Carbohydrates – Function Overview

- **Energy supply**
  - Storehouses of chemical energy for plants .... Glucose, starch, ...
    - approximately 3/4th of dry weight of plants
  - Source of energy for animals too ... typically not in a stored form ...
    - animals get most of their carbohydrates from plants .... Less than 1% of animal body weight is carbohydrates
  - In lean times, animals utilize glycogen as source of energy .... Glycogen is a polymer of glucose ... α (1→4)-linked

- **Skeletal material**
  - Supportive structure for plants .... Cellulose, chitin ... called structural polysaccharides .... Cellulose is β (1→4)-linked ... mere change from α to β completely alters the function!
  - Connective tissue in animals ... acidic polysaccharides ... examples include hyaluronic acid, chondroitin sulfate, ....
Carbohydrates – Function Overview

- **Biological importance**
  
  - RNA and DNA contain ribose or deoxyribose
  
  - Cell surfaces have many carbohydrate-based molecules ... e.g., heparan sulfate
  
  - Differentiation of A, B, AB and O blood types ... the type of tri- or tetrasaccharide present on RBCs determines the blood type

**TYPE A**

\[ \text{D-GalNp2Ac(1} \rightarrow 4)\] \(\alpha\)-D-Galp(1 \(\rightarrow\) 3)-\(\beta\)-D-GlcNp2Ac

\[ \alpha\-L\-Fucp(1 \rightarrow 2) \]

**TYPE B**

\[ \text{D-Galp(1} \rightarrow 4)\] \(\alpha\)-D-Galp(1 \(\rightarrow\) 3)-\(\beta\)-D-GlcNp2Ac

\[ \alpha\-L\-Fucp(1 \rightarrow 2) \]

**TYPE O**

\[ \alpha\-D\-Galp(1 \rightarrow 3)-\(\beta\)-D-GlcNp2Ac

\[ \alpha\-L\-Fucp(1 \rightarrow 2) \]

Type A person has antibodies for type B … cannot accept type B blood & vice versa. Type O person has antibodies for both type A and B … cannot accept either A or B blood. Type O blood has no antigens … therefore is accepted by all … universal donor Type AB blood has neither A nor B antibodies … therefore is a universal acceptor
Carbohydrates - Function Overview

- Biological importance … Major roles in Biology
  - Vitamin C
    
    ![Chemical structures](image)
    
    L-ascorbic acid ... not synthesized by humans ... obtained from plants ... prolonged deficiency results in scurvy (impairment of collagen formation) ... fresh foods have vitamin C ... not otherwise because of oxidation to DHA

  - Heparin
    
    ![Heparin structure](image)
    
    Glycosaminoglycan that is present in mast cells that line arterial walls, especially in the liver, lungs and skin ... inhibits clotting ...
Carbohydrates - Nomenclature

- **Word ‘carbohydrate’ implies “hydrate of carbon”** … \( C_n(H_2O)_m \)
  - Glucose (a monosaccharide) \( C_6H_{12}O_6 \) … \( C_6(H_2O)_6 \)
  - Sucrose (a disaccharide) \( C_{12}H_{22}O_{11} \) … \( C_{12}(H_2O)_{11} \)
  - Cellulose (a polysaccharide) \( (C_6H_{12}O_6)_n \)… \( (C_6(H_2O)_6)_n \)

- **Not all carbohydrates have this formula … some have nitrogen … Yet the name is retained**
  - Glucosamine (glucose + amine) …. \( C_6H_{13}O_5N \) … -NH\(_2\) at the 2-position of glucose
  - N-acetyl galactosamine (galactose + amine + acetyl group) …. \( C_8H_{15}O_6N \) … -NHCOCH\(_3\) at the 2-position of galactose

- **Typical prefixes and suffixes used in naming carbohydrates**
  - Suffix = ‘-ose’ & prefix = ‘tri-’, ‘tetr-’, ‘pent-’, ‘hex-’
  - Pentose (a five carbon monosaccharide) or hexose (a six carbon monosaccharide)

- **Functional group types**
  - Monosaccharides with an aldehyde group are called aldoses … e.g., glyceraldehyde
  - Those with a keto group are called ketoses … e.g., dihydroxyacetone
Monosaccharides

Structure

✓ Have a general formula \( C_nH_{2n}O_n \) and contain a carbonyl group
✓ Common monosaccharides have 3 → 9 carbons
✓ Two molecules form the class of smallest monosaccharides ... glyceraldehyde and dihydroxyacetone

\[
\begin{align*}
\text{CHO} & \quad \text{CH}_2\text{OH} \\
\text{CHOH} & \\
\text{CH}_2\text{OH} & \\
\text{Glyceraldehyde} & \\
\end{align*}
\]

\[
\begin{align*}
\text{CH}_2\text{OH} & \\
\text{CH}_2\text{OH} & \\
\text{Dihydroxyacetone} & \\
\end{align*}
\]
Monosaccharides

✓ Glyceraldehyde has a chiral carbon

\[
\begin{align*}
\text{CHO} \\
* \text{CHOH} \\
\text{CH}_2\text{OH}
\end{align*}
\]

* = chiral carbon

... 2 stereoisomers

✓ 3-Dimensional arrangement

\[
\begin{align*}
\text{CHO} & \quad \text{CHO} \\
\text{HO} & \quad \text{HOCH}_2 \\
\text{CH}_2\text{OH} & \quad \text{OH} \\
(R) & \quad (S)
\end{align*}
\]

✓ 2-Dimensional representation

\[
\begin{align*}
\text{CHO} & \quad \text{CHO} & \quad \text{CHO} & \quad \text{CHO} \\
\text{H} & \quad \text{H} & \quad \text{HO} & \quad \text{HO} \\
\text{OH} & \quad \text{OH} & \quad \text{H} & \quad \text{H} \\
\text{CH}_2\text{OH} & \quad \text{CH}_2\text{OH} & \quad \text{CH}_2\text{OH} & \quad \text{CH}_2\text{OH} \\
(D) & \quad (R) & \quad (L) & \quad (S)
\end{align*}
\]
Monosaccharides

Emil Fischer’s representation ... arbitrarily assigned the dextrorotatory enantiomer as D-glyceraldehyde, which fortuitously proved correct

\[
\begin{array}{ccc}
\text{CHO} & \text{CHO} \\
\text{H} & \text{HO} \\
\text{CH}_2\text{OH} & \text{CH}_2\text{OH} \\
(D) & (L) \\
(+ ) & (- )
\end{array}
\]

Note: This does not mean that all D-saccharides are dextrorotatory; likewise it does not mean that all D-saccharides are also (R) in the Cahn-Ingold-Prelog system.
Monosaccharides

✓ A D-monosaccharide has the same configuration on its penultimate carbon as the D-glyceraldehyde

![Chemical structures of monosaccharides]

✓ Exactly similar series is possible for the L-monosaccharides starting with L-glyceraldehyde

✓ Likewise similar series exists for L and D-ketoses starting from dihydroxyacetone
Monosaccharides

✓ A L-ketoses starting from dihydroxyacetone

Dihydroxyacetone
(no D- or L-form)

L-erythulose

L-psicose

L-fructose

L-sorbose

L-ribulose

L-tagatose
**Monosaccharides**

- D-glucose is also called dextrose because it is dextrorotatory.
- D-glucose is the most abundant monosaccharide; it is present in most fruit juices.
- D-glucose is also called blood sugar ….. it is present in about 65 – 100 mg per 100 mL of blood.
- The dextrose solution for iv drip contains about 5% glucose + 0.15% saline (KCl).
- Fructose is one of the monosaccharides present in disaccharide sucrose (table sugar) … the other is D-glucose.
- Galactose is part of lactose (milk sugar).
- Several aminosugars are known including D-glucosamine, D-mannosamine, D-galactosamine and N-acetyl-D-glucosamine. These have a nitrogen at position 2.

![Chemical structures](image-url)
Monosaccharides

Cyclic Structure of Aldoses

Earlier you have studied that aldehydes and ketones react with alcohols to give hemi-acetals

\[
\begin{align*}
\text{HCHO} \quad &+ \quad \text{R'OH} \quad \leftrightarrow \quad \text{ROH} \\
\end{align*}
\]

An anomer represents a stereoisomer that differs in configuration only at the anomeric carbon

What is an epimer?
Monosaccharides

Cyclic Structure of Ketoses

- Similar cyclic structures exist for five membered saccharides ... e.g., ribose.
- These five membered cyclic hemiacetals are well known for nucleic acids ... e.g., RNA (ribonucleic acid) and DNA (deoxyribonucleic acid)

D-fructose

α-D-fructofuranose
(α-D-fructose)

β-D-fructofuranose
(β-D-fructose)

HAWORTH Projections

2-deoxy-α-D-fructofuranose
(2-deoxy-α-D-fructose)

2-deoxy-β-D-fructofuranose
(2-deoxy-β-D-fructose)
**Monosaccharides**

- **Conformations of the pyranose form of D-glucose**

![Chair Conformations](image)

**Chair Conformations**

- Why is β-D-glucose the most common sugar in nature?
Monosaccharides

Conformations of the pyranose form of D-galactose

Chair Conformations
Monosaccharide Derivatives

- **Uronic Acids**

![Diagram of D-Glucose and D-Glucuronic Acid]

