CARBOHYDRATES

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Course content

- Chemistry: chemical nature, Classification, physical and chemical properties and biologic importance of carbohydrates with emphasis on role of heteropolysaccharides.

- Metabolism: Glucose Transporters, Glycolysis, Glycogen metabolism, HMP shunt and uronic acid pathway, Gluconeogenesis, Overview of inborn errors of carbohydrate metabolism (glycogen storage diseases, Galactosemia, Pentosuria etc.)

- Regulation of Blood Glucose level, Insulin receptor and Insulin Resistance, metabolism in starvation and Diabetes mellitus, Lab diagnosis and monitoring of Diabetes Mellitus; Biochemical basis of acute and chronic complications of Diabetes Mellitus.

OBJECTIVES

- Introduction and Definition
- Isomerism in Sugars
- Classification
- Important Carbohydrates
- Biomedical Importance of Carbohydrates

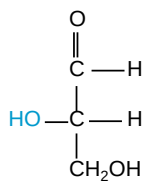
INTRODUCTION

- Hydrates of carbon
- Saccharides — sugars
- Some contain N and S
- Synthesized in
  - Plants
  - Animals

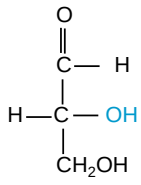
DEFINITION

- Carbohydrates are polyhydroxylated compounds having at least 3 carbon atoms and a potentially active carbonyl group which may be an aldose or a ketose group.
- Examples are: glucose, ribose.

GLYCERALDEHYDE

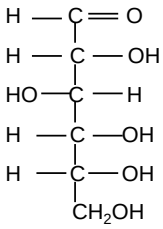


L-GLYCEROSE



D-GLYCEROSE

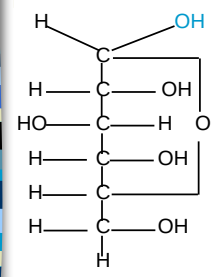
GLUCOSE



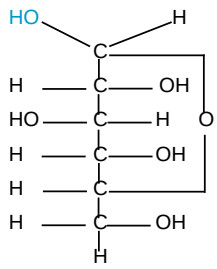
GLUCOSE

- **ANOMERIC CARBON ATOM**
  - ➢The carbon atom which is part of the carbonyl group
  - ➢Alpha(α) and Beta(β) anomers differ from each other only in respect to configuration around anomeric carbon atom.

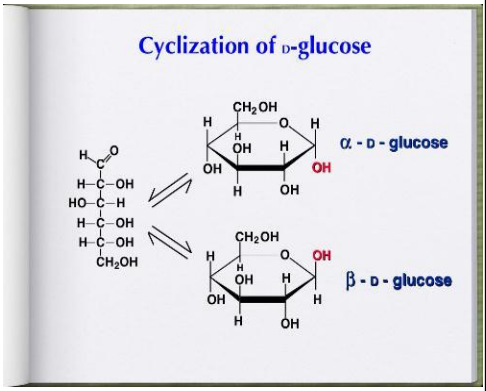
Alpha and Beta anomers of glucose



α-D-GLUCOPYRANOSE



β-D-GLUCOPYRANOSE



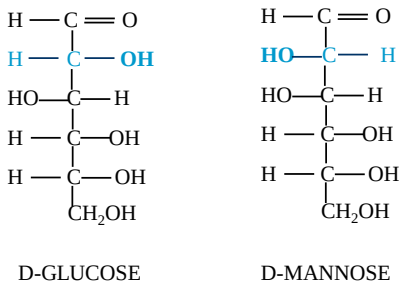
ISOMERISM IN SUGARS

- Isomers/Stereo-isomers: Compounds having the same chemical formulae but differing in the arrangement of their atoms in space and having different physical properties are called isomers.

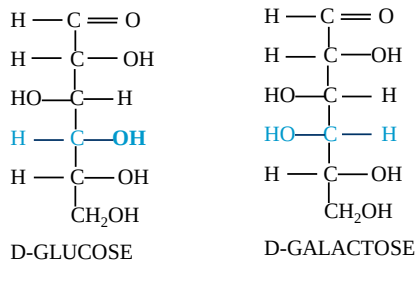
EPIMERS

- Monosaccharides which differ in configuration around one specific C-atom are called epimers of one another
- C-2 epimers
  - glucose and mannose
- C-4 epimers
  - glucose and galactose

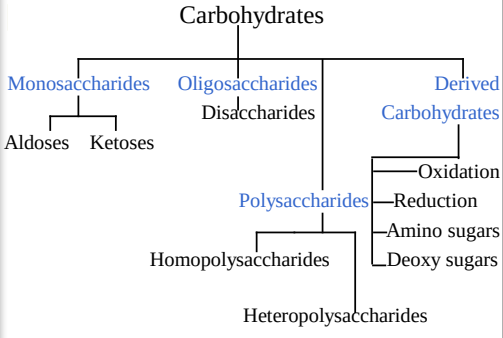
CARBON-2 EPIMERS



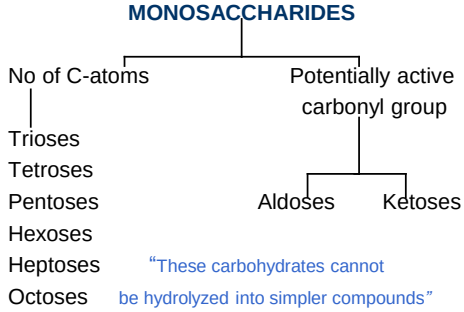
CARBON-4 EPIMERS



CLASSIFICATION OF CARBOHYDRATES

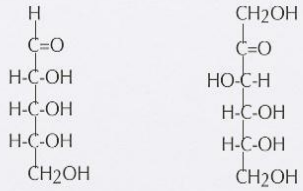


MONOSACCHARIDES



Monosaccharide classifications

Based on location of C=O



Aldose

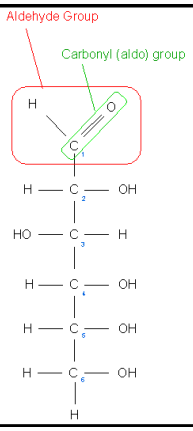
Aldehyde CHO

Ketose

Ketone C=O

Reducing and Non-Reducing Sugars

- Reduction is the chemist's term for electron gain
- A molecule that gains an electron is thus……
  - "reduced"
- A molecule that donates electrons is called a……
  - "reducing agent"
- A sugar that donates electrons is called a……
  - "reducing sugar"
- The electron is donated by the **carbonyl group**
- **Benedict's reagent** changes colour when exposed to a reducing agent

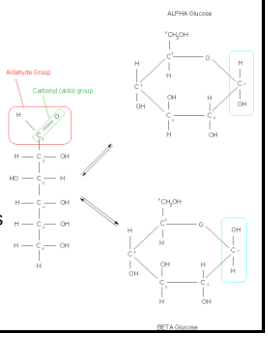


Benedict's Test

- Benedict's reagent undergoes a complex colour change when it is reduced
- The intensity of the colour change is proportional to the concentration of reducing sugar present
- The colour change sequence is:
  - Blue…
  - green…
  - yellow…
  - orange…
  - brick red

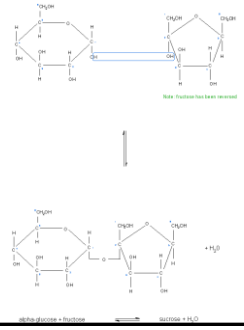
The carbonyl group - monosaccharides

- The carbonyl group is "free" in the straight chain form
- But not free in the ring form
- BUT remember – the ring form and the straight chain form are interchangeable
- So **all** monosaccharides are reducing sugars
- All monosaccharides reduce Benedict's reagent



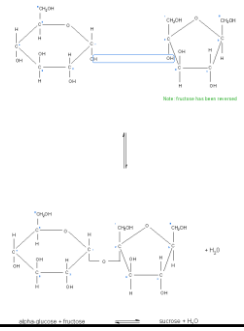
The carbonyl group – disaccharides - sucrose

- In some disaccharides e.g. sucrose **both** of the carbonyl groups are involved in the glycosidic bond
- So there are **no** free carbonyl groups
- Such sugars are called **non-reducing sugars**
- They **do NOT** reduce Benedict's reagent



The carbonyl group – disaccharides - sucrose

- The subunits of sucrose (glucose and fructose) are reducing sugars
- If sucrose is hydrolysed the subunit can then act as reducing sugars
- This is done in the lab by **acid hydrolysis**
- After acid hydrolysis sucrose **will** reduce Benedict's reagent



OLIGOSACCHARIDES

- These are the condensation products of 2 to 10 monosaccharide units
- Disaccharides: These are the condensation products of two monosaccharide units e.g. sucrose, lactose.

