Carbohydrates are the major recognition molecules in many cell-cell interaction events in nature.

Carbohydrates- Chapter 10

• Introduction and definition monosaccharides
• Aldoses and Ketoses
• Cyclic glycosyl residues, Haworth Projections
• Modified monosaccharides
• Glycosidic bond
• Disaccharides
• Polysaccharides
• Peptidoglycans
• Proteoglycans
• Glycoproteins
**Carbohydrates**

* ____________ organic molecule on earth
* ______________________________ (or yield these upon hydrolysis)
* __________: energy storage (glycogen, starch)
  metabolic intermediates (ATP, coenzymes)
  part of DNA & RNA
  structural elements in cell walls of bacteria, fungi & plants
  exoskeleton of arthropods
  extracellular matrix of animals
  cell-cell communication/signalling

• Individual monomeric units are called _________________ \((\text{CH}_2\text{O})_n\) where \(n \geq 3\)

• ________________ (contain 2-20 monosaccharides)
  ________________ (two linked monosaccharides)

• ________________ (> 20 monosaccharides)

• pure mono- & disaccharides are water-soluble, colorless in solution & sweet

• ___________________________: aldoses & ketoses
 carbohydrate polymer

 carbohydrate derivative where carbohydrate(s) are linked to a peptide, protein or lipid (i.e. proteoglycans, peptidoglycans, glycoproteins, glycolipids)

 study of role of glycans and glycoconjugates in living organisms

 compounds with the same molecular formula but different spatial arrangement of their atoms

 D & L sugars differ only in steric arrangement of atoms about central C. They are non-superimposable mirror images (i.e. ____________)

 They differ in orientation of the crystals, in directions in which solutions rotate polarized light, and in selectivity of reaction with other asymmetric molecules
Fischer projections of: (a) L- and D-glyceraldehyde, (b) dihydroxyacetone

(a) \[
\begin{align*}
&\text{L-Glyceraldehyde} \\
&\text{D-Glyceraldehyde}
\end{align*}
\]

(b) \[
\begin{align*}
&\text{Dihydroxyacetone}
\end{align*}
\]

See pg. 158

Stereo view of L- and D-glyceraldehyde

See pg. 158
<table>
<thead>
<tr>
<th>N (# of Cs)</th>
<th>Name</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>triose</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>tetrose</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>pentose</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>hexose</td>
<td></td>
</tr>
</tbody>
</table>

For sugars with >1 asymmetric (chiral) carbon, D & L refer to chiral C furthest from aldehyde (or ketone) & correspond to D & L glyceraldehyde

# of stereoisomers = $2^n$ where $n =$ # of chiral C’s

__________: stereoisomers that differ in configuration at only one chiral center

---

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Structure of the 3-6 carbon D-aldoses
(blue are the most common)

You must memorize the structures of all the sugars in blue!

(aldoses continued)
(aldoses continued)

Fisher projections of the 3 to 6 carbon
D-ketoses (blue structures are most common)

Ketotriose

\[
\begin{array}{c}
\text{CH}_2\text{OH} \\
\text{C} = \text{O} \\
\text{CH}_2\text{OH}
\end{array}
\]

Dihydroxyacetone

Ketotetrose

\[
\begin{array}{c}
\text{CH}_2\text{OH} \\
\text{C} = \text{O} \\
\text{H} - \text{C} - \text{OH} \\
\text{CH}_2\text{OH} \\
\text{d-erythrose}
\end{array}
\]
(ketoses continued)

Ketopentoses

\[
\begin{align*}
\text{CH}_2\text{OH} & \quad \text{CH}_2\text{OH} \\
\text{C} & \quad \text{C} \\
\text{H} & \quad \text{H} \\
\text{C} & \quad \text{C} \\
\text{OH} & \quad \text{OH} \\
\text{d-Ribulose} & \quad \text{d-Xylulose}
\end{align*}
\]

Ketohexoses

\[
\begin{align*}
\text{CH}_2\text{OH} & \quad \text{CH}_2\text{OH} & \quad \text{CH}_2\text{OH} & \quad \text{CH}_2\text{OH} \\
\text{C} & \quad \text{C} & \quad \text{C} & \quad \text{C} \\
\text{H} & \quad \text{H} & \quad \text{H} & \quad \text{H} \\
\text{C} & \quad \text{C} & \quad \text{C} & \quad \text{C} \\
\text{OH} & \quad \text{OH} & \quad \text{OH} & \quad \text{OH} \\
\text{d-Psicose} & \quad \text{d-Fructose} & \quad \text{d-Tagatose} & \quad \text{d-Sorbose}
\end{align*}
\]
Cyclization of Aldoses and Ketoses

Reaction of an alcohol with:
(a) An aldehyde to form a hemiacetal
(b) A ketone to form a hemiketal

See pg. 159-160

Carbohydrates- Chapter 10

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(a) Pyran and (b) Furan ring systems

(a) Six-membered sugar ring is a ____________

(b) Five-membered sugar ring is a ____________

Cyclization of D-glucose to form glycopyranose

See pg. 159-160
(cyclization of D-glucose, continued)

Haworth Projection

- Reaction of C-5 hydroxyl with one side of C-1 gives α, reaction with the other side gives β

* anomeric carbon
* α and β refer to the anomeric configurations

See Fig. 10.3

![Haworth Projection Diagram]

---

**α-β-Glucopyranose (Haworth projection)**

**β-β-Glucopyranose (Haworth projection)**

---

**α-β-Fructofuranose (a cyclic form of fructose)**

**α-β-Fructofuranose (a cyclic form of fructose)**

---

Fig. 10.4
Aldoses where $C_n \ (n \geq 5)$ or ketoses ($n \geq 6$) yield cyclic hemiacetals (or hemiketals) in solution

6 member ring = ___________
5 member ring = ___________

_________ C = most oxidized C of cyclic monosaccharide. It is chiral (i.e. $\alpha$ or $\beta$) = anomeric configuration

*** In solution the ring & linear form of monosaccharides are in equilibrium!
Example: D-glucose at 31°C
64% $\beta$-D-pyranose
36% $\alpha$-D-pyranose
< 1% furanose or linear
Cyclization of D-ribose to form $\alpha$- and $\beta$-D-ribopyranose and $\alpha$- and $\beta$-D-ribofuranose

Continued on next slide

(Cyclization of D-ribose continued)

Continued next slide
(Cyclization of D-ribose continued)

31°C at equilibrium

Conformations of Monosaccharides

Conformations of $\beta$-D-ribofuranose

Ten possible envelope & ten possible twist conformations

see Fig. 10.5

$\alpha$-D-Ribopyranose (Haworth projection) $\beta$-D-Ribopyranose (Haworth projection) $\alpha$-D-Ribofuranose (Haworth projection) $\beta$-D-Ribofuranose (Haworth projection)

21.5% 58.5% 6.5% 13.5% <1% open chain
Conformations of $\beta$-D-glucopyranose

*Axial substituent: perpendicular to plane of ring

** Equatorial substituent: parallel to plane of ring

2 possible conformations (generally more stable)

6 possible conformations

(b) Stereo view of chair (left), boat (right)

Conformations of $\beta$-D-glucopyranose

- Top conformer is more stable because it has the bulky hydroxyl substituents in equatