of the paper, away from the reader.

The chiral carbon presents at the intersection of vertical and horizontal lines

- **Perspective formula** solid wedge-shaped bonds point toward the reader, dashed wedges point away.



Ball-and-stick models



Lehninger, Principles of Biochemistry, 4th ed.

Monosaccharides (Cont.)

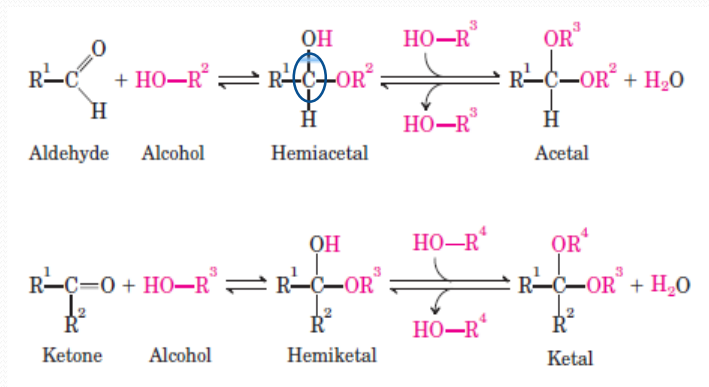
The Common Monosaccharides Have Cyclic Structures

In fact, in aqueous solution, aldotetroses and all monosaccharides with five or more carbon atoms in the backbone occur predominantly as **cyclic (ring)** structures in which the **carbonyl group has formed a covalent bond** with the oxygen of a hydroxyl group along the chain.

The formation of these ring structures is the result of a general reaction between **alcoholic OH** and the **carbonyl group of the aldehydes or ketones** to form derivatives called **hemiacetals or hemiketals**, respectively.

This results in the formation of an additional asymmetric carbon atom and thus can exist in two stereoisomeric forms (α and β).

Formation of hemiacetals and hemiketals.



- An aldehyde or ketone can react with an alcohol to form a hemiacetal or hemiketal, respectively, creating a **new chiral center** at the carbonyl carbon.
- Substitution of a second alcohol molecule produces an acetal or ketal.
- When the second alcohol is part of another sugar molecule, the bond produced is a **glycosidic bond**.

Anomers

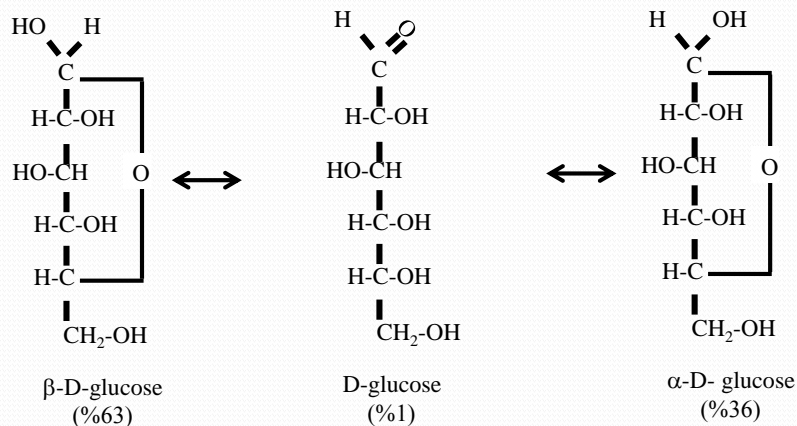
Formation of the two cyclic forms of D-glucose Alpha (α) versus Beta (β) form

- **Anomers** are isomeric forms of **the same** monosaccharide that differ only in their configuration about the hemiacetal or hemiketal carbon atom.
- The hemiacetal carbon atom (or carbonyl) is called the **anomeric carbon**.
- For example, D-glucose exists in solution as an intramolecular **hemiacetal** in which the free hydroxyl group at C-5 has reacted with the aldehydic C-1, rendering the latter carbon asymmetric and producing two anomers designated as **α** and **β** .

Formation of the two cyclic forms of D-glucose

Mutarotation is the interconversion of α - and β - anomers when polarized light is passed through an aqueous solution of the monosaccharide to reach equilibrium.

Q₁

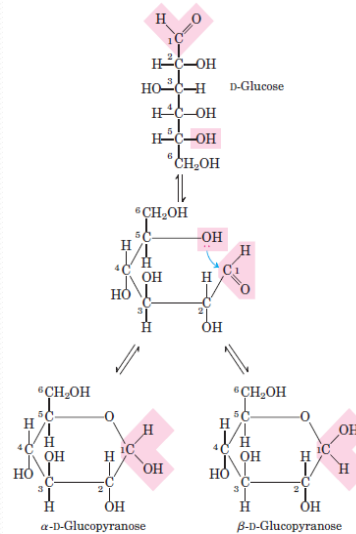


Formation of the two cyclic forms of D-glucose (Haworth perspective formulas)

Reaction between the aldehyde group at C-1 and the hydroxyl group at C-5 forms a **hemiacetal** linkage, producing either of two stereoisomers, the α and β anomers, which differ only in the stereochemistry around the hemiacetal carbon.

These six-membered ring compounds are called **pyranoses** because they resemble the six membered ring compound pyran.

The systematic names for the two ring forms of D-glucose are α -D-glucopyranose and β -D-glucopyranose.



Lehninger, Principles of Biochemistry, 4th ed.

Pyranoses versus furanoses (Haworth perspective form) and Chair conformation

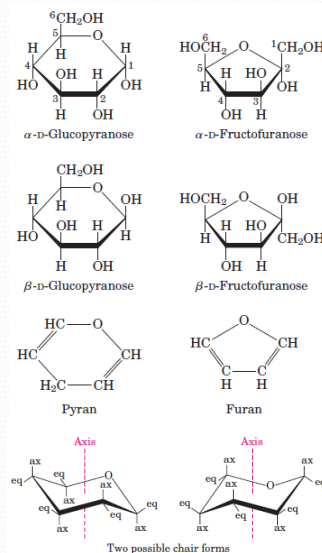
Like glucose (aldohexose), fructose (ketohexose) forms ring structure.

Reaction between the ketone group at C-2 and the hydroxyl group at C-5 forms a hemiketal linkage, producing the α and β anomers of fructose, which differ only in the stereochemistry around the hemiketal carbon (C2).

In Haworth perspective formulas of glucose and fructose, the edges of the ring nearest the reader are represented by bold lines.

Surprisingly, fructose form both pyranose and furanose rings.

Although the Haworth perspective form is commonly used in biochemistry, the six-membered pyranose ring is not planar, as Haworth perspectives suggest, but tends to assume either of two "chair" conformations.



Quiz

Remember:

Enantiomers and anomers:

are two forms of the *same* sugar D/L and α/β , respectively)

Epimers:

are isomers two different sugars

- Indicate whether each of the following pairs of sugars consists of
- A- anomers,
- B- epimers,
- C- aldose-ketose pair:
- () D-glyceraldehyde and dihydroxyacetone
- () D-glucose and D-mannose
- () D-glucose and D-fructose
- () α -D-glucose and β -D-glucose
- () D-ribose and D-ribulose
- () D-galactose and D-glucose

Stryer

Quiz (to be covered in the practical)

Q1

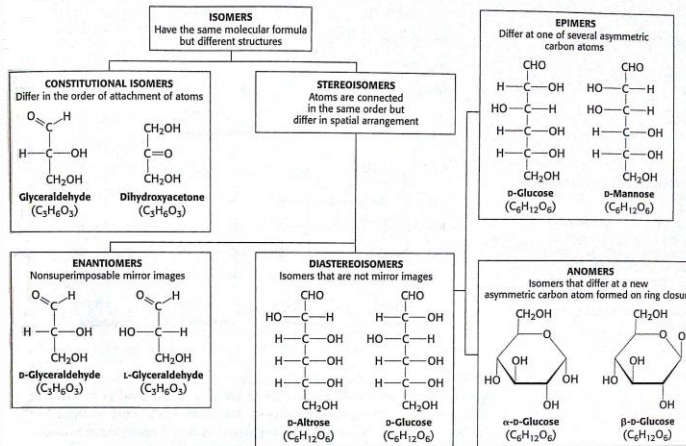
- The specific rotations of the α and β anomers of D-glucose are +112 degrees and +19 degrees, respectively.
- Specific rotation, $[\alpha]_D$, is defined as the observed rotation of light of wavelength 589 nm (the D line of a sodium lamp) passing through 10 cm of a 1 g ml⁻¹ solution of a sample.
- When a crystalline sample of α -D-glucopyranose is dissolved in water, the specific rotation decreases from 112 degrees to an equilibrium value of 52.5 degrees.
- On the basis of this result, what are the proportions of the α and β anomers at equilibrium? Assume that the concentration of the open-chain form is negligible.
- Percentage of D-Glucose?
- Specific Rotation at Equilibrium = +52.5
Specific Rotation of alpha Glucose = +112
Specific Rotation of beta Glucose = +19
Calculate the percentage of each of the two forms of D-Glucose present at equilibrium.

Answer:

- 19 beta (100% beta) = 0 % alpha
- 112 (100 % alpha) = 0% beta
- Hence 112 - 19 = 93
at equilibrium 52.5 represent alpha + beta
- Alpha at equilibrium = 52.5 - 19 = 33.5
- 93 alpha \rightarrow 100
- 33.5 \rightarrow ?
- 33.5 x 100/93 = 36.02 % alpha glucose
- 100-36 = 64% beta anomer

Stryer

Summary: Types of isomers of carbohydrates



Biochemistry, Berg, et al., 8th Ed. (Stryer)

FIGURE 11.1 Isomeric forms of carbohydrates.

Solubility of carbohydrates

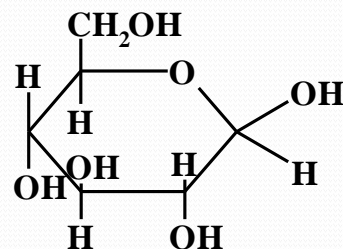
- In a common monosaccharide, most carbon atoms have a hydroxyl group attached. This accounts for their high solubility in water: the hydroxyl groups are very polar and prone to hydrogen bonding.
- As a rule:
 - If something has hydrogen bonding its an extreme form of polar bonds as well as vanderwaals forces.
 - Water is a polar compound that also has hydrogen bonding.
 - So if you have hydrogen bonding you have a polar compound which will be soluble in water.
- All monosaccharides are soluble in water
- Smaller sugars are more soluble in water than larger ones.
- Oligosaccharides are less soluble than monosaccharides.
- Polysaccharides like starch and glycogen are slightly soluble or nearly insoluble although they have too many –OH groups because of their high molecular weight.

Examples of monosaccharides

<https://quizlet.com/7700478/biochem3-carbsglycobio-flash-cards/>
<https://quizlet.com/86700718/biochemistry-exam-3-carbs-flash-cards/>
<https://quizlet.com/101806993/biochemistry-exam-3-carbs-pt-2-flash-cards/>

Glucose

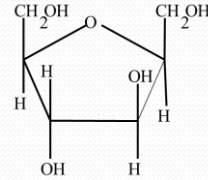
- The main source of energy
- Binds to other sugars to give disaccharides, oligo and poly saccharides
- It is also hexose, glucopyranose
- It is called Dextrose
- (dextro-rotatory) +52.5 (this value represents the mix of α and β at equilibrium)
- i.e it rotates the route of polarized light to the right by 52.5 degree
- It is reducing sugar
- It is called also grape sugar



β -D-Glucose

Fructose

- It is Keto hexose
- The most sweet sugar
- It is called levulose (levo rotatory) -92.3
- It is reducing sugar
- It is called also fruit sugar
- It binds to glucose to give sucrose
- Surprisingly, *fructose form both pyranose and furanose rings.*
- The pyranose form predominantly found when fructose is free in solution while furanose is predominant in many fructose derivatives.
- β -D-Fructopyranose, found in honey, is one of the sweetest chemicals known.
- The β -D-Fructofuranose form isn't nearly as sweet.
- Heating converts β -pyranose into β -furanose form, reducing sweetness.
- For this reason, corn syrup with high concentration of fructose in β -D-pyranose form is used as sweetener in cold drinks but not in hot drinks.



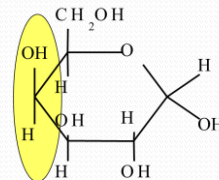
α -D-Fructose

Fructose of highest sweet taste is the form of

- a- β -D-Fructofuranose b- β -D-Fructopyranose c- α -D-Fructofuranose d- α -D-Fructopyranose

Galactose

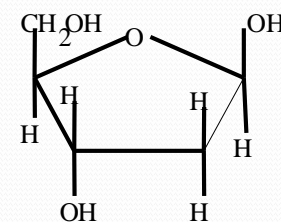
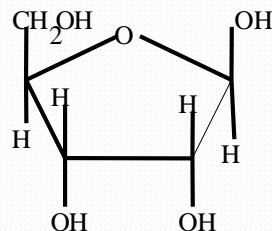
- It does not found free in nature
- Binds to glucose to give lactose
- It is also hexose
- It is reducing sugar
- It is epimer to glucose at C-4
- Galactose can be converted in the cell into glucose to be used for energy production.
- It has an important role in *cell communication*.
- It is also synthesized by the body and *forms part of glycolipids* (carbohydrates-containing lipids), *glycoproteins* (carbohydrates-containing proteins) and *galactolipids* that occur in the brain and other tissues of most animals.



α -D-Galactose

Ribose

- The sugar in the nucleic acid
- Aldo pentose
- Also, it forms part of some enzyme's cofactors
- The DNA contains the deoxy form of ribose, *lack of Oxygen in position C2*
- The RNA contains the normal form of ribose
- It is reducing sugar

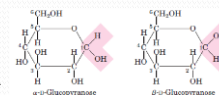


Quiz (to be covered in the practical)

- 4. Interconversion of D-Glucose Forms A solution of one enantiomer of a given monosaccharide rotates plane-polarized light to the left (counterclockwise) and is called the levorotatory isomer, designated (-); the other enantiomer rotates plane-polarized light to the same extent but to the right (clockwise) and is called the dextrorotatory isomer, designated (+).
- An equimolar mixture of the (-) and (+) forms does not rotate plane-polarized light.
- The optical activity of a stereoisomer is expressed quantitatively by its optical rotation, the number of degrees by which plane-polarized light is rotated on passage through a given path length of a solution of the compound at a given concentration.
- The specific rotation $[\alpha]_D^{25^\circ\text{C}}$ of an optically active compound is defined thus:

$$[\alpha]_D^{25^\circ\text{C}} = \frac{\text{observed optical rotation } (^\circ)}{\text{optical path length (dm)} \times \text{concentration (g/mL)}}$$

- The temperature (t) and the wavelength of the light (λ) employed (usually, as here, the D line of sodium, 589 nm) must be specified.
- A freshly prepared solution of α -D-glucose shows a specific rotation of 150.7° .
- Over time, the rotation of the solution gradually decreases and reaches an equilibrium value corresponding to 80.2° .
- In contrast, a freshly prepared solution of β -D-glucose has a specific rotation of 52.8° .
- The rotation of this solution increases over time to the same equilibrium value as that shown by the α anomer.
- (a) Draw the Haworth perspective formulas of the α and β forms of D-glucose. What feature distinguishes the two forms?
- (b) Why does the specific rotation of a freshly prepared solution of the α form gradually decrease with time? Why do solutions of the α and β forms reach the same specific rotation at equilibrium?
- (c) Calculate the percentage of each of the two forms of D-glucose present at equilibrium.



- Answer (a)
- The α and β forms of D-glucose differ only at the hemiacetal carbon (C-1; the anomeric carbon).

- (b) A fresh solution of the α form of glucose undergoes mutarotation to an equilibrium mixture containing both the α and β forms. The same applies to a fresh solution of the β form.

- (c) The change in specific rotation of a solution in changing from 100% α form (150.7°) to 100% β form (52.8°) is 97.9° .
- For an equilibrium mixture having 80.2° , the fraction of D-glucose in the α form is

$$\frac{80.2^\circ - 52.8^\circ}{150.7^\circ - 52.8^\circ} = \frac{27.4^\circ}{97.9^\circ} = 0.279 \approx 28\%$$

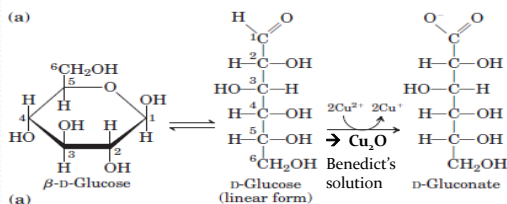
Reactions of simple sugars

- The anomeric carbon can react with alcohol, nitrogen of amine or phosphate to form glycosidic bond
- Other carbons in the sugar backbone can react phosphate or with amine to form sugar Phosphate or sugar amine, respectively.
- These modifications give the carbohydrate more characteristics enabling them to serve as signal molecules or facilitate the metabolism of the carbohydrate.
- **So, we can divide the reaction of sugar into:**
 - Oxidation-reduction (required for monosaccharide metabolic breakdown)
 - Esterification, Phosphorylation (reaction with alcohol, production of phosphate esters)
 - Amino derivatives (used to produce structural components)
 - Glycoside formation (linkage of monosaccharides to form oligo- and polysaccharides)

<https://www.youtube.com/watch?v=iuW3nk5EADg>

Reducing vs nonreducing sugars

- The hemiacetal linkage is weak and can be dissociated to give the open form.
- This process makes the carbonyl group available to reduce mild oxidizing agent such as ferric (Fe^{+3}) or cupric (Cu^{+2}) ion and the *carbonyl carbon* is oxidized to a *carboxyl group* plus ferrous (Fe^{+2}) or cuprous (Cu^{+}).
- This property is the basis of Fehling's reaction, a test for the presence of reducing sugar.
- By measuring the amount of oxidizing agent reduced by a solution of a sugar, we estimate the concentration of that sugar.
- **Sugars with a free or potentially free aldehyde or ketone group (hemiacetal or hemiketal) have reducing properties and are called *reducing sugars*.**
- So, all monosaccharides are reducing sugars.
- In case of converting **all** the hemiacetal or hemiketal linkage to the strong acetal or ketal, the sugar loses the reducing ability and is called nonreducing sugar.



- Oxidation of aldoses (using Fehling reagent)

The presence of the **hydrogen atom in the aldehyde group** gives reducing properties to the aldehyde molecule.

Aldehydes are easily oxidized by mild oxidizing agents such as Fehling's reagent to carboxylic acids

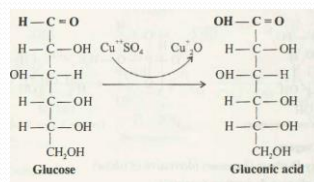
Thus, aldoses are reducing agents.

Any sugar that has a free aldehyde group is referred to as a reducing sugar.

The product name is made by changing the -ose ending to -onic acid (-onate)

Glucose → gluconic acid or gluconate

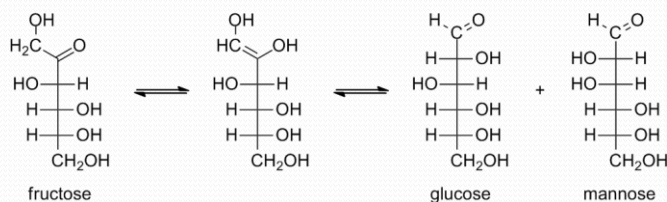
Tests for reducing sugars: Fehling's reaction [Cu(II) → Cu(I)]



<https://www.youtube.com/watch?v=iuW3nk5EADg>

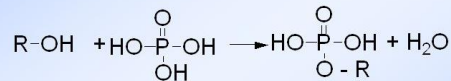
- Oxidation of ketoses (using Fehling reagent)

- Ketones do not have such reducing properties of the aldehyde group due to the lack of H attached to C=O and are not oxidized under similar conditions.
- **BUT**, fructose reduces such reagents even though it contains no aldehyde group.
- Reduction occurs because **the reagents are basic solutions** and fructose is readily isomerized to a mixture of aldoses (glucose and mannose) under basic conditions.



2-Esterification

The most important biological esters of carbohydrates are **phosphate esters**. In the cell, phosphate esters are produced **NOT** by using the very acidic phosphoric acid, but most often by transfer of phosphate group from **ATP** to carbohydrate hydroxyl group, a reaction catalyzed by enzymes called **kinases**.

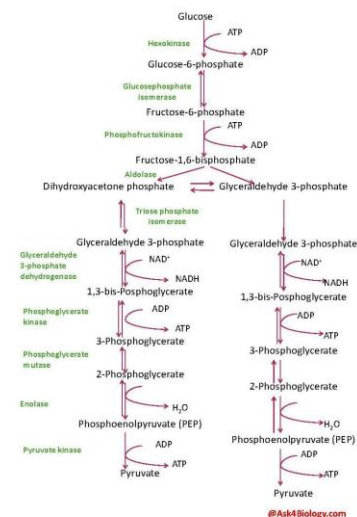


Example. Phosphoryl group from ATP forms an ester with D-glucose, catalyzed by kinases.



2-Esterification-Phosphorylation

- The addition of phosphoryl groups is common in sugar metabolism.
- Glucose is converted in the glycolysis pathway to glucose 6-phosphate, which undergoes a series of reactions, all of them contain phosphate groups including fructose 6-phosphate, Fructose 1,6-bisphosphate, Glyceraldehyde 3-phosphate, Dihydroxyacetone phosphate, 6-Phosphoglycerate and Phosphoenolpyruvate.
- Phosphorylation makes sugars **anionic**, **negative charge** prevents sugars from spontaneously leaving the cell by crossing lipid-bilayer membranes. Creates reactive intermediates that will more readily form linkages to other molecules.



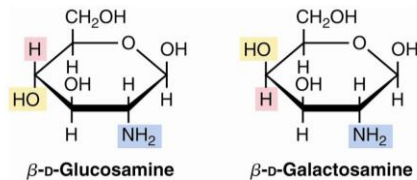
3- Amino derivatives

- The replacement of a hydroxyl group on a carbohydrate with amino group results in an amino sugar.

- Uses for amino sugars:**

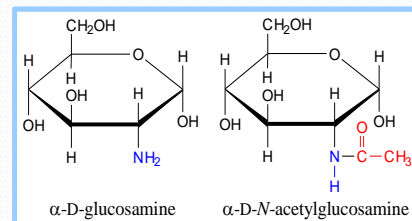
It is used to produce **structural component** in many organisms

- Structural components of bacteria; cell wall.
- A component of chitin, the carbohydrate polymer forming the exoskeleton of insects.
- A major structural unit of chondroitin sulphate, a component of cartilage of vertebrates.
- A component of glycoproteins and glycolipids.



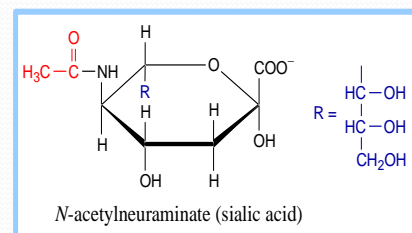
3- Amino derivatives (cont.)

The amino group of glucosamine may be **acetylated**, as in *N*-acetylglucosamine.



N-acetylneuraminate (N-acetylneuraminic acid, also called **sialic acid**) is often found as a *terminal residue* of oligosaccharide chains of glycoproteins.

Sialic acid imparts **negative charge** to glycoproteins, because its carboxyl group tends to dissociate a proton at physiological pH,



4- Glycoside formation

Do you remember the anomeric carbon?

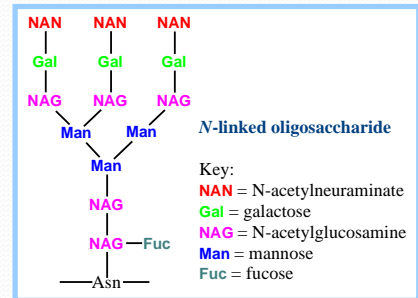
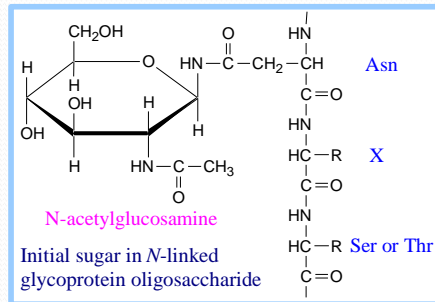
- There are many types of glycosidic bond.
- It is formed between the **anomeric carbon** of a carbohydrate and the oxygen, nitrogen or phosphorous of other compound.
- $$R-OH + HO-R' \rightarrow R-O-R' + H_2O$$
- After glycosidic bond formation, the anomeric carbon involved in bond formation is stabilized and the bond converts to acetal or ketal (strong bond) with no potentially free aldehyde or keto groups.
- Glycosidic bonds between monosaccharides yields oligo- and polysaccharides.
- The glycosidic bond has *direction and orientation* and could affect the reducing character of the sugar (see the disaccharides coming next lecture).

Glycosylation Reaction

- There are several types of glycosylation, although the first two are the most common.
 - **In N-glycosylation**, sugars are attached to nitrogen, typically on the amide side-chain of asparagine.
 - **In O-glycosylation**, sugars are attached to oxygen, typically on serine or threonine but also on non-canonical amino acids such as hydroxylysine & hydroxyproline. Also bond between monosaccharides to form oligosaccharides and polysaccharides is o-glycosylation.
 - **In P-glycosylation**, sugars are attached to phosphorus on a phosphoserine.
 - **In C-glycosylation**, sugars are attached directly to carbon, such as in the addition of mannose to tryptophan.
 - **In glypiation**, is the covalent bond of **G**lycosyl **P**hosphatidyl **I**nositol (GPI) anchor and is a common post-translational modification that localizes proteins to cell membranes. Glycolipid is attached to the C-terminus of a polypeptide, serving as a membrane anchor.

N-linked glycosylation

Sugar molecules can be attached to asparagine or glutamine by *N*-linked glycosylation



***N*-linked oligosaccharides** of glycoproteins tend to be complex and branched.

First ***N*-acetylglucosamine** is linked to a protein via the side-chain N of an asparagine residue in a ***particular 3-amino acid sequence (-Asn-X-Ser/Thr)***.

Additional monosaccharides are added, and the *N*-linked oligosaccharide chain is modified by removal and addition of residues, to yield a characteristic branched structure

O-linked glycosylation

Oligosaccharides **can bind** to a protein via *O-glycosidic bond* between the sugar residue & the **serine or threonine OH** to form linear or branched chains.

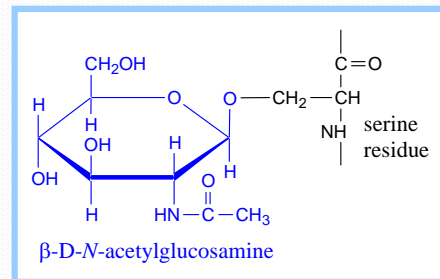
O-linked oligosaccharide chains of glycoproteins vary in complexity.

O-linked oligosaccharides have roles in **recognition, interaction, and enzyme regulation**.

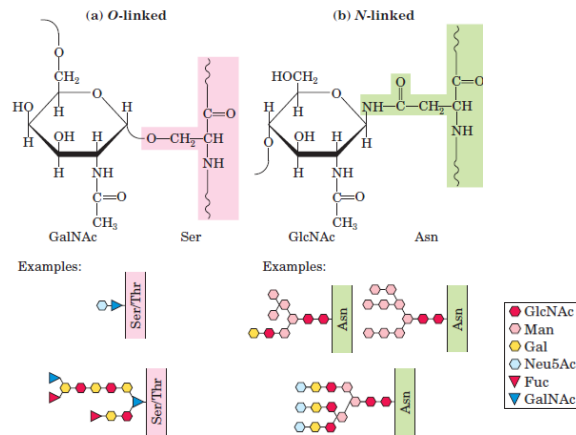
***N*-acetylglucosamine (GlcNAc)** is a common O-linked glycosylation of protein serine or threonine residues.

Many cellular proteins, including enzymes & transcription factors, are **regulated** by reversible GlcNAc attachment.

Often attachment of GlcNAc to a protein OH **alternates with phosphorylation**, with these 2 modifications having opposite regulatory effects (stimulation or inhibition).



O-linked versus N-linked glycosidic bond



Oligosaccharide linkages in glycoproteins.

(a) *O-linked oligosaccharides* have a glycosidic bond to the hydroxyl group of Ser or Thr residues (shaded pink), illustrated here with GalNAc as the sugar at the reducing end of the oligosaccharide. One simple chain and one complex chain are shown.

(b) *N-linked oligosaccharides* have an *N-glycosyl bond* to the amide nitrogen of an Asn residue (shaded green), illustrated here with GlcNAc as the terminal sugar. Three common types of oligosaccharide chains that are *N-linked* in glycoproteins are shown.

What is the difference between glycosides, glycosidic bond, O-glycosidic bond and N-glycosidic bond

- Q1-
- **Glycoside formation**
- Hemiacetals/Hemiketals react with alcohols to form acetal/ketal

O-glycosidic bond

- OH reacts with anomeric C, lose OH and replaced with RO
- O attached to anomeric C
- linkage between 2 sugars
- form of oligo/polysaccharides from these reactions
- Thr and Ser (not Tyr) can be used to make glycoprotein

N-glycosidic bond

- amine (NH) substitutes for OH,
 - N reacts with anomeric C
 - seen in formation of nucleic acids
 - asparagine can be used to make glycoprotein
- N-Glycosides can substitute for hydroxyl groups and react at the anomeric carbon center of carbohydrates
- This linkage is called an N-glycosidic bond .
- This type of bond is of paramount importance in the construction of nucleotides such as ATP and in the nucleic acids RNA and DNA

Glucose in the blood and the glycated hemoglobin

Glucose is the main sugar in our diet and in the body. The normal blood glucose is 70-110 mg%.

Blood glucose reacts with the *N-terminal of the beta chain of the hemoglobin* nonenzymatically.

This glycosylation (glycation) reaction forms a Schiff base which is itself converted to *1-deoxyfructose*.

In diabetic patients, the blood glucose levels are high, glucose molecules attach to the hemoglobin in red blood cells. So, the glycated hemoglobin is higher.

The level of glycated hemoglobin within the red cell, therefore, reflects the average level of glucose to which the cell has been exposed during the RBCs life-cycle (120 days).

So, measuring glycated hemoglobin in the form of plasma glucose concentration assesses the effectiveness of therapy by monitoring long-term serum glucose regulation during 3 months.

| % | HbA _{1c} | eAG (estimated average glucose) | |
|----|-------------------|---------------------------------|---------------|
| | (mmol/mol) | (mmol/L) | (mg/dL) |
| 5 | 31 | 5.4 (4.2-6.7) | 97 (76-120) |
| 6 | 42 | 7.0 (5.5-8.5) | 126 (100-152) |
| 7 | 53 | 8.6 (6.8-10.3) | 154 (123-185) |
| 8 | 64 | 10.2 (8.1-12.1) | 183 (147-217) |
| 9 | 75 | 11.8 (9.4-13.9) | 212 (170-249) |
| 10 | 86 | 13.4 (10.7-15.7) | 240 (193-282) |
| 11 | 97 | 14.9 (12.0-17.5) | 269 (217-314) |
| 12 | 108 | 16.5 (13.3-19.3) | 298 (240-347) |
| 13 | 119 | 18.1 (15-21) | 326 (260-380) |
| 14 | 130 | 19.7 (16-23) | 355 (290-410) |
| 15 | 140 | 21.3 (17-25) | 384 (310-440) |
| 16 | 151 | 22.9 (19-26) | 413 (330-480) |
| 17 | 162 | 24.5 (20-28) | 441 (460-510) |
| 18 | 173 | 26.1 (21-30) | 470 (380-540) |
| 19 | 184 | 27.7 (23-32) | 499 (410-570) |

https://en.wikipedia.org/wiki/Glycated_hemoglobin

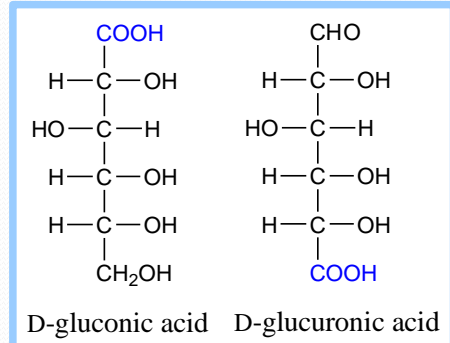
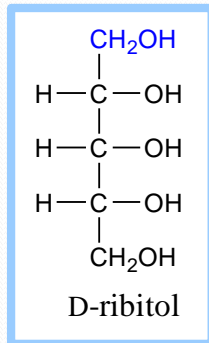
Quiz

Q: In the monosaccharide derivatives known as sugar alcohols, the carbonyl oxygen is reduced to a hydroxyl group. For example, D-glyceraldehyde can be reduced to glycerol. However, this sugar alcohol is no longer designated D or L. Why?

Ans: Because with reduction of the carbonyl oxygen to a hydroxyl group, the stereochemistry at C-1 is the same; and the anomeric carbon is no longer chiral.

<https://quizlet.com/107516204/biochem-chapter-11-flash-cards/>

Sugar derivatives



- ♦ **Sugar alcohol** - lacks an aldehyde or ketone; e.g., **ribitol**.
- ♦ **Sugar acid** - the aldehyde at C1, or OH at C6, is oxidized to a carboxylic acid; e.g., **gluconic acid**, **glucuronic acid**.

Examples of oligosaccharides

<https://quizlet.com/7700478/biochem3-carbsglycobio-flash-cards/>
<https://quizlet.com/86700718/biochemistry-exam-3-carbs-flash-cards/>
<https://quizlet.com/101806993/biochemistry-exam-3-carbs-pt-2-flash-cards/>

Disaccharides Contain a Glycosidic Bond

- Disaccharides (such as maltose, lactose, and sucrose) consist of two monosaccharides joined covalently by an **O-glycosidic** bond, which is formed by dehydration (removal of H₂O), a hydroxyl group of one sugar and hydrogen from OH of other sugar.
- This reaction form an **acetal** from a hemiacetal.
- Glycosidic bonds are readily **hydrolyzed by acid** but **resist cleavage by base**.
- Thus, disaccharides can be hydrolyzed to yield their free monosaccharide components by boiling with dilute acid.

Maltose

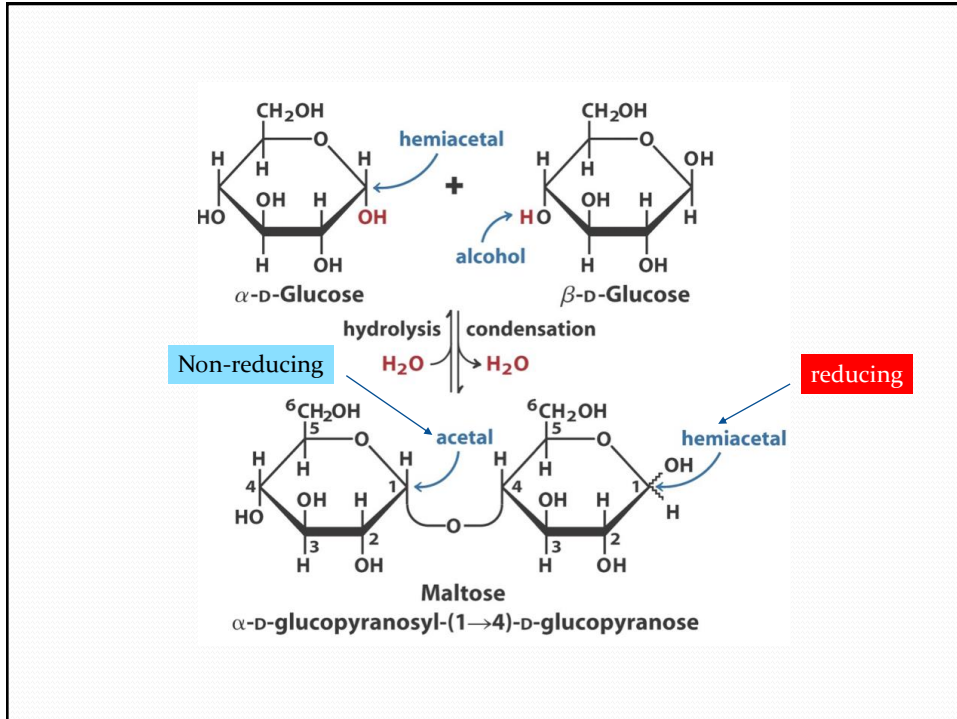
It is also called maltobiose or malt sugar.

The disaccharide **maltose** contains two D-glucose residues joined by a O-glycosidic linkage between C-1 (the anomeric carbon) of one glucose residue and C-4 of the other.

Because the disaccharide retains **ONE** free anomeric carbon **maltose is a reducing sugar**.

The configuration of the anomeric carbon atom in the glycosidic linkage is α -(1 \rightarrow 4).

The glucose residue with the free anomeric carbon is capable of existing in α - and β -pyranose forms.

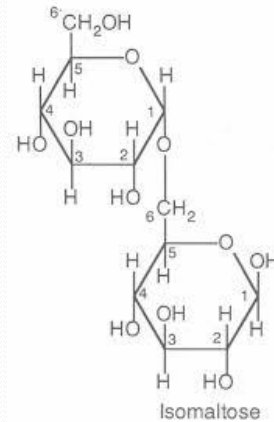


Isomaltose

Two units of glucose bound by α -1 \rightarrow 6 glycosidic bond.

Because the disaccharide retains **ONE** free anomeric carbon **isomaltose is a reducing sugar**.

It is produced by the hydrolysis of glycogen or amylopectin.



Lactose

It is also called milk sugar.

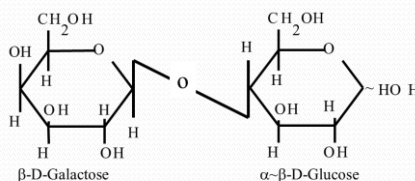
It is composed of galactose and glucose linked by is β -(1 \rightarrow 4) glycosidic bond.

So, *galactose* lose its reducing ability because the hemiacetal is converted to acetal bond, while the anomeric carbon of the *glucose* residue is available for oxidation and retains its reducing potential.

Thus **lactose is a reducing disaccharide**.

Its abbreviated name is Gal(1 \rightarrow 4)Glc.

How you can define the reducing ability from the sugar name without looking for the chemical structure?



Sucrose

Sucrose (table sugar or cane sugar) is a disaccharide of glucose and fructose.

It is formed by plants but not by animals.

In contrast to maltose and lactose, **sucrose contains no free anomeric carbon atom**;

the anomeric carbons of both monosaccharide units are involved in the glycosidic bond (α , β 1 \rightarrow 2).

So, sucrose is therefore a **non-reducing sugar**.

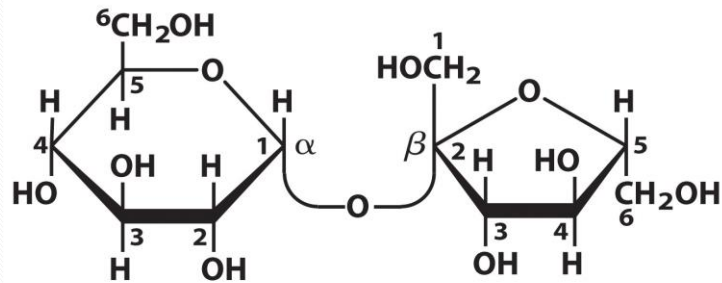
Explain why sucrose is nonreducing while maltose is reducing sugar?

-The hydrolysis of sucrose by acid makes the following changes:

- It gives glucose and fructose. So, it is more sweet,
- It changes from non-reducing to reducing,
- The optical rotation changes from right to left (+52.5, -92.3 for glu and fru, respectively)
- It is called invert sugar

What are the changes that appear on sucrose when treated with acid and heating?

- The full name of sucrose is α -D-glucopyranosyl-(1 \rightarrow 2)- β -D-fructopyranose).



Sucrose

α -D-glucopyranosyl β -D-fructofuranoside
 Glc(α 1 \leftrightarrow 2 β)Fru

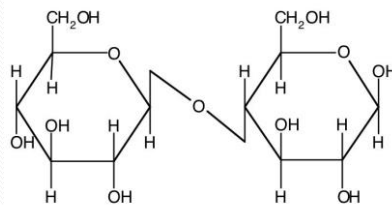
Compare and contrast between sucrose, maltose and lactose?