POLYSACCHARIDES

- These are the condensation products of more than 10 molecules of monosaccharide units
- They include starch, glycogen.
- Stores of fuel
- Structural elements of cells

POLYSACCHARIDES

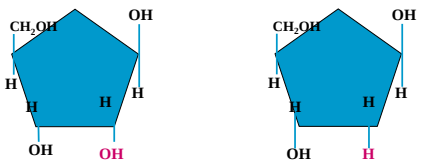
- Homopolysaccharides
  - *Starch
  - *Glycogen
  - *Cellulose
  - *Dextrins
  - * Inulin
- Heteropolysaccharides
  - Glycoseaminoglycans
    - *Hyaluronic acid
    - *Heparin
    - *Chondoitin SO_4
    - *Serum mucoids
    - *Blood gp polysaccharides
  - Mucilages
    - *Agar
    - *Vegetable gums
    - *Pectins
    - *Hemicellulose

DERIVED CARBOHYRATES

Oxidation Products	Reduction Products	Amino Sugars	Deoxy Sugars
Gluconic acid	Glycerol	Glucosamine	Deoxyribose
Glucuronic acid	Ribitol	Galactoseamine	
Glucaric acid		Mannoseamine	

"These are derived from carbohydrates by various chemical reactions"

DEOXYRIBOSE SUGARS



IMPORTANT CARBOHYDRATES

- MONOSACCHARIDES
  - PENTOSES
- Ribose:
- Found in nucleic acids
- Forms structural elements of nucleic acid and coenzymes
- Intermediates of pentose phosphate pathway
- ATP, NAD, NADP, flavoproteins etc

HEXOSES

Glucose

- Found in fruits, fruit juices, hydrolysis of starch, maltose and lactose.
- Body sugar and the principal one used by the tissues
- Excess in the blood is called *hyperglycemia* and presence in urine (*glucosuria*) indicates diabetes mellitus
- *Cataract* due to sorbitol

Fructose

- Latin word for fruit — "fructus"
- Found in fruit juices, honey
- Released by the hydrolysis of inulin
- Main nutritional source of energy for the spermatozoa and is found in the seminal fluid
- Can be converted to glucose in the liver
- It is the sweetest sugar
- Lack of enzymes of metabolism can lead to *essential fructosuria*

Galactose

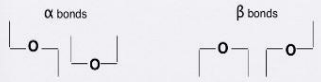
- Greek word for milk--"galact", found as a component of lactose in milk
- Formed by the hydrolysis of lactose
- Synthesized in the lactating mammary gland
- Constituent of glycolipids and glycoproteins
- Can be converted to glucose in the liver
- Accumulation can lead to *galactosemia* and *cataract* (galactitol)

Glycosidic bonds

Type is based on the position of the C-1 OH

α glycosidic bond
linkage between a C-1 α OH and a C-4 OH

β glycosidic bond
linkage between a C-1 β OH and a C-4 OH

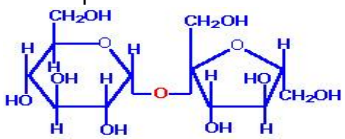


C-4 end can be either up or down depending on the orientation of the monosaccharide.

OLIGOSACCHARIDES

Sucrose

- Known as table sugar
- α-D-glucose ------ β-D- fructose
- α-1 ⟶ β-2



Sucrose

α-D-glucopyranosyl-(1 2)-β-D-fructofuranoside

Lactose

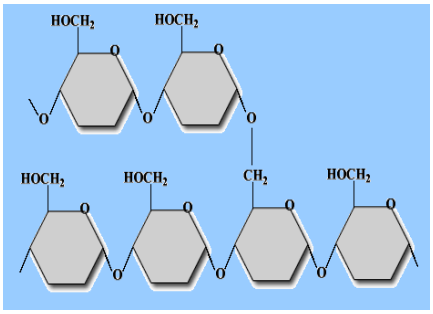
- Synthesized by lactating mammary gland
- Milk sugar (lac-milk)
- β-D-galactose ⟶ β-D-glucose
- β 1⟶ 4 linkage
- Enzyme – lactase and lactose intolerance
- Least sweet sugar – 16% of sucrose
- Possesses one potential aldehyde group
  - reducing sugar
  - forms osazone crystals

HOMOPOLYSACCHARIDES

Starch

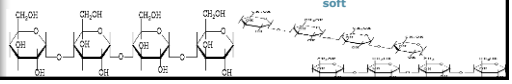
- Main storage form of glucose in plants
- Polysaccharide units
  - Amylose (20—28%)
  - Amylopectin 72—80%)
- Polymer of α-D-glucose
- α-1⟶4 glycosidic linkage
- At branching points α-1⟶6 linkage
- No free aldehyde group
- Found in wheat, rice, corn, potatoes

