Principles of Biochemistry
Fourth Edition

Chapter 8
Carbohydrates

Structures of Monosaccharides
8.1 Monosaccharides are chiral compounds
8.2 Cyclization of Aldoses and ketoses
8.3 Conformation of Monosaccharides
8.4 Derivatives of Monosaccharides

Disaccharides and Polysaccharides
8.5 Disaccharides and Other Glycosides
8.6 Polysaccharides
8.7 Glycoconjugates
Chapter 8 - Carbohydrates

- Carbohydrates ("hydrate of carbon") have empirical formulas of \((\text{CH}_2\text{O})_n\), where \(n \geq 3\)
- **Monosaccharides** one monomeric unit
- **Oligosaccharides** ~2-20 monosaccharides
- **Polysaccharides** > 20 monosaccharides
- **Glycoconjugates** linked to proteins or lipids

8.1 Most Monosaccharides are Chiral Compounds

- **Aldoses** - polyhydroxy aldehydes
- **Ketoses** - polyhydroxy ketones
- **Trioses** (3 carbon) - smallest monosaccharides

\[ \text{HO-CH-CH}_2\text{OH} \quad \text{H-C-OH} \quad \text{CH}_2\text{OH} \]

\[ \text{L-Glyceraldehyde} \quad \text{D-Glyceraldehyde} \quad \text{Dihydroxyacetone} \]
Aldotriose (Glyceraldehyde) is Chiral

Carbon-2 of Glyceraldehyde is chiral.
L-isomer: OH left
D-isomer: OH right
Enantiomers and Epimers

**Enantiomers**
- mirror image pairs (all chiral centers inverted)

**Epimers**
- differ at only one chiral center
8.2 Cyclization of Aldoses and Ketoses

(a) $\text{H}^+ \rightarrow \text{Aldehyde}$

$\text{R}_1\text{C}^=\text{O} \text{H} \leftrightarrow \text{H}_2\text{O} \text{R}_1\text{C}^=\text{H}$

$\text{R}_1\text{C}^=\text{H}$

Alcohol

(b) $\text{H}^+ \rightarrow \text{Ketone}$

$\text{R}_1\text{C}^=\text{O} \text{H} \leftrightarrow \text{H}_2\text{O} \text{R}_1\text{C}^=\text{R}_2$ $\text{R}_1\text{C}^=\text{R}_2$

Alcohol

Hemiacetal (chiral)

Hemiketal (chiral)
Cyclization of D-glucose to form glycopyranose

Pyran = 6-membered ring with oxygen

Furan = 5-membered Ring with oxygen
8.3 Conformations of Monosaccharides (Ribofuranoses)

Conformations of $\beta$-D-glucopyranose

Which is more stable?
1,3-Diaxial Interactions in β-D-glucopyranose (pyranoses)

Top conformer is more stable (no 1,3 interactions)

What is the order of the ring stability of the β-D-isomers of Glc, Gal and Man?

8.4 Derivatives of Monosaccharides

A. Sugar phosphates
B. Deoxy sugars
C. Amino sugars
D. Sugar alcohols
E. Sugar acids
F. Vitamin C

| TABLE 8.1: Abbreviations for some monosaccharides and their derivatives |
|--------------------|-------------------|
| Monosaccharide or derivative | Abbreviation |
| Pentoses           |                  |
| Ribose             | Rib              |
| Xylose             | Xyl              |
| Hexoses            |                  |
| Fructose           | Fru              |
| Galactose          | Gal              |
| Glucose            | Glc              |
| Mannose            | Man              |
| Deoxy sugars       |                  |
| Aldose             | Abe              |
| Fucose             | Fuc              |
| Amino sugars       |                  |
| Glucosamine        | GlcN             |
| Galactosamine      | GalN             |
| N-Acetylglucosamine| GlcNAc           |
| N-Acetylgalactosamine| GalNAc       |
| N-Acetylneuraminic acid| NeuNAc   |
| N-Acetylmannosamine| ManNAc           |
| Sugar acids        |                  |
| Glucuronic acid    | GlcUA            |
| Iduronic acid      | IduA             |