Cellulose

Two units of glucose bound by β -1 \rightarrow 4 glycosidic bond.

Because the disaccharide retains **ONE** free anomeric carbon
 cellulose is a reducing sugar.

It is produced by the hydrolysis of cellulose.



Quiz

1-Which of the following is non-reducing sugar?

A- Glucose

B- sucrose

C- maltose

D- galactose

2-An example of ketohexose is

A- Fructose

B- glucose

C- lactose

D- sucrose

3-Glucose is

A- aldohexose

B- dextrose

C- Grape sugar

D- all of the above

4-We can find the acetal bond in

A- All mono saccharides

B- disaccharides

C- polypeptide

D- protein

5-The bond between the sugars of maltose is

A- $\beta(1 \rightarrow 4)$

B- $\alpha(1 \rightarrow 4)$

C- $\beta(1 \rightarrow 6)$

D- hydrogen bond

6-The molecular formula $C_5H_{10}O_5$ could be of

A- ribose

B- fructose

C- tetrose

D- sucrose

7- Sucrose is formed from and

A- 2 Glucose

B- Glucose + fructose

C- Glucose + galactose

D- ribose + Glucose

8- The glycosidic bond between the sugarse of lactose is

A- $\beta(1 \rightarrow 4)$

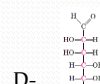
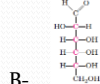
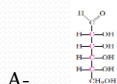
B- $\alpha(1 \rightarrow 4)$

C- $\beta(1 \rightarrow 6)$

D- hydrogen bond

Quiz

1-Circle the structure of glucose



2-The following compound is

A- Monosaccharide

B- dipeptide

C- disaccharide

D- non of the above



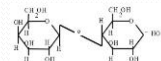
3-The following structure represents

A- sucrose

B- lactose

C- maltose

D- mannose



4-The sugars lactose, maltose and sucrose all belong to which category of carbohydrates?

A- Monosaccharides

B- Disaccharides

C- oligosaccharides

D- polysaccharide

Quiz

- **How many different oligosaccharides can be made by linking one glucose, one mannose, and one galactose? Assume that each sugar is in its pyranose form. Compare this number with the number of tripeptides that can be made from three different amino acids.**
- Three amino acids can be linked by peptide bonds in only six different ways. However, three different monosaccharides can be linked in a plethora of ways.
 - - linear or branched manner,
 - - α or β linkages,
 - - with bonds between C-1 and C-3, between C-1 and C-4, between C-1 and C-6, and so forth.
- Consequently, the number of possible trisaccharides greatly exceeds the number of tripeptides.

Stryer

Quiz

Q: A disaccharide, which you know to be either maltose or sucrose, is treated with Fehling's solution, and a red color is formed. Which sugar is it, and how do you know?

Ans: Maltose is the reducing sugar; sucrose has no reducing (oxidizable) group, as the anomeric carbons of both monosaccharides are involved in the glycosidic bond.

Q: Although lactose exists in two anomeric forms, no anomeric forms of sucrose have been reported. Why?

Ans: Lactose ($\text{Gal}(\beta\ 1\rightarrow4)\text{Glc}$) has a free anomeric carbon (on the glucose residue).
In sucrose ($\text{Glu}(\alpha\ 1\rightarrow2\beta)\text{Fru}$), the anomeric carbons of both monosaccharide units are involved in the glycosidic bond, and the disaccharide has **no free anomeric carbon to undergo mutarotation**.

Quiz

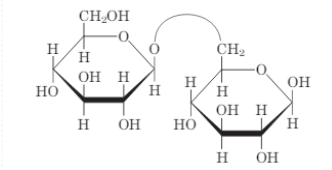
- **Invertase “Inverts” Sucrose** The hydrolysis of sucrose (specific rotation 66.5) yields an equimolar mixture of D-glucose (specific rotation 52.5) and D-fructose (specific rotation -92).
- (a) Suggest a convenient way to determine the rate of hydrolysis of sucrose by an enzyme preparation extracted from the lining of the small intestine.
- (b) Explain why an equimolar mixture of D-glucose and D-fructose formed by hydrolysis of sucrose is called invert sugar in the food industry.
- (c) The enzyme invertase (now commonly called sucrase) is allowed to act on a 10% (0.1 g/mL) solution of sucrose until hydrolysis is complete. What will be the observed optical rotation of the solution in a 10 cm cell? (Ignore a possible small contribution from the enzyme.)
- **Answer**
- (a) An equimolar mixture of D-glucose and D-fructose, such as that formed from sucrose hydrolysis, has optical rotation
- $-52.5 + (-92.0) = -39.5^\circ$.
- Enzyme (sucrase) activity can be assayed by observing the change in optical rotation of a solution of 100% sucrose (specific rotation +66.5 as it is converted to a 1:1 mixture of D-glucose and D-fructose).
- (b) The optical rotation of the hydrolysis mixture is negative (inverted) relative to that of the unhydrolyzed sucrose solution.
- (c) The addition of 1 mol of water (Mr 18) in the hydrolysis of 1 mol of sucrose (Mr 342) gives the products an increase in weight of $(18/342)(100\%) = 5.26\%$ with respect to the starting sugar.
- Accordingly, a 10% sucrose solution yields a $[10 + (0.053 \times 10)]\% = 10.5\%$ solution of invert sugar.
- Of this 10.5%, 5.25% (0.0525 g/mL) is D-glucose and 5.25% is D-fructose.
- By rearranging the equation

$$[\alpha]_D^{25^\circ} = \frac{\text{observed optical rotation } (^\circ)}{\text{optical path length (dm)} \times \text{concentration (g/mL)}}$$

- we can determine the optical rotation of each sugar in the mixture in a 10 cm cell:
- Optical rotation of glucose $\alpha = (52.5^\circ)(1 \text{ dm})(0.0525 \text{ g/mL}) = 2.76^\circ$
- Optical rotation of fructose $\alpha = (92^\circ)(1 \text{ dm})(0.0525 \text{ g/mL}) = -4.8^\circ$.
- The observed optical rotation of the solution is $2.76^\circ + (-4.8^\circ) = -2.0^\circ$.

Quiz

- **Q: Gentiobiose (D-Glu(β1->6)D-Glu) is a disaccharide found in some plant glycosides. Draw the structure of gentiobiose based on its abbreviated name. Is it a reducing sugar? Does it undergo mutarotation?**



- **Ans:** It is a reducing sugar; it undergoes mutarotation.

Examples of Polysaccharides

<https://quizlet.com/7700478/biochem3-carbsglycobio-flash-cards/>
<https://quizlet.com/86700718/biochemistry-exam-3-carbs-flash-cards/>
<https://quizlet.com/101806993/biochemistry-exam-3-carbs-pt-2-flash-cards/>

Polysaccharides

Most carbohydrates found in nature occur as polysaccharides, polymers of medium to high molecular weight.

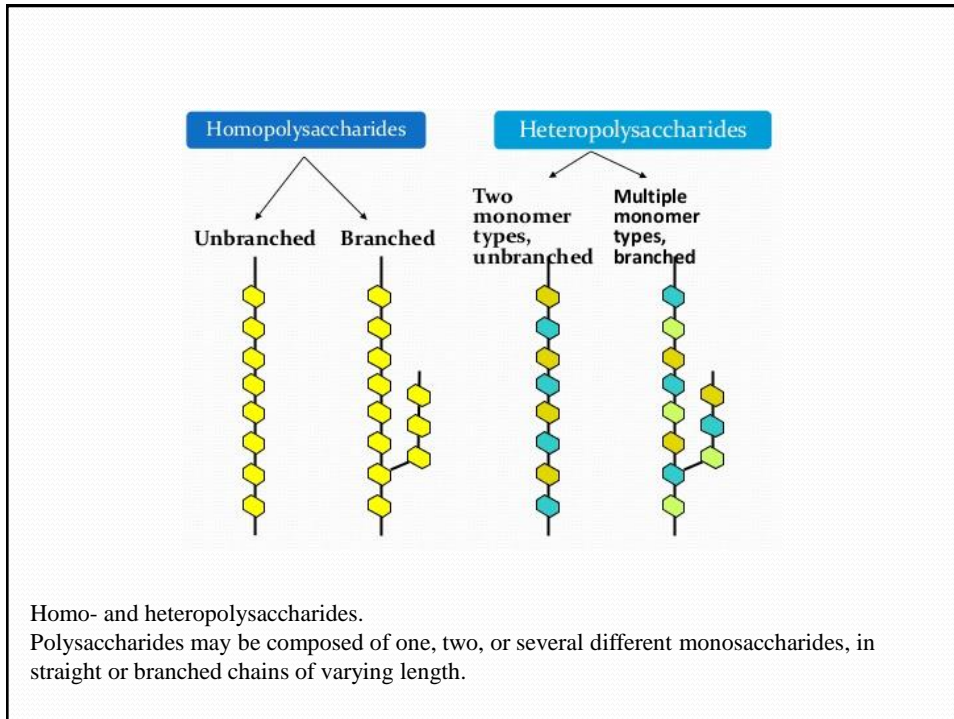
Polysaccharides do NOT have a defined molecular weight (WHY?)

Polysaccharides, also called *glycans*, differ from each other in:

- the identity of their recurring monosaccharide units,
- the length of their chains,
- the orientation of bonds linking the units, and
- the degree of branching.

We can classify them into:

- Homopolysaccharides contain only a single type of monomer;
- Heteropolysaccharides contain two or more different kinds.
- Unlike proteins, there is **NO template** (gene) used to make polysaccharides.



Homopolysaccharides

Some *homopolysaccharides* serve as storage forms of monosaccharides that are used as fuels;

Starch and glycogen are homopolysaccharides of this type.

Other homopolysaccharides (like cellulose and chitin) serve as structural elements in plant cell walls and animal exoskeletons, respectively.

Heteropolysaccharides

It provides *extracellular support* for organisms of all kingdoms. For example, the rigid layer of the bacterial cell envelope (the peptidoglycan) is composed in part of a heteropolysaccharide built from two alternating monosaccharide units.

In animal tissues, the extracellular space is occupied by several types of heteropolysaccharides, which form a matrix that holds individual cells together and provides protection, shape, and support to cells, tissues, and organs.

Homopolysaccharides

The most important storage polysaccharides are **starch** in plant cells and **glycogen** in animal cells.

Both polysaccharides occur intracellularly as large clusters or granules.

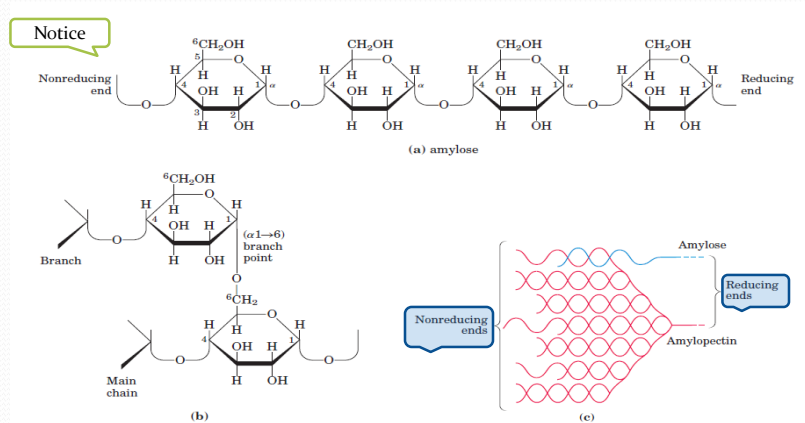
Starch and glycogen molecules are heavily hydrated, because they have many exposed hydroxyl groups available to hydrogen-bond with water.

Most plant cells have the ability to form starch, but it is especially abundant in tubers, such as potatoes, and in seeds.

Starch

- **Glucose** is not stored in plant cell because of its high solubility.
- Alternatively, it is polymerized in the form of starch granules that have different forms depending on the plant source.
- **Starch:** contains two types of glucose polymers (homopolysaccharide), amylose and amylopectin.
 - **Amylose** consists of long, **unbranched** chains of D-glucose residues connected by (α 1 \rightarrow 4) linkages. Such chains vary in molecular weight from a few thousands to more than a million. It takes a helical shape with about **6 glucose residues per turn**.
 - **Amylopectin** also has a high molecular weight (up to 100 million Dalton) but unlike amylose is **highly branched**.
- The glycosidic linkages joining successive glucose residues in amylopectin chains are (α 1 \rightarrow 4); the branch points (**occurring every 24 to 30 residues**) are (α 1 \rightarrow 6) linkages.

Starch (cont.)



Amylose and amylopectin, the polysaccharides of starch.

(a) A short segment of *amylose*, a linear polymer of D-glucose residues in (α 1 \rightarrow 4) linkage. A single chain can contain several thousand glucose residues. *Amylopectin* has stretches of similarly linked residues between branch points.

(b) An (α 1 \rightarrow 6) branch point of amylopectin.

(c) A cluster of amylose and amylopectin like that believed to occur in starch granules. Strands of amylopectin (red) form **double-helical structures** with each other or with amylose strands (blue).

Starch (cont.)

