Carbohydrates and Glycobiology

Functions of Carbohydrates

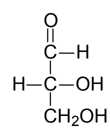
1. Energy source for plants and animals
2. Source of carbon in metabolic processes
3. Storage form of energy
4. Structural elements of cells and tissues
5. Recognition (e.g. contact inhibition of cells)

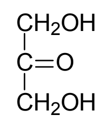
Carbohydrates

- Originally thought to have the formula $(C{\cdot}H_2O)_n$.
- Now known that only simple monosaccharides obey this rule.

<u>Carbohydrate</u>- polyhydroxy aldehyde or ketone or a larger molecule which can be hydrolyzed to a polyhydroxy aldehyde or ketone.

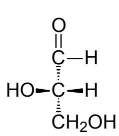
Simplest Carbohydrates Two Hydroxyls Minimum

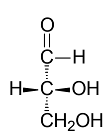




aldose	ketose
triose	triose
aldotriose	ketotriose
glyceraldehyde	dihydroxyacetone

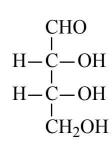
Stereochemistry



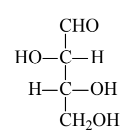


In biochemistry, we use the D-L system (similar principle to the R-S system usually used in organic, but everything is compared with glyceraldehyde)

Moving Up



Erythrose
D



Threose
D or L?

The D and L designation of sugars with $n > 3$ are taken from the chiral carbon furthest from the carbonyl carbon.

Stereochemistry: Other Important Terminology to Review

<u>Enantiomers</u>- mirror image molecules

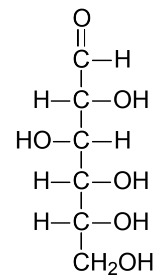
D- and L-sugars are enantiomers

<u>Diastereomers</u>- nonsuperimposable, non mirror image

<u>Epimers</u>- differ in arrangement about <u>one</u> other chiral carbons. (Glc *vs*. Man, e.g.)

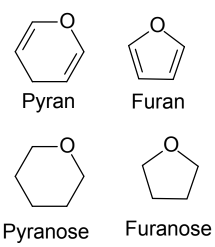
Fischer Projections

- Emil Fischer
- Vertical lines into plane (away from you)
- Horizontal lines out of plane (towards you)
- C1 (IUPAC nomenclature) on top



Most 5 and 6 Carbon Sugars are in Ring Form (Chair Conformation)

- Based on molecules Pyran and Furan
- Carbohydrates can exist in either, but generally one is much more common.



Interchanging Fisher and Haworth Projections

<u>Haworth Projection</u>- shows the ring configuration.

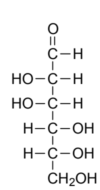
1. Carbonyl reacts with OH of carbon 5.
2. H of C5 OH is transferred to carbonyl O.
3. O of C5 OH becomes part of ring.
4. α- and ß-*anomers* are possible.

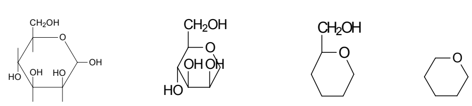
<u>Anomer</u>- differ in arrangement around carbonyl carbon.

Shortcut Interconversions

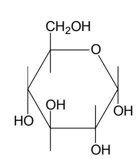
- 6C aldose ⇒ pyranose

- D sugar #6 up
- Right down and left up
- Anomeric anything

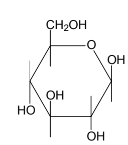




α- and ß-Anomers: Inspect C6 and Anomeric Hydroxyl

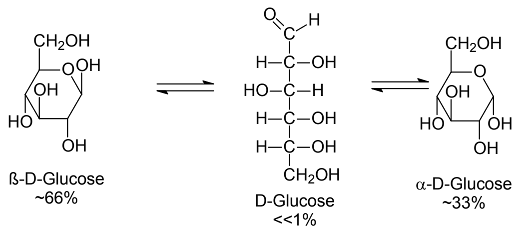


α-anomer
opposite direction



ß-anomer
same direction

An Equilibrium Exists Between Possible Structures



Specific Rotation Problem

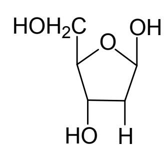
$$\text{specific rotation} = \frac{\text{observed rotation}}{\ell \times c}$$

- ß-D-Gal has a specific rotation of +52.8^o
- α-D-Gal has a specific rotation of +150.7^o
- After *mutarotation* of either α or ß, the rotation is +80.2^o
- What is the % α and ß?
- A: 28% α and 72 % ß

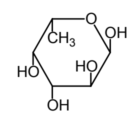
Important Simple Monosaccharides

1. Glucose
2. Mannose
3. Galactose
4. Fructose
5. Ribose

Important Monosaccharide Derivatives: Deoxysugars



Deoxyribose
Important in: DNA



L-Fucose
Important in: immune recognition, e.g.