Starch



Characteristics of Amylose and Amylopectin

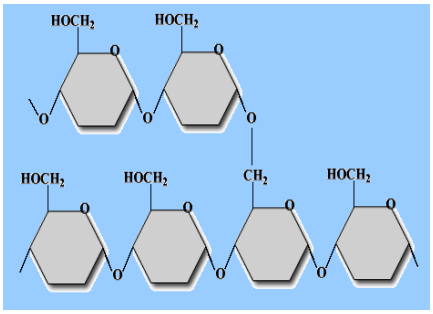
Characteristic	Amylose	Amylopectin
Form	Linear	Branch
Linkage	α-1,4 (some α-1,6)	α-1,4; α-1,6
Polymer units	200-2,000	Up to 2,000,000
Molecular weight	Generally <0.5 million	50-500 million
Gel formation	Firm	Non-gelling to soft

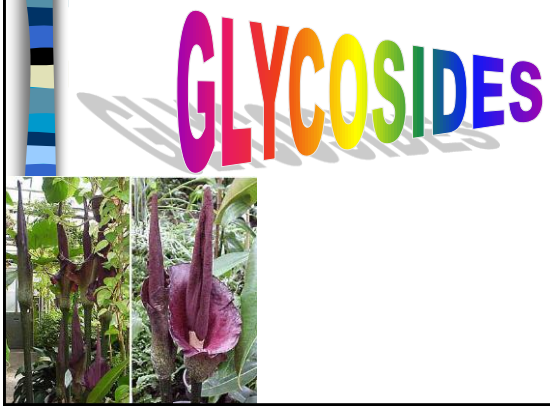


Glycogen

- Known as animal starch
- Present in the liver and muscle
- Both α-1⟶4 and α-1⟶6 linkages are found
- More branched structure than starch
- Gives red color with iodine

Glycogen





GLYCOSIDES

A glycoside is an organic compound, usually of plant origin, that is composed of a sugar portion linked to a non-sugar moiety. The sugar portion is called glycone, while the non-sugar portion is called aglycone .

GLYCOSIDES

The linkage between the sugar and the aglycone is an acetal linkage.

Types of Glycosides :

According to atoms involved in the glycosidic linkage:

1- O-glycosides
2- C-glycosides
3- S-glycosides
4- N-glycosides

GLYCOSIDES

- **Cardiac glycosides Digitalis useful in Congestive cardiac failure. They contain Steroid as aglycone.**

BIOMEDICAL IMPORTANCE OF CARBOHYDRATES

BIOMEDICAL IMPORTANCE

- Glucose — most important carbohydrate
- Glucose can be converted into
  - glycogen
  - ribose
  - galactose
- Glycoproteins — molecular targeting
- Antibodies and blood clotting factors
- Structural components of cell membranes

- Neuronal adhesion in development of nervous system (protein-glycan-heparan-sulfate)
- Constituents of extra cellular matrix
- Diseases associated with carbohydrates
  - Diabetes mellitus
  - Galactosemia
  - Lactose intolerance
  - Glycogen storage diseases

ISOMERISM

Structural isomers
Compounds with the same molecular formula but with different structures

Functional group isomers
with different functional groups
E.g. glyceraldehyde and dihydroxyacetone

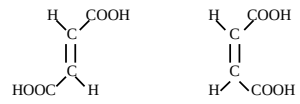
Positional isomers
with substituent groups on different C-atoms
E.g.

COO^--$CHOPO_3^-$-CH_2OH and COO^--$CHOH$-$CH_2OPO_3^-$
2-Phosphoglycerate 3-Phosphoglycerate

ISOMERISM

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

cis-trans isomers
with different conformation around double bonds



Fumaric acid (*trans*) Maleic acid (*cis*)

ISOMERISM

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

optical isomers
with different conformation around chiral or asymmetric carbon atoms

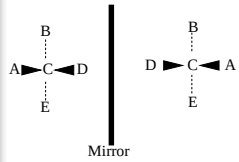
The carbon C is asymmetric if A, B, D, and E are four different groups

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

ISOMERISM

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

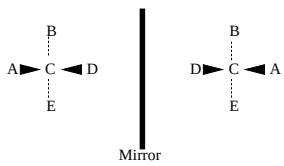
optical isomers
with different conformation around chiral or asymmetric carbon atoms