- Starch is non-reducing polysaccharide.
- **Notice**, amylopectin has **one reducing** end and **many non-reducing ends**.
- Although starch has free terminal hemiacetal bond, it is non reducing because this terminus represents very small proportion in comparison to the number of internal acetal bonds of the whole molecule.
- Although starch has too many hydroxyl groups, it is not soluble in water because of its high molecular weight.
- Small quantity of starch can be dissolved with gentle heating.
- Starch is detected by the addition of iodine solution which upon binding with starch turns from yellow to dark blue, as iodine enters the helix of amylose and absorb all colors and reflect the blue. This color disappears by heating because the helix extends and the iodine liberates.

Glycogen

Glycogen is the main storage polysaccharide of animal (up to 120,000 glucose residues).

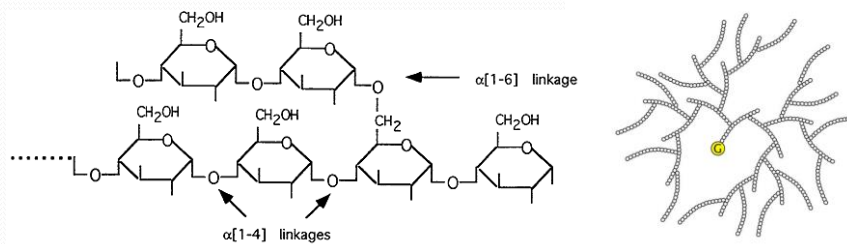
It is similar to amylopectin, a homopolymer of (α 1 \rightarrow 4)-linked subunits of glucose, with (α 1 \rightarrow 6)-linked branches, but glycogen is more extensively branched (on average, **every 8 to 12 residues**) and more compact than starch.

Glycogen is especially abundant in the liver, where it may constitute as much as 7% of the wet weight; it is also present in skeletal muscle (1% of muscle weight). The total amount of muscle glycogen is 3-4 times the quantity in the liver.

In hepatocytes glycogen is found in large granules of several million Daltons (Mwt), which are themselves clusters of smaller granules composed of single, highly branched glycogen molecules with an average molecular weight of several million.

Such glycogen granules also contain, in tightly bound form, the enzymes responsible for the synthesis and degradation of glycogen.

What is the difference between glycogen and glycogenin?
Make a search.....



Glycogen is similar to plant amylopectin have **one reducing end** and **many non-reducing end**.

Glycogen represents the main store of carbohydrate in mammals when person fed carbohydrate rich food.

This store is used only when the concentration of blood glucose fall below 70 mg%. Then glycogen starts to degrade to glucose to compensate the decrease of blood glucose.

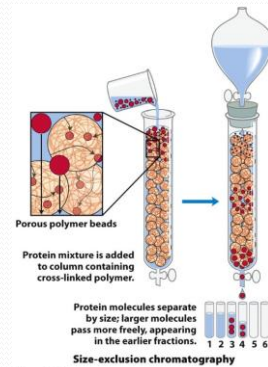
The liver glycogen can be consumed after 12-18 hour of fasting but the muscular lasts longer.

Glycogen gives red color in the iodine test.

Compare and contrast between glycogen and starch?

Dextrans

- Dextrans are bacterial and yeast homopolysaccharides made up of (α 1 \rightarrow 6)-linked poly-D-glucose; all have (α 1 \rightarrow 3) branches, and some also have (α 1 \rightarrow 2) or (α 1 \rightarrow 4) branches.
- Dental plaque, formed by bacteria growing on the surface of teeth, is rich in dextrans.
- Synthetic dextrans are used in several commercial products (for example, Sephadex) that serve in the fractionation of proteins by size-exclusion (gel filtration) chromatography. The dextrans in these products are chemically cross-linked to form insoluble materials of various porosities, to separate the macromolecules depending on their molecular sizes.



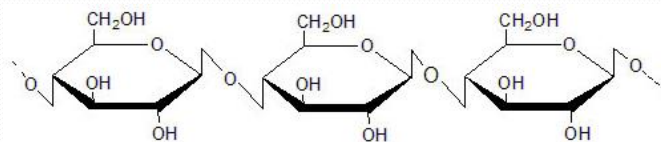
Cellulose

Cellulose, a fibrous, tough, water-insoluble substance, is found in the cell walls of plants, and in all woody portions of the plant.

Cotton is almost pure cellulose.

The cellulose molecule is a linear, **unbranched** homo-polysaccharide, consisting of 10,000 to 15,000 D-glucose units. Cellulose chains bring together by hydrogen bonds.

The glucose residues are linked by β - (1 \rightarrow 4) glycosidic bonds.



Cellulose: β -1,4 glucosidic bonds

The glucose residues in cellulose are linked by (β 1 \rightarrow 4) glycosidic bonds, in contrast to the (α 1 \rightarrow 4) bonds of amylose, starch, and glycogen.

This difference gives cellulose and amylose very different structures and physical properties. Glycogen and starch ingested in the diet are hydrolyzed by α -amylases, enzymes in saliva and intestinal secretions that break α 1 \rightarrow 4 (but not β 1 \rightarrow 4) glycosidic bonds between glucose units.

Most animals cannot use cellulose as an energy source, because they lack the enzyme that hydrolyze the (β 1 \rightarrow 4) linkages.

Termites readily digest cellulose (and therefore wood), because their intestine harbors a symbiotic microorganism, *Trichonympha*, that secretes enzyme called cellulase, which hydrolyzes the (β 1 \rightarrow 4) linkages.

Ruminants have microbes in stomach.

Wood-rot fungi and bacteria also produce cellulase.

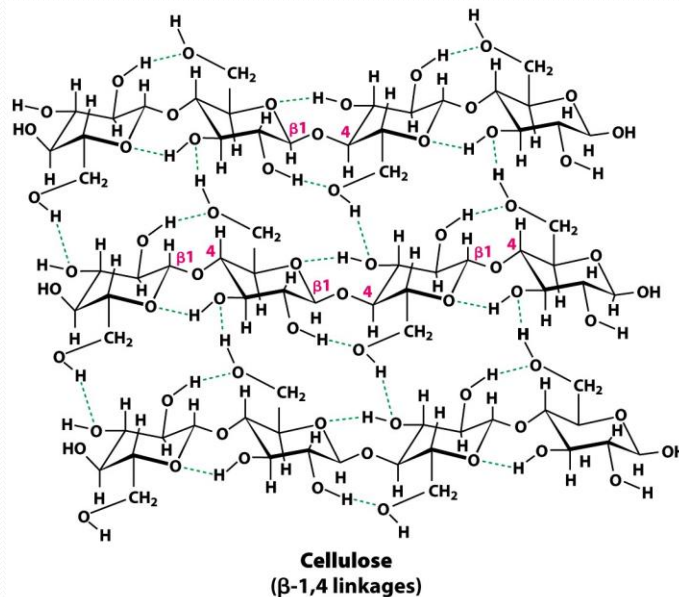


Figure 9.14a
Biochemistry: A Short Course, First Edition
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Chitin

Chitin is a linear homopolysaccharide composed of *N-acetylglucosamine residues* in β 1 \rightarrow 4 linkage.

The only chemical difference from cellulose is the replacement of the hydroxyl group at C-2 with an acetylated amino group.

Chitin forms extended fibers similar to those of cellulose, and like cellulose cannot be digested by vertebrates.

Chitin is the principal component of the hard exoskeletons of million species of arthropods—insects, lobsters, and crabs, for example—and is probably the second most abundant polysaccharide, next to cellulose, in nature.

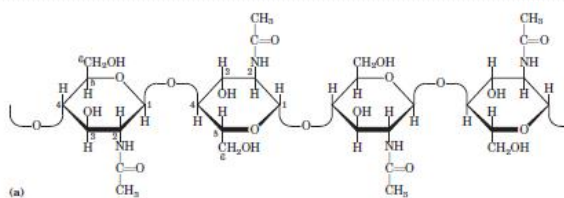
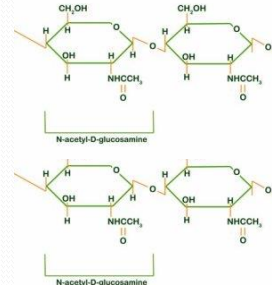


FIGURE 7-18 Chitin. (a) A short segment of chitin, a homopolymer of *N*-acetyl-D-glucosamine units in (β 1 \rightarrow 4) linkage. (b) A spotted June beetle (*Pellodonta punctatata*), showing its surface armor (exoskeleton) of chitin.



Chitin. (a) A short segment of chitin, a homopolymer of *N*-acetyl-D-glucosamine units in (β 1 \rightarrow 4) linkage.

Compare and contrast between cellulose and chitin?

Quiz

1-All of the following are polysaccharides except

A- cellulose.

B- lactose

C- glycogen D- amylopectin

2-Cellulose, $\beta(1\rightarrow4)$ -linked glucose polysaccharide, differs from starch in that starch is

A- $\beta(1\rightarrow6)$ -linked mannose polysaccharide

B- $\alpha(1\rightarrow6)$ -linked glucose polysaccharide.

C- $\alpha(1\rightarrow4)$ -linked glucose polysaccharide.

D- $\beta(1\rightarrow6)$ -linked glucose polysaccharide.

- <https://quizlet.com/144383786/test>

Quiz

- **Q: Physical Properties of Cellulose and Glycogen.**

The almost pure cellulose obtained from the seed threads of *Gossypium* (cotton) is tough, fibrous, and completely insoluble in water.

In contrast, glycogen obtained from muscle or liver disperses readily in hot water to make a turbid solution. Although they have markedly different physical properties, both substances are composed of $(1\rightarrow4)$ -linked D-glucose polymers of comparable molecular weight.

What structural features of these two polysaccharides underlie their different physical properties?

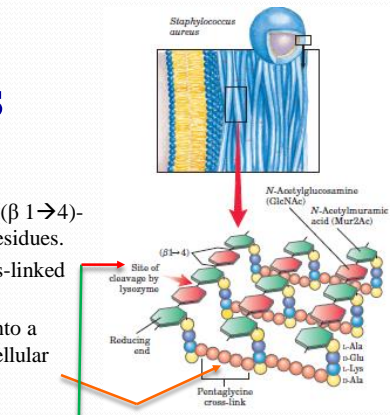
Explain the biological advantages of their respective properties.

Quiz

- **Q:**Cellulose could provide a widely available and cheap form of glucose, but humans cannot digest it. *Why not?*
- **If you were offered a procedure that allowed you to acquire this ability, would you accept? Why or why not?**
- **Ans:** Humans cannot break down cellulose to its monosaccharides because they lack cellulases, a family of enzymes, produced chiefly by fungi, bacteria, and protozoans, that catalyze the hydrolysis of cellulose to glucose.
- In ruminant animals (such as cows and sheep), the rumen (one of four stomach compartments) acts as an anaerobic fermenter in which bacteria and protozoa degrade cellulose, making its glucose available as a nutrient to the animal.
- If cellulase were present in the human digestive tract, we could use foods rich in cellulose as nutrients. This would greatly increase the forms of biomass that could be used for human nutrition. This change might require some changes in the teeth that would allow cellulosic materials to be ground into small pieces to serve as cellulase substrates.

Structural Heteropolysaccharides Bacterial Cell Walls

- The bacterial cell walls is a heteropolymer of alternating (β 1 \rightarrow 4)-linked *N*-acetylglucosamine and *N*-acetylmuramic acid residues.
- The linear polymers lie side by side in the cell wall, cross-linked by short **peptides**.
- The **peptide cross-links** weld the polysaccharide chains into a strong sheath that envelops the entire cell and prevents cellular swelling and lysis due to the osmotic entry of water.
- The enzyme **lysozyme** kills bacteria by hydrolyzing the (β 1 \rightarrow 4) glycosidic bond between *N*-acetylglucosamine and *N*-acetylmuramic acid.
- Lysozyme is notably present in tears, presumably as a defense against bacterial infections of the eye.
- It is also produced by certain bacterial viruses to ensure their release from the host bacterial cell.
- Penicillin and related antibiotics kill bacteria by preventing synthesis of the cross-links, leaving the cell wall too weak to resist osmotic lysis.



Not to be **confused** with
n-acetyl neuraminic acid

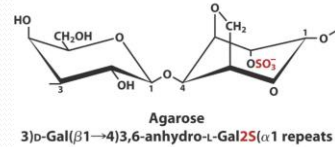
Structural Heteropolysaccharides

Algal Cell Walls

Certain marine red algae have **agar** in its cell walls.

Agar is composed of two major polysaccharides:

- **Agarose**, is unbranched linear polymer ($M_r \sim 120,000$) made up of repeating units of **agarobiose** (a disaccharide made up of D-galactose and 3,6-anhydro-L-galactopyranose bound by $\beta 1 \rightarrow 4$ glycosidic bond in which an ether ring connects C-3 and C-6). These units are joined by $(1 \rightarrow 3)$ glycosidic links to form a polymer 600 to 700 residues long.
- **Agaropectin**, is branched chain **sulphated** polysaccharide composed of alternating units of D-galactose and an L-galactose .



- **Agar and agarose have many applications:**
 - Agar is also used to form a surface for the growth of bacterial colonies.
 - Agar is used for the capsules in which some vitamins and drugs are packaged; the dried agar material dissolves readily in the stomach and is metabolically inert.
 - Agarose has a remarkable gel-forming property when a suspension of agarose in water is heated and cooled. This gel has a three-dimensional structure that traps large amounts of water and it is used in the laboratory for the electrophoretic separation of nucleic acids.

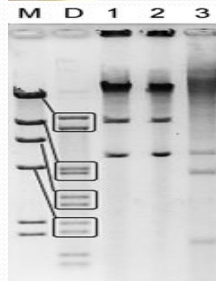
- Agar --- growth of bacterial colonies.



- Agar ---- capsules



- Agarose ----- laboratory for the electrophoretic separation of nucleic acids.



True or false

Agar is a sulfated glycosaminoglycan composed of a chain of alternating sugars
(F) It is not glycosaminoglycan

Conflicting terms

- **Glycosaminoglycans** (mucopolysaccharides) are linear polysaccharides of repeating disaccharides containing amino sugar, either glucosamine or galactosamine
- Polysaccharides containing aminosugars
- **Peptidoglycans** are polysaccharides consisting of sugars and few amino acids.
- Polysaccharides + few amino acids
- **Proteoglycans** are proteins that are heavily glycosylated (95% carbohydrates of the biomolecule by weight). It consists of core protein covalently bound to glycosaminoglycans.
- Protein + polysaccharide in the form of glycosaminoglycans.
- **Glycoproteins** are proteins that contain covalently bound oligosaccharide chains (1-30% carbohydrates).
- Protein + few sugars

Glycosaminoglycans: Anionic polysaccharide chains made of repeating disaccharide units

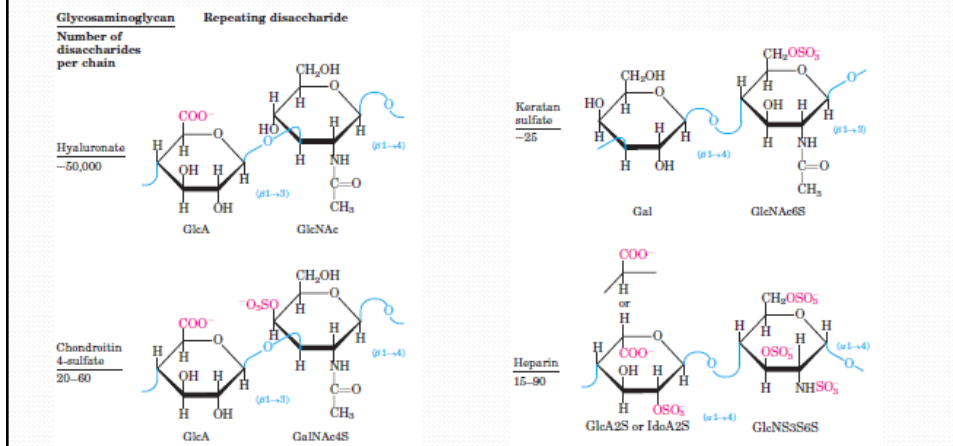
- **Glycosaminoglycans** present on the animal cell surface and in the extracellular matrix.
- Glycosaminoglycans (mucopolysaccharides) are linear polymers of repeating disaccharides units containing a derivative of an amino sugar, either glucosamine or galactosamine
- The constituent monosaccharides tend to be modified, with acidic groups, amino groups, and sulfated hydroxyl etc.
- Glycosaminoglycans tend to be negatively charged. It is large complexes of negatively charged heteropolysaccharide chains. This negative charge comes from the prevalence of acidic groups (carboxylate) or due to the presence of sulfate group.
- The sulfate esters on some of the hydroxyl groups give these polymers a high density of negative charge, forcing them to assume extended conformations.

Glycosaminoglycans:

(cont.)

- So, glycosaminoglycans have the following properties:
 - Can bind large amounts of water
 - Gel-like matrix
 - Viscous, Lubricating
 - Shock absorbing
 - Negatively charged
- Examples: Chondroitin sulfate, keratan sulfate, heparin, dermatan sulfate, and hyaluronate
- Glycosaminoglycans are usually attached with a small (<5%) amount of protein forming proteoglycans

Repeating units of some common glycosaminoglycans of extracellular matrix



Examples of Glycosaminoglycans

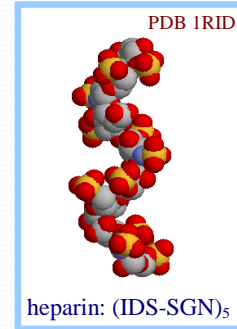
Heparin, is a soluble glycosaminoglycan act as natural anticoagulant and is synthesized in the mast cells in a nonsulfated form, which is then deacetylated and sulfated.

When released into the blood, it inhibits clot formation by interacting with the protein antithrombin.

It has a structure similar to that of heparan sulfates, but is more **highly sulfated**.

Heparin has an **extended helical conformation**.

Heparin shown has 10 residues, alternating IDS (iduronate-2-sulfate) & SGN (N-sulfo-glucosamine-6-sulfate).



Heparin has the highest negative charge density of any known biological macromolecule. The charge repulsion by the many negatively charged groups may contribute to its conformation.

Purified heparin is routinely added to blood samples obtained for clinical analysis, and to blood donated for transfusion, to prevent clotting.

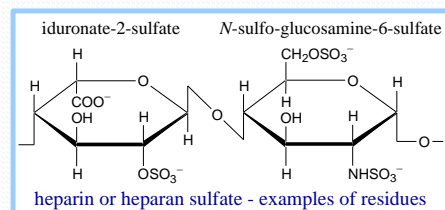
Examples of Glycosaminoglycans Heparan sulfate

Heparan sulfate is initially synthesized on a membrane-embedded core protein as a polymer of alternating **N-acetylglucosamine** and **glucuronate** residues.

Heparan sulfate is like heparin except that it has :

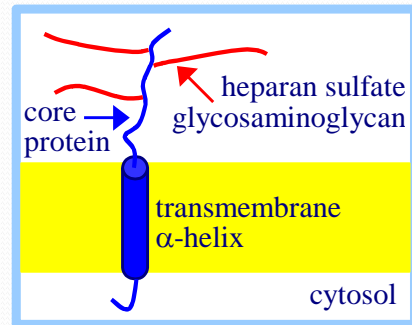
- fewer N- and O-sulfate groups
- more acetyl groups.

Later, in segments of the polymer, glucuronate residues may be converted to the sulfated sugar **iduronic acid**, while N-acetylglucosamine residues may be deacetylated and/or sulfated to give heparin.



Some **cell surface heparan sulfate glycosaminoglycans** remain covalently linked to core proteins embedded in the plasma membrane.

The core protein of a **syndecan** heparan sulfate proteoglycan includes a single **transmembrane α -helix**.



Syndecans are single transmembrane domain proteins that act as co-receptors. These core proteins carry three to five heparan sulfate and chondroitin sulfate chains, which allow for interaction with a large variety of ligands

The core protein of a **glypican** heparan sulfate proteoglycan is attached to the outer surface of the plasma membrane via **covalent linkage to a modified phosphatidylinositol lipid**.

Glypicans constitute one of the two major families of heparan sulfate proteoglycans. They seem to play a vital role in morphogenesis, and have been suggested as regulators for some cell signaling pathways.

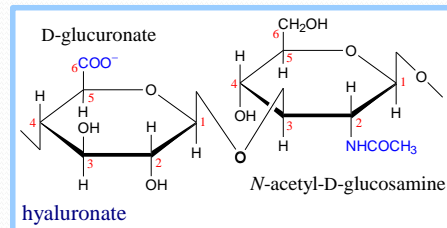
Proteins involved in **signaling & adhesion** at the cell surface recognize & bind heparan sulfate chains.

E.g., binding of some **growth factors** (small proteins) to cell surface receptors is enhanced by their binding also to heparan sulfates.

Regulated cell surface **Sulf** enzymes may **remove sulfate** groups at particular locations on heparan sulfate chains to **alter affinity** for signal proteins, e.g., growth factors.

Examples of Glycosaminoglycans Hyaluronate

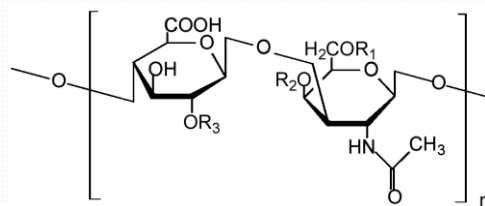
Hyaluronate (*hyaluronan*) is an α -glycosaminoglycan that is found in extracellular tissue space, the synovial fluid of joints, and the vitreous humor of the eyes and acts as a binding, lubricating, and protective agent.



Hyaluronate is a repeating disaccharide consisting of 2 glucose derivatives, glucuronate (glucuronic acid) & *N*-acetyl-glucosamine.

The glycosidic linkages are $\beta(1\rightarrow3)$ & $\beta(1\rightarrow4)$.

Examples of Glycosaminoglycans Chondroitin sulfate



- **Chondroitin sulfate** is unbranched polysaccharides.
- It is a sulfated glycosaminoglycan (GAG) composed of a chain of alternating sugars (N-acetylgalactosamine and glucuronic acid). Typically attached to proteins as part of a proteoglycan.
- It helps with tensile strength of cartilage, tendons, and ligaments.

Peptidoglycan

- Peptidoglycan, also known as **murein**, is a polymer consisting of sugars and amino acids that forms a mesh-like layer outside the plasma membrane of most bacteria, forming the cell wall.
- The sugar component consists of alternating residues of β -(1,4) linked *N*-acetylglucosamine and *N*-acetylmuramic acid.
- Attached to the *N*-acetylmuramic acid is a peptide chain of three to *five amino acids*.
- *In case of Escherichia coli (a Gram-negative bacterium) the amino acids are:*
 - L-alanine, D-glutamic acid, *meso*-diaminopimelic acid, and D-alanine
- *In case of Staphylococcus aureus (a gram-positive bacterium) the amino acids are:*
 - L-alanine, D-glutamine, L-lysine, and D-alanine with a 5-glycine
- The peptidoglycan layer is substantially thicker in gram-positive bacteria (20 to 80 nanometers) than in gram-negative bacteria (7 to 8 nanometers).

Proteoglycans

- **Proteoglycans** are **glycosaminoglycans** that are covalently linked to **serine** residues of specific **core proteins**. The glycosaminoglycan chain is synthesized by sequential addition of sugar residues to the core protein.
 - It resembles polysaccharides more than proteins (heavily glycosylated proteins) in as much as the carbohydrate makes up as much as **95%** of the biomolecule by weight.
 - Proteoglycans function as lubricants and structural components in connective tissue and mediate adhesion of cells to the extracellular matrix.
- Some proteoglycans** of the extracellular matrix **bind** non-covalently to **hyaluronate** via protein domains called **link modules**. e.g.:
- Multiple copies of the **aggrecan** proteoglycan associate with hyaluronate in cartilage to form large complexes.
 - **Versican**, another proteoglycan, binds hyaluronate in the extracellular matrix of loose connective tissues.

Glycoproteins

- Glycoproteins contain less carbohydrate than proteoglycans (1-30%).
- **Glycoproteins** have one or several oligosaccharides of varying complexity joined covalently to a protein.
- They are found inside and outside the cells:
 - Inside cells they are found in specific organelles such as Golgi complexes, secretory granules, and lysosomes.
 - Outside the cell on the outer face of the plasma membrane, in the extracellular matrix, and in the blood.
- The oligosaccharide portions of glycoproteins are rich in information, forming highly specific sites for recognition and high-affinity binding by other proteins.
- Cell-surface molecules are contributed to:
 - antigen determinants
 - mediator of cell-cell interaction
 - attachment sites for viruses

Functions of Glycoproteins

- Glycoproteins have many biological functions:
 - 1- Immunological protection
 - 2- Cell-cell recognition
 - 3- Blood clotting
 - 4- Host-pathogen interaction

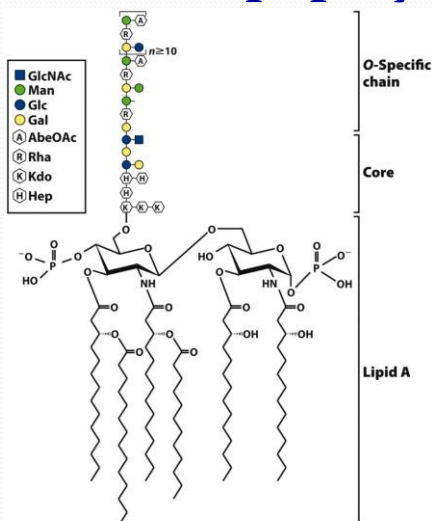
Linkage between sugar and protein part in glycoproteins

- Carbohydrates link through the *anomeric* carbon to:
 - The amide nitrogen in the side chain of *asparagine* (N-glycosidic bond) or
 - The hydroxyl oxygen of *serine or threonine* (O-glycosidic bond)

Lipo-oligo vs lipo-polysaccharides

- The term lipo-oligosaccharide ("LOS") is used to refer to a low-molecular-weight small number of sugar molecules bound to lipid core.
- Lipopolysaccharides (LPS) or lipoglycans are larger molecules consisting of a lipid and a polysaccharide.
- It is composed of outer core and inner core joined by a covalent bond and found in the outer membrane of Gram-negative bacteria.