Table 8.1: Principles of Biochemistry, 4/e
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A. Sugar Phosphates (Intermediates in Glc, Rib or Glycogen Metabolism)

Dihydroxyacetone phosphate

\[
\text{CH}_2\text{OH} \quad \text{CH}_2\text{OPO}_3^2
\]

D-Glyceraldehyde 3-phosphate

\[
\text{H} \quad \text{CH}_2\text{OPO}_3^2
\]

\[\text{\textbullet \ D}_3\text{POCH}_2\]

\[\alpha-D-\text{Ribose} 5\text{-phosphate}\]

\[\alpha-D-\text{Glucose} 6\text{-phosphate}\]

\[\alpha-D-\text{Glucose} 1\text{-phosphate}\]

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B. Deoxy Sugars (Deoxy-D-Ribose is a Structural Components of DNAs)

\[\beta-2\text{-Deoxy-D-ribose}\]

\[\alpha-L\text{-Fucose (6-Deoxy-L-galactose)}\]

DNA structure

Synthesized from D-ribose nucleotides using NADPH as a reducing agent
C. Amino Sugars

Amino sugars of glucose and galactose occur commonly in glycoconjugates (glycans; glycoproteins)

D. Sugar Alcohols (polyhydroxy alcohols)

Sugar alcohols: carbonyl group is reduced by 2e-

Glyceraldehyde \( \text{C}_3\text{H}_8\text{O}_3 \) vs

Glycerol \( \text{C}_3\text{H}_6\text{O}_3 \) ⇌ TG component
E. Sugar Acids

Carboxylic Acids Produced by:

C-1 oxidation \(\Rightarrow\) aldonic acid
Glucono-\(\delta\)-lactone – Metabolic Intermediate)

C-6 oxidation \(\Rightarrow\) alduronic acid
Glucuronate – glycan structural component)

F. Ascorbic Acid (Vitamin C)

• L-Ascorbic acid is derived from D-glucuronate
8.5 Disaccharides and Other Glycosides

**Glycosidic bond** – chiral bond used to link monosaccharides together to form glycosides

![Glycosidic bond](image)

A. Structures of Disaccharides

- **β anomer of maltose**
  \((α-D-Glucopyranosyl-1\rightarrow4)β-D-glucopyranose\)

- **β anomer of cellobiose**
  \((β-D-Glucopyranosyl-1\rightarrow4)β-D-glucopyranose\)

- **α anomer of lactose**
  \((β-D-Galactopyranosyl-1\rightarrow4)α-D-glucopyranose\)

- **Sucrose**
  \((α-D-Glucopyranosyl-1\rightarrow2)β-D-fructofuranose\)
B. Reducing and Nonreducing Sugars

- Monosaccharides and most disaccharides are hemiacetals (contain a reactive carbonyl group)
- This carbonyl group reduces metal ions (Cu$^{2+}$, Ag$^+$) \( \Rightarrow \) reducing sugars
- Glc, Maltose, cellobiose and lactose are reducing sugars (free reactive carbonyl)
- Sucrose is not reducing even though Glc and Fru are reducing monosaccharides

C. Nucleosides and Other Glycosides

Anomeric carbons of sugars can form glycosidic linkages with alcohols, amines and thiols

N-Glycosides - nucleosides attached via a ring nitrogen in a glycosidic linkage
8.6 Polysaccharides