Specific enzymes in the body

- **Uronic acids and Biology**
  - Several other uronic acids occur in our body, e.g., D-mannuronic acid (from D-mannose), L-iduronic acid (from L-idose), D-galacturonic acid
  - Components of many polysaccharides
  - Add to the conformational complexity, e.g., L-iduronic acid can exist in several conformations other than chair – $^2S_0$, $^0S_2$, $^1C_4$ and $^4C_1$
Monosaccharide Derivatives

- Finding ground state conformations

D-Glucose
Monosaccharide Derivatives

- Finding ground state conformations of L-iduronic Acid from D-glucose

![Chemical Structures]

D-Glucose

L-Iduronic Acid

\[\text{D-Glucose} \rightarrow \text{L-Iduronic Acid}\]
Disaccharides

Sucrose

Sucrose (table sugar) is a disaccharide made from \( \alpha\)-D-glucose and \( \beta\)-D-fructose, where the inter-glycosidic bond is \( \alpha\)-1,2.

How do we find out which atoms are connected in polysaccharides and what is their orientation?

How do we know what conformation does a sugar adopt?
Lactose

Lactose (milk sugar) is a disaccharide made from \( \beta-D\)-galactose and D-glucose, where the inter-glycosidic bond is \( \beta-1,4 \)

\[
\begin{align*}
\text{Galactose} & \quad \beta-D\text{-galactose} \\
\text{Gluco} & \quad D\text{-glucose}
\end{align*}
\]

\( \beta-1,4\)-interglycosidic bond

Lactose intolerance? ... cow’s milk ... 4 – 6% lactose ... some infants, most blacks and many Orientals have low level of lactase, which hydrolyzes the \( \beta(1,4) \) bond of lactose ... lactose accumulates in colon where bacterial fermentation produces large quantities of \( CO_2, H_2 \) and organic acids
Monosaccharide Derivatives

Is lactose (D-galactose-β (1 → 4)-D-glucose) is same as D-glucose-β (1 → 4)-D-galactose?

Remember! D-glucose is consumed by our body; L-glucose is left untouched!
Oligosaccharides

- **Glycoproteins**
  - **O-linked oligosaccharides**
    Attachment through the side-chain of Ser or Thr
  - **N-linked oligosaccharides**
    Attachment through Asn side chain

- **Importance**
  - **N- and O-glycans that determine blood group A, B, & O discussed earlier**
  - **N- and O-glycans containing sialic acid on their terminus are present to a high extent on outer cell membranes (>10 million molecules/RBC), on the interior of lysosomal membranes and on secreted glycoproteins ... roles in stabilization of molecules and membranes ... stability of platelets in circulation**
  - **Glycan recognition is important for immunity ... pathogens are marked for destruction ... example of glycans as specific ligands for cell-microbe interactions**
  - **Glycan recognition is also important cell – cell interactions ... selectin family of adhesion molecules mediate interactions between blood cells and vascular cells in a variety of conditions**
Representative N- and O-Glycans

O-linked Glycan:

N-linked glycan:
Polysaccharides

Starch, cellulose & glycogen

- A number of polysaccharides are known in nature. Starch, cellulose and glycogen are most common.
- Starch from each plant may be different. Starch consists of two principal polysaccharides – amylose and amylopectin. Complete hydrolysis of both amylose and amylopectin yields D-glucose only. Different ways in which glucose is joined together yields different polysaccharides.
- Cellulose is plant skeletal polysaccharide. Cotton is almost pure cellulose. It is a linear polysaccharide of β-1,4-linked glucose units.
- Glycogen is made up of α-1,4- and α-1,6-linked D-glucose units.
Polysaccharides

Cellulose

A portion of Amylose

✓ Why is cellulose a skeletal material and amylose not?
Polysaccharides

- Cellulose geometry affords extensive inter-chain interactions (side-by-side and one over other)
Polysaccharides

- Amylose ($\alpha(1 \rightarrow 4)$-linked) geometry disfavors inter-chain interactions and favors intra-chain hydrogen bonding
Polysaccharides

- Many other polysaccharides also form helical structures, e.g., heparin, dermatan sulfate, hyaluronate, ...

Structure of heparin determined by NMR and molecular modeling in which each IdoAp residue is either in $^1C_4$ form (A) or in $^2S_0$ form (B) {Taken from Mulloy et al. (1993) Biochem. J. 293, 849-855}. This does not imply that all IdoAp residues are always either $^1C_4$ or $^2S_0$. See text for details.
Glycosaminoglycans

GAGs are heterogeneous, polydisperse, acidic polysaccharides