Lipopolysaccharides

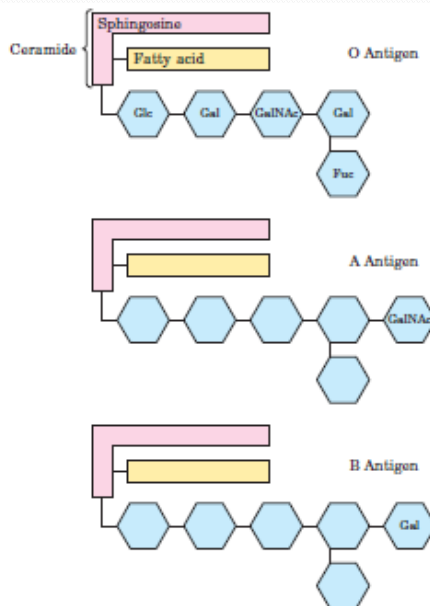


Lipopolysaccharide of
the outer membrane of
the bacterium
Salmonella
typhimurium

Figure 7-31
Lehninger Principles of Biochemistry, Sixth Edition
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The addition of sugar moiety determines the blood group

- Sugars attached to glycoproteins and glycolipids on the surfaces of red blood cells determine the blood group termed A, B, and O.
- The A and B antigens differ from the O antigen by the addition of one extra monosaccharide through an α -1,3 linkage to a galactose moiety of the O antigen
 - *N*-acetylgalactosamine (for A)
 - galactose (for B).
- The addition of *N*-acetylgalactosamine or galactose is mediated by specific enzyme called **glycosyltransferases** which add the extra monosaccharide to the O antigen.
- Each person inherits the gene for one glycosyltransferase of this type from each parent.
 - The type A **glycosyltransferases** specifically adds *N*-acetylgalactosamine,
 - The type B **glycosyltransferases** adds galactose.
 - The O phenotype lack that enzyme due to mutation that leads to premature termination of translation and, hence, it produces inactive glycosyltransferase.



Sugars determining blood groups.

Abbreviations:

Fuc, fucose;

Gal, galactose;

GalNAc, *N*-acetylgalactosamine;

GlcNAc, *N*-acetylglucosamine.

Principles of Biochemistry 4th ed - Lehninger

- **Type A**
 - has lots of sugar bound but there is a different sugar at non-reducing end
 - people have antibodies against B sugars
 - donors (receive blood from): A or O
- **Type B**
 - has lots of sugar bound but there is a different sugar at non-reducing end
 - people have antibodies against A sugars
 - donor (receive blood from): B or O
- **Type AB**
 - mix of both types of sugars as A and B
 - people have no antibodies towards A or B
 - donors (receive blood from): A, B or AB or O
- **Type O**
 - Lack of sugars specific for A and B (lack of terminal *N*-acetylgalactosamine; or terminal galactose)
i.e. missing sugar at non-reducing end
 - people have antibodies towards both A or B
 - donors (receive blood from): O only
 - Universal donor : give blood to all groups (A, B, AB and O)

Quiz

- <https://quizlet.com/56413759/test>

Carbohydrates as informational Molecules: The Sugar Code

Many proteins **secreted** by cells have attached N-linked oligosaccharide chains.

Genetic diseases have been attributed to deficiency of particular enzymes involved in synthesizing or modifying oligosaccharide chains of these glycoproteins.

Such diseases, and **gene knockout studies in mice**, have been used to define pathways of modification of oligosaccharide chains of glycoproteins and glycolipids.

Carbohydrate chains of plasma membrane glycoproteins and glycolipids usually face the **outside of the cell**.

They have roles in cell-cell **interaction** and **signaling**, and in forming a protective layer on the surface of some cells.

Lectins are glycoproteins that **recognize** and **bind** to specific **oligosaccharides**.

Concanavalin A & **wheat germ agglutinin** are plant lectins that have been useful research tools.

The **C-type lectin-like domain** is a **Ca⁺⁺-binding** carbohydrate recognition domain in many **animal lectins**.

Recognition/binding of CHO moieties of glycoproteins, glycolipids & proteoglycans **by** animal **lectins** is a factor in:

- cell-cell recognition
- adhesion of cells to the extracellular matrix
- interaction of cells with chemokines and growth factors
- recognition of disease-causing microorganisms
- initiation and control of inflammation.

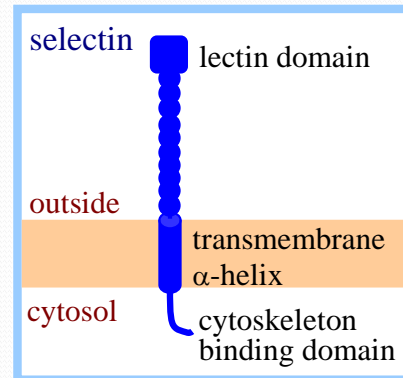
Examples of animal lectins:

Mannan-binding lectin (MBL) is a glycoprotein found in blood plasma.

It binds cell surface carbohydrates of **disease-causing microorganisms** & promotes phagocytosis of these organisms as part of the immune response.

Selectins are integral proteins of mammalian cell plasma membranes with roles in **cell-cell recognition** & binding.

The C-type **lectin-like domain** is at the end of a multi-domain extracellular segment extending out from the cell surface.



A **cleavage site** just outside the transmembrane α -helix provides a mechanism for regulated release of some lectins from the cell surface.

A **cytosolic domain** participates in regulated interaction with the actin cytoskeleton.

Carbohydrate digestion and metabolism

Dietary carbohydrates

- Starch
 - Sucrose
 - Glucose and fructose
 - Lactose
- } Digestible
- Cellulose
 - Other plant polysaccharides
- } Non-digestible
by humans

Only monosaccharides are absorbed into the bloodstream from the gut.

Digestion of carbohydrates involves their hydrolysis into monosaccharides

Digestive Enzymes

Enzymes for carbohydrate digestion

| Enzyme | Source | Substrate | Products |
|-------------------|----------------------------|--------------------------|--------------------|
| α -Amylase | Salivary gland Pancreas | Starch, glycogen | Oligosaccharides |
| Dextrinase | Small intestine | Oligosaccharides | Glucose |
| Isomaltase | Small intestine | α -1,6-glucosides | Glucose |
| Maltase | Small intestine | Maltose | Glucose |
| Lactase | Small intestine | Lactose | Galactose, glucose |
| Sucrase | Small intestine | Sucrose | Fructose, glucose |

Lactase deficiency produces lactose intolerance

Blood glucose concentrations

It can be measured in mmol/L = mM or in mg/dL

Conversion factor: 1 mM = 18 mg/dL

Normal plasma glucose concentrations roughly contains 3.9 – 8.3 mM

Hypoglycemia (low blood glucose): < 2.2 mM

Hyperglycemia ((low blood glucose)or Diabetes: > 7.0 mM (fasting)
> 11.1 mM 2 h after ingestion of 75 g glucose

All cells can use glucose as an energy source
Brain cells and erythrocytes require glucose as an energy source

Quiz

- **Q: Volume of Chondroitin Sulfate in Solution One critical function of chondroitin sulfate is to act as a lubricant in skeletal joints by creating a gel-like medium that is resilient to friction and shock. This function seems to be related to a distinctive property of chondroitin sulfate: the volume occupied by the molecule is much greater in solution than in the dehydrated solid. Why is the volume so much larger in solution?**
- **Ans:** In solution, the negative charges on chondroitin sulfate repel each other and force the molecule into an extended conformation. The polar molecule also attracts many water molecules (water of hydration), further increasing the molecular volume. In the dehydrated solid, each negative charge is counterbalanced by a counterion, such as Na⁺, and the molecule collapses into its condensed form.

Quiz

- **Q: Heparin Interactions** Heparin, a highly negatively charged glycosaminoglycan, is used clinically as an anticoagulant. It acts by binding several plasma proteins, including antithrombin III, an inhibitor of blood clotting. The 1:1 binding of heparin to anti thrombin III seems to cause a conformational change in the protein that greatly increases its ability to inhibit clotting. What amino acid residues of anti-thrombin III are likely to interact with heparin?
- **Ans:** Positively charged amino acid residues would be the best candidates to bind to the highly negatively charged groups on heparin. In fact, Lys residues of anti thrombin III interact with heparin.

Quiz

- **Q: Glucose Oxidase in Determination of Blood Glucose** The enzyme glucose oxidase isolated from the mold *Penicillium notatum* catalyzes the oxidation of β -D-glucose to D-glucono-d-lactone. This enzyme is highly specific for the β anomer of glucose and does not affect the α anomer. In spite of this specificity, the reaction catalyzed by glucose oxidase is commonly used in a clinical assay for total blood glucose—that is, for solutions consisting of a mixture of β - and α -D-glucose. What are the circumstances required to make this possible? Aside from allowing the detection of smaller quantities of glucose, what advantage does glucose oxidase offer over Fehling's reagent for the determination of blood glucose?
- **Ans:** The rate of mutarotation (interconversion of the α and β anomers) is sufficiently high that, as the enzyme consumes β -D-glucose, more α -D-glucose is converted to the β form, and, eventually, all the glucose is oxidized. Glucose oxidase is specific for glucose and does not detect other reducing sugars (such as galactose). Fehling's reagent reacts with any reducing sugar.

Quiz

- Q: As the table shows, certain pairs of derivatives have the same melting points, although the underivatized monosaccharides do not. Why do glucose and mannose, and similarly galactose and talose, form osazone derivatives with the same melting points?

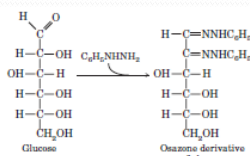
| Monosaccharide | MP of anhydrous monosaccharide (°C) | MP of osazone derivative (°C) |
|----------------|-------------------------------------|-------------------------------|
| Glucose | 146 | 205 |
| Mannose | 132 | 205 |
| Galactose | 165-168 | 201 |
| Talose | 128-130 | 201 |

- Ans: The configuration at C-2 of an aldose is lost in its osazone derivative, so aldoses differing only at the C-2 configuration (C-2 epimers) give the same derivative, with the same melting point. Glucose and mannose are C-2 epimers and thus form the same osazone; the same is true for galactose and talose.

Quiz

Q3: Melting Points of Monosaccharide Osazone Derivatives

Many carbohydrates react with phenylhydrazine (C₆H₅NHNH₂) to form bright yellow crystalline derivatives known as osazones:



The melting temperatures of these derivatives are easily determined and are characteristic for each osazone. This information was used to help identify monosaccharides before the development of HPLC or gas-liquid chromatography.

Listed below are the melting points (MPs) of some aldoseosazone derivatives:

| Monosaccharide | MP of anhydrous monosaccharide (°C) | MP of osazone derivative (°C) |
|----------------|-------------------------------------|-------------------------------|
| Glucose | 146 | 205 |
| Mannose | 132 | 205 |
| Galactose | 165-168 | 201 |
| Talose | 128-130 | 201 |

As the table shows, certain pairs of derivatives have the same melting points, although the underivatized monosaccharides do not. Why do glucose and mannose, and galactose and talose, form osazone derivatives with the same melting points?

Ans: The configuration at C-2 of an aldose is lost in its osazone derivative, so aldoses differing only at the C-2 configuration (C-2 epimers) give the same derivative, with the same melting point.

Glucose and mannose are C-2 epimers and thus form the same osazone; the same is true for galactose and talose (see Fig. 7-3).

Quiz

- **A Taste of Honey:** The fructose in honey is mainly in the -D-pyranose form. This is one of the sweetest carbohydrates known, about twice as sweet as glucose. The -D-furanose form of fructose is much less sweet. The sweetness of honey gradually decreases at a high temperature. Also, high-fructose corn syrup (a commercial product in which much of the glucose in corn syrup is converted to fructose) is used for sweetening *cold* but not *hot* drinks.. Draw the two forms and explain why it may not always be wise to cook with honey.
- Heating converts the very sweet pyranose form to the more stable but less sweet furanose form. Consequently, it is difficult to accurately control the sweetness of the preparation, which also accounts for why honey loses sweetness with time.

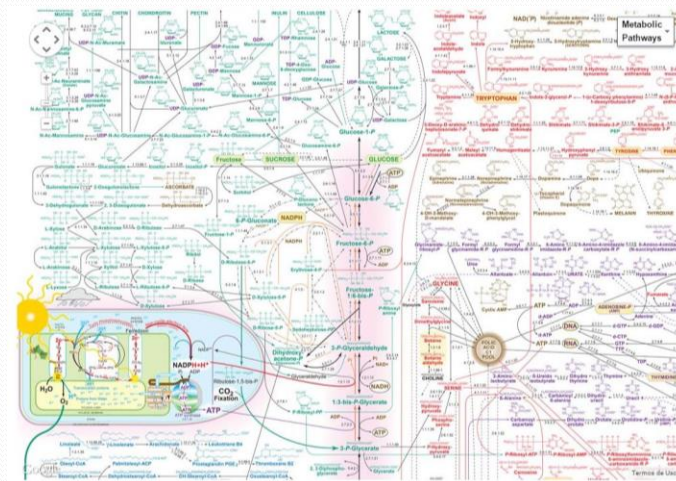
Stryer- Lehninger

Quiz

- **Q: Manufacture of Liquid-Filled Chocolates** The manufacture of chocolates containing a liquid center is an interesting application of enzyme engineering. The flavored liquid center consists largely of an aqueous solution of sugars rich in fructose to provide sweetness. The technical dilemma is the following: the chocolate coating must be prepared by pouring hot melted chocolate over a solid (or almost solid) core, yet the final product must have a liquid, fructose-rich center. Suggest a way to solve this problem. (Hint: Sucrose is much less soluble than a mixture of glucose and fructose.)
- **Ans:** Prepare the core as a semisolid slurry of sucrose and water. Add a small amount of sucrase (invertase), and quickly coat the semisolid mixture with chocolate. After the chocolate coat has cooled and hardened, the sucrase hydrolyzes enough of the sucrose to form a more liquid center: a mixture of fructose, glucose, and sucrose.

- <https://quizlet.com/128350306/test>
- <https://quizlet.com/128350306/lehninger-biochem-ch-7-flash-cards>
- <https://quizlet.com/161793298/test>
- <https://quizlet.com/161793298/c8-carbohydrates-biochemistry-flash-cards/>

Introduction to Carbohydrate metabolism



Some metabolic pathways of carbohydrates

- 1- Glycolysis
- 2- Krebs cycle
- 3- Glycogenesis
- 4- Glycogenolysis
- 5- Glyconeogenesis

- - Pentose Phosphate Pathway (PPP)
- - Curi cycle
- - Biological oxidation

Metabolism

Metabolism involves :

- *Catabolic reactions* that break down large, complex molecules to provide energy and smaller molecules.
- *Anabolic reactions* that use ATP energy to build larger molecules.

Stages of Carbohydrate Metabolism

Stage 1: Digestion and hydrolysis - break down large molecules to smaller ones that enter the bloodstream.

Stage 2: Degradation - breaks down molecules to two- and three-carbon compounds.

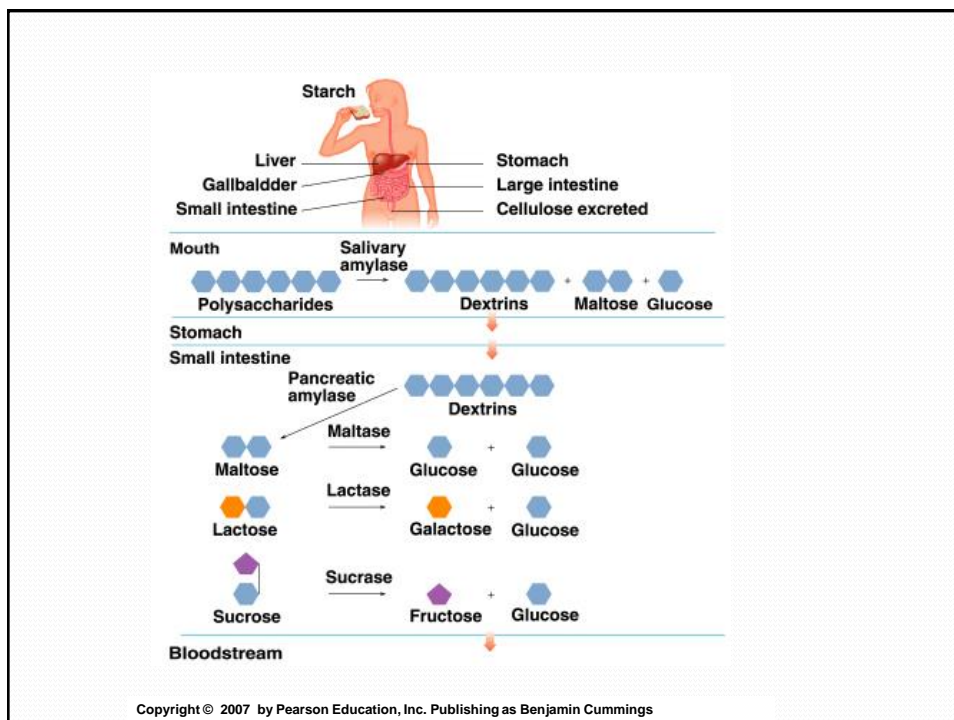
Stage 3: Oxidation of small molecules in the citric acid cycle and electron transport provide ATP energy.

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Stage 1: Digestion of Carbohydrates

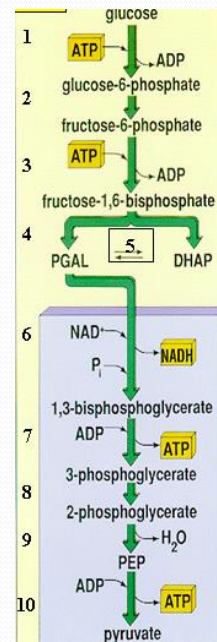
The digestion of carbohydrates:

- Begins in the mouth where salivary amylase breaks down polysaccharides to smaller polysaccharides (dextrins), disaccharide (maltose), and some glucose.
- Continues in the small intestine where pancreatic amylase hydrolyzes dextrins to maltose and glucose.
- Hydrolyzes of disaccharides; maltose, lactose, and sucrose to monosaccharides, mostly glucose, which enter the bloodstream for transport to the cells.



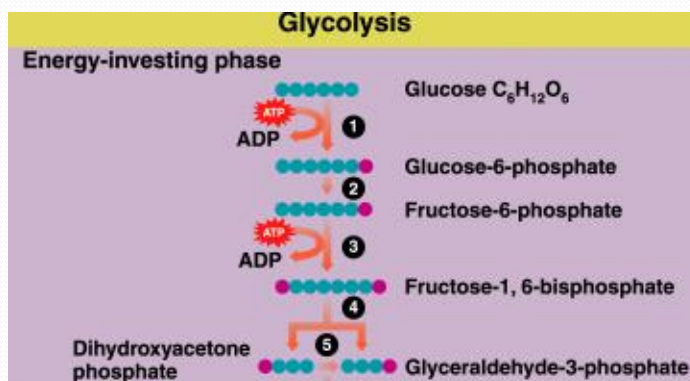
Stage 2: Glycolysis

- Glycolysis is a metabolic pathway that degrades glucose (a six-carbon) to pyruvate (a three-carbon molecules).
- It is an anaerobic process (no oxygen) and occur in the cytoplasm.
- It is divided into two stages:
 - A- five reactions and consume energy
 - B- five reactions that produce energy



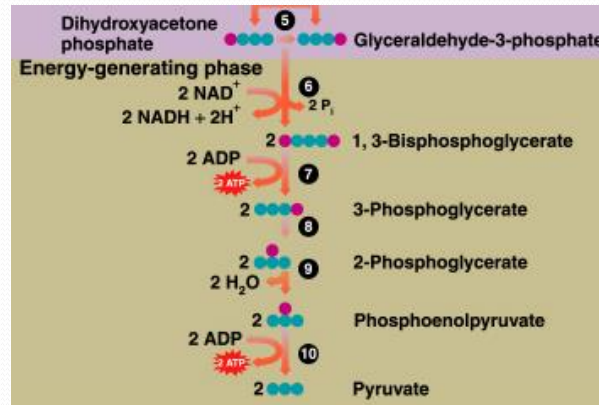
In reactions 1-5 of glycolysis,

- Energy is required to add phosphate groups to glucose.
- Glucose is converted through five enzymatically catalyzed reactions to two three-carbon molecules.



In reactions 6-10 of glycolysis, energy is generated as:

- Sugar phosphates are cleaved to triose phosphates.
- Four ATP molecules are produced.



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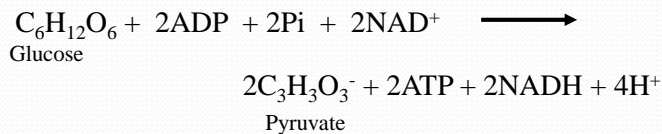
Glycolysis: Overall Reaction

In glycolysis,

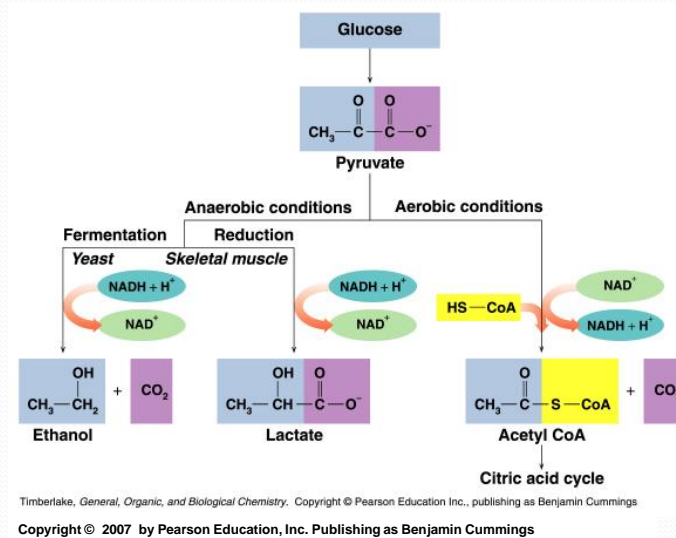
- Two ATP add phosphate to glucose and fructose-6-phosphate.
- Four ATP are formed in energy-generation by direct transfers of phosphate groups to four ADP.
- There is a net gain of 2 ATP and 2 NADH.

In other pathway

- In mitochondria, each of the 2NADH is converted to NAD⁺ and 3ATP are produced (2x 3 = 6ATP)

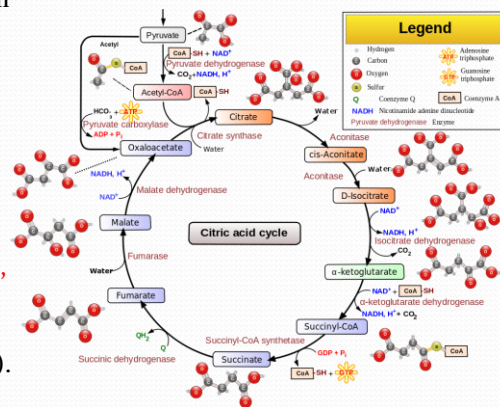


The Fate of pyruvate produced from glycolysis



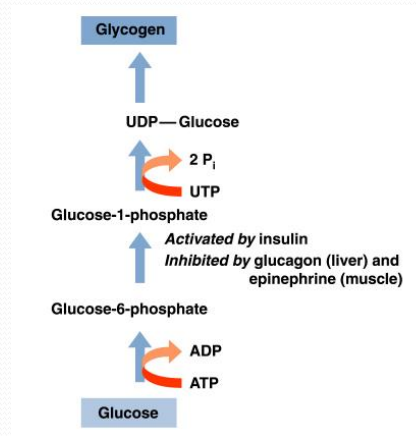
Krebs cycle

- It needs oxygen, so it occurs in all aerobic organisms.
- It is called **citric acid cycle**, **tricarboxylic acid (TCA) cycle** or the **Krebs cycle**.
- It generates energy through the oxidation of acetyl-CoA derived from **carbohydrates**, **fats** and **proteins** into CO_2 and chemical energy in the form of adenosine triphosphate (ATP).
- It occurs only in mitochondria which is called the "Power House"



Glycogenesis

- It is the storing of glucose (monosaccharide) by converting to glycogen (polysaccharide) in liver and muscles.
- It operates when high levels of glucose-6-phosphate are formed in the first reaction of glycolysis.
- It does not operate when energy stores (glycogen) are full, which means that additional glucose is converted to body fat.

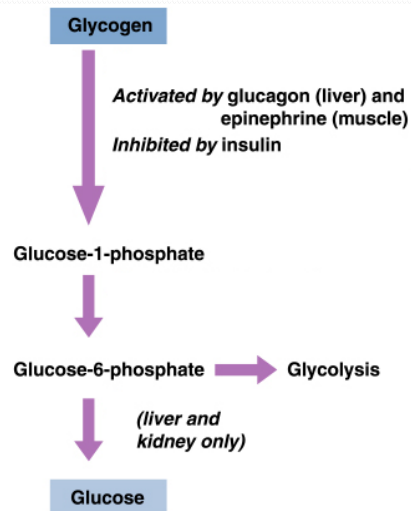


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Glycogenolysis

In **glycogenolysis**

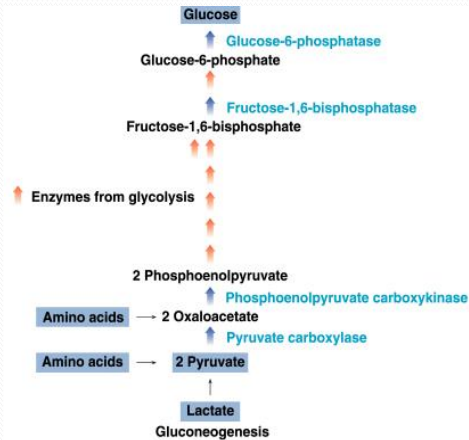
- Glycogen stores in liver and muscles is broken down to glucose.
- Glucose molecules are removed one by one from the end of the glycogen chain to yield glucose-1-phosphate.
- It occurs when the blood glucose level is decreasing to less than the lower limit (70 mg%) to compensate this decrease.



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Gluconeogenesis

- It is the generation of glucose from certain non-carbohydrate carbon substrates like the **metabolic products of carbohydrates, amino acids and lipid**.
- It occurs when glycogen stores are depleted as a result of starvation or if the body can not utilize glucose as in the case of diabetes.



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Pentose Phosphate Pathway (PPP)

- The **pentose phosphate pathway** is a metabolic pathway parallel to glycolysis.
- It generates NADPH and pentoses as well as Ribose 5-phosphate, the last one a precursor for the synthesis of nucleotides.

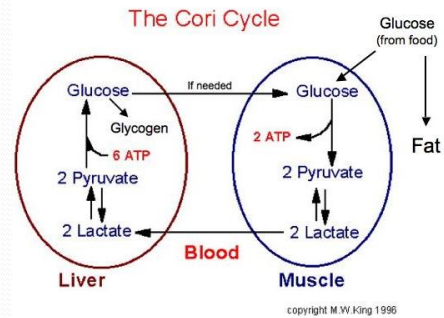


↳ 5 glucose 6-phosphate

Cori Cycle

The Cori cycle

- It is the flow of lactate and glucose between the muscles and the liver.
 - It occurs when anaerobic conditions occur in active muscle and glycolysis produces lactate.
 - It operates when lactate moves through the blood stream to the liver, where it is oxidized back to pyruvate.
 - It converts pyruvate to glucose, which is carried back to the muscles.
- **Notice:** the formation of glucose from lactate consumes 6 ATP molecules.



Pathways for Glucose