Important Monosaccharide Derivatives: Amino sugars

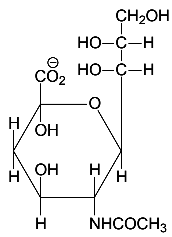
Glucosamine
Galactosamine
N-Acetylglucosamine
N-Acetylgalactosamine

Important Monosaccharide Derivatives: Oxidized Sugars

Gluconolactone: C1 ketone
Gluconic acid: C1 carboxylate
Glucuronic acid: C6 carboxylate

Important Monosaccharide Derivatives: Others

N-Acetylneuraminic acid, a sialic acid (many modified sialic acids exist)



Reactions of Monosaccharides

Acid stable but *epimerize* in base
1. Mutarotation
2. Oxidation to CO_2 + H_2O

Reactions due to aldehyde group

3. Reducing sugars.
4. Reduction to polyols.

Reactions due to alcohol groups

5. Esterification.
6. Formation of *acetals*, also called *glycosides*

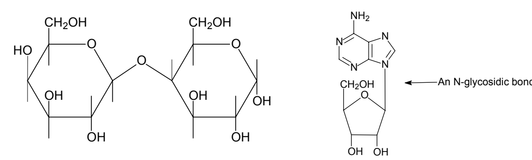
Classification of Carbohydrates

<u>Monosaccharide</u>- one sugar residue.

<u>Oligosaccharide</u>- a few (2-9) sugar residues.

<u>Polysaccharide</u>- many sugar residues.

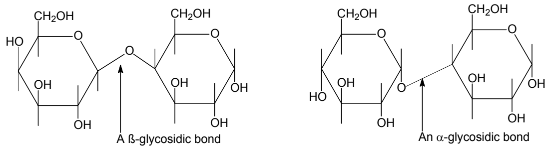
Disaccharides: The Glycosidic Bond



<u>Glycosidic bond</u>- bond between a sugar and an alcohol (another sugar) or amine (a base) through an O- or N- linkage.

α- versus ß-Glycosidic Bonds

Refers to the configuration at the anomeric carbon involved in the bond.



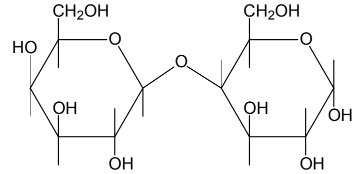
α-linkages are digestible, ß-linkages are not.

Disaccharides: Use Common Names

O-ß-D-galactopyranosyl-1→4-D-glucopyranose

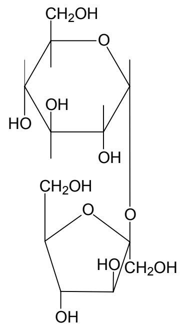
Short-hand: Galß1→4Glc

Common: Lactose

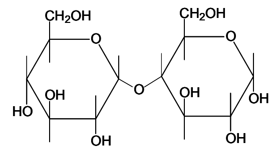


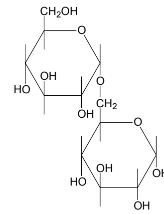
Disaccharides: Use Common Names

Sucrose: Glc (α1→ß2) Fru



Disaccharides: Maltose and Isomaltose





What are the shorthand notations for these molecules?

Reactions of Disaccharides

1. Mutarotation.
2. Oxidation to CO_2 + H_2O.

Reactions due to aldehyde group

3. Reducing sugars.
4. Reduction to polyols.

Reactions due to alcohol groups

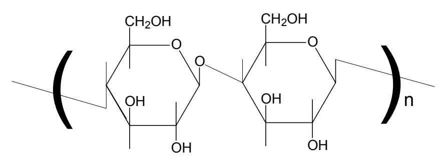
5. Esterification.
6. Formation of *acetals*.

Reactions due to glycosidic bond

7. Acid-catalyzed hydrolysis

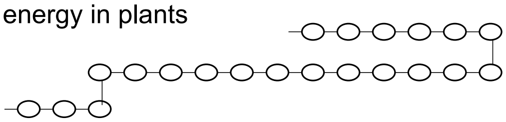
Homopolysaccharides: Cellulose

Cellulose: ß1,4 linked glucose
linear; undigestable by mammals
Plays a structural role in plants: hydrogen bonds



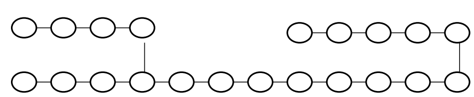
Homopolysaccharides: Starch

- α1,4 linked glucose with <u>some</u> α1,6 linkages (branched)
- branch every 12-20 Glc residues
- digestable by mammals- storage form of energy in plants



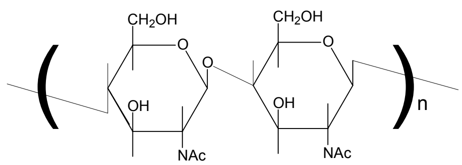
Homopolysaccharides: Glycogen

- α1,4 linked glucose with <u>many</u> α1,6 linkages (branched)
- branch every 8-12 Glc residues
- energy storage in mammals



Homopolysaccharides: Chitin

Chitin: ß1,4 linked GlcNAc used by insects and crustaceans for shells (structural)



Heteropolysaccharides: Glycosaminoglycans

Mucopolysaccharides: used in lubricating joints, mucous secretions

- Hyaluronic acid: GlcNAc - Glucuronic acid in alternating ß1,3 and ß1,4 linkages
- Chondroitin sulftate: GalNAc-6-SO_4 - Glucuronic acid in alternating ß1,3 and ß1,4 linkages
- Others exist

Oligosaccharides

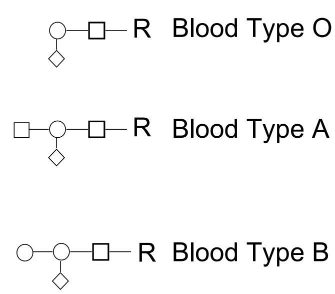
Can be arranged in a plethora of ways.

α and ß linkages

1,3; 1,4; 1,6 linkages

any two (or more) monosaccharides can be linked together

Glycoproteins and Recognition

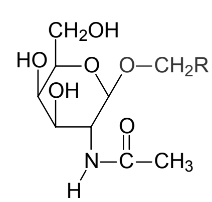


Oligosaccharides

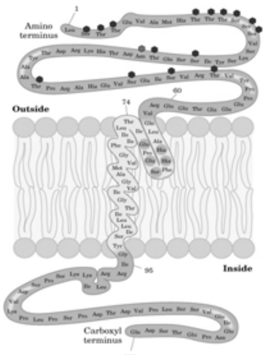
1. Function in recognition: parasites
2. Modulate solubility, viscosity, charge
3. Affect proteolytic processing
4. Cellular localization
5. Affect binding to receptor
6. Affect embryonic development/differentiation

O-linked Glycoprotein

- GalNAc linked to Ser or Thr alcohol group
- Often just MS
- Sometimes DS- SA also

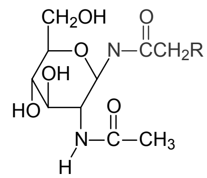


Lehninger, POB 3rd Ed. Fig 12-10



- GalNAc linked to Ser or Thr alcohol group
- Often just MS
- Sometimes DS- SA also
- Ser/Thr rich regions

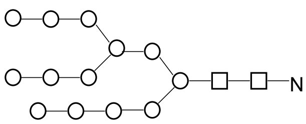
N-linked Glycoprotein



- GlcNAc linked to Asn
- In sequence NXT
- 3 types

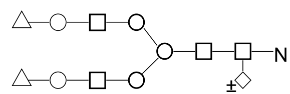
"Typical" High Mannose

- Lower eukaryotes such as yeast



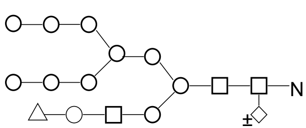
"Typical" Complex Biantennary

- Default pathway in mammals



"Typical" Hybrid

- Part high mannose, part complex



Glycoprotein Analysis

1. Get a pure species
2. Acid hydrolysis to det'n composition
3. Methylate and hydrolyze to det'n linkage
   OR use glycosidases of known specificity
   OR use specific *lectins*

NMR or MS can be used, but fewer people know how

Glycolipids and Lipopolysaccharides

- Talk about with lipids