The mirror images can't be superimposed on each other, i.e. they are different

The mirror image isomers constitute an ***enantiomeric pair***; one member of the pair is said to be the ***enantiomer*** of the other

ISOMERISM



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 (+)

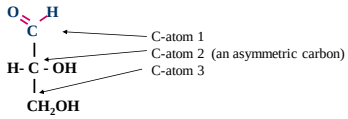
The other member of the pair will then rotate the light in a counterclockwise direction.
It is said to be *levorotatory* which is labelled (-)

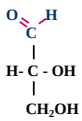
ISOMERISM

Fischer projection formula

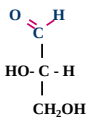
Perspective formula

Reference compound for optical isomers is the simplest monosaccharide with an asymmetric carbon: glyceraldehyde

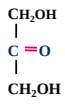




D-Glyceraldehyde



L-Glyceraldehyde



Dihydroxyacetone

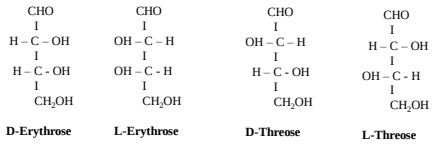
D-Glyceraldehyde is assigned to be the isomer that has the hydroxyl group on the right when the aldehyde group is at the top in a Fischer projection formula.

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

If a compound has n asymmetric carbon atoms then there are 2^n different optical isomers

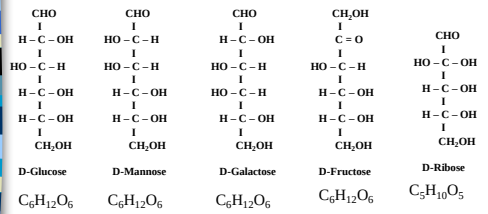
Number of carbon atoms	Aldose/Ketose	Number of asymmetric carbon atoms	Number of optical isomers
3	Aldose	1	2
4	Aldose	2	4
5	Aldose	3	8
6	Aldose	4	16
3	Ketose	0	-
4	Ketose	1	2
5	Ketose	2	4
6	Ketose	3	8

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



Optical isomers that are not enantiomers are *diastereomers*

Diastereomers that differ by their configuration on a <u>single</u> asymmetric carbon are *epimers*



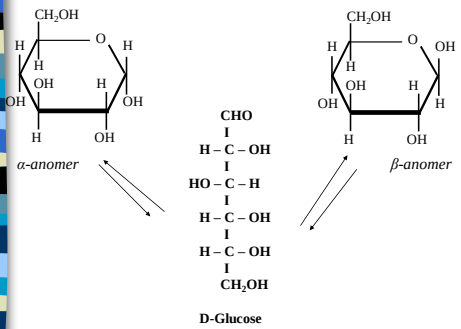
With ring formation involving the aldehyde- or ketone-carbon atom, this carbon atom also becomes asymmetric, giving two possible isomers called
anomers

The carbon atom is the *anomeric* carbon
The hydroxyl group bound to the anomeric carbon is the *anomeric* hydroxyl group.

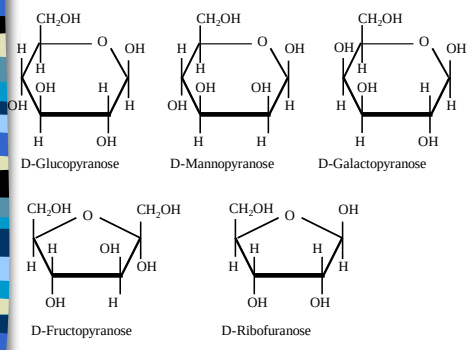
In Haworth formulas of D-pentoses and D-hexoses,
the *α-anomer* has the anomeric hydroxyl written below the ring plane
the *β-anomer* has the anomeric hydroxyl written above the ring plane

6-membered ring:	Pyranose
5-membered ring:	Furanose

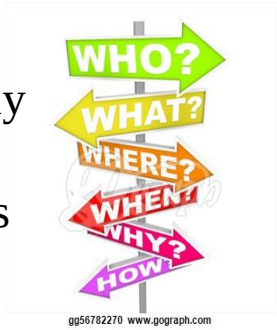
Mutarotation: Spontaneous conversion of one anomer to the other



Equilibrium: 36% α-anomer, 63% β-anomer, <1% open-chain form



Frequently Asked Questions



FAQs

- Define & classify carbohydrates.
- Physiological significance of carbohydrates.
- Different types of isomerisms
- Mutarotation
- Mucopolysaccharides