**Homoglycans** - one type of monosaccharide

**Heteroglycans** - more than one type

### Table 8.2: Structures of some common polysaccharides

<table>
<thead>
<tr>
<th>Polysaccharide</th>
<th>Component(s)</th>
<th>Linkage(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Storage homoglycans</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Starch</td>
<td>Glc</td>
<td>α-(1→4)</td>
</tr>
<tr>
<td>Amylose</td>
<td>Glc</td>
<td>α-(1→4)</td>
</tr>
<tr>
<td>Amylopectin</td>
<td>Glc</td>
<td>α-(1→4), α-(1→6) (branches)</td>
</tr>
<tr>
<td>Glycogen</td>
<td>Glc</td>
<td>α-(1→4), α-(1→6) (branches)</td>
</tr>
<tr>
<td><strong>Structural homoglycans</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cellulose</td>
<td>Glc</td>
<td>β-(1→4)</td>
</tr>
<tr>
<td>Chitin</td>
<td>GlcNAc</td>
<td>β-(1→4)</td>
</tr>
<tr>
<td><strong>Heteroglycans</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glycosaminoglycans</td>
<td>Disaccharides (amino sugars, sugar acids)</td>
<td>Various</td>
</tr>
<tr>
<td>Hyaluronic acid</td>
<td>GlcUA and GlcNAc</td>
<td>β-(1→3), β-(1→4)</td>
</tr>
</tbody>
</table>

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**A. Starch and Glycogen**

**Starch** (plants) & **glycogen** (animals) are polymers of Glc with α(1→4) linkages

**Starch**: amylose (unbranched) & amylopectin (branched via α(1→6) linkages)

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Figure 8-22a: Principles of Biochemistry 4/e © 2006 Prentice Hall, Inc.
**Conformation of amylose**

Assumes a left-handed helical conformation in water

Hydrated well with H2O

No intermolecular H-bonds

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**Structure of amylopectin**

**Glycosidases**
- Exo-glycosidase
  - Cleaves terminal bond
- Endo-glycosidase
  - Cleaves internal bond

**Enzymes**
- Lysozyme
- α-Amylase
- β-Amylase
- α-Amylase
- β-Amylase
B. Cellulose (top) and Chitin (bottom)

H-Bonds hold Cellulose fibrils together

H-Bonds
Intra-strand
C₃OH ⇆ O
C₆OH ⇆ C₂OH
Inter-strand
All other –OH used ⇆
Water Insoluble
8.7 Glycoconjugates

Glycoconjugates = polysaccharide covalently linked to proteins or peptides

Heteroglycans are used for the polysaccharide part of the glycoconjugate

Proteoglycans = Proteins $\rightarrow$ Heteroglycans
Peptidoglycans = Peptides $\rightarrow$ Heteroglycans
Glycoproteins = Heteroglycans $\rightarrow$ Proteins

A. Proteoglycans

Proteoglycans – glycosaminoglycan + protein

Glycosaminoglycans – Unbranched, Repeating disaccharides:

1. Amino sugar
   (D-galactosamine or D-glucosamine)
2. Sugar Acid
   (Alduronic acid w/ sulfated hydroxyl/amino groups)
Repeating disaccharide of hyaluronic acid

Amino sugar: GlcN\textsubscript{Ac} = N-acetylglucosamine

Sugar Acid: GlcUA = D-glucuronate

Cartilage Contains Proteoglycan (Bottle-Brush Structure) and Collagen Fibrils

Proteoglycans (core proteins with glycosaminoglycan chains attached) Central strand of hyaluronic acid

Hydrated Shock Absorbers of Extracellular Matrix
B. Peptidoglycans (Bacterial cell walls)

Peptidoglycans = Heteroglycan + peptides

Heteroglycan unbranched, alternating disaccharide \([\text{GlcNAc} \rightarrow \text{N-acetylmuramic acid}]\) by a \(\beta-(1 \rightarrow 4)\) linkage

Structure of the peptidoglycan

(S. aureus Cell Wall)

Tetrapeptide linked to every MurNAc residue by amide bond
Covalently Linked L- and D- Amino Acids w/ nonstandard Amide Bonds

C. Glycoproteins

Glycoprotein = Sugar + Proteins (O-Linked or N-Linked Glycosidic Bonds)

Glycoforms - proteins with identical amino acid sequences but different oligosaccharide chains
Four subclasses of O-glycosidic linkages

(a) GalNAc-Ser/Thr (most common)

(b) 5-Hydroxylysine (collagen)

(c) Gal-Gal-Xyl-Ser- (proteoglycan)

(d) GlcNAc-Ser/Thr (less common)

Structures of N-linked oligosaccharides

(a) High Mannose

(b) Complex Chain

(c) Hybrid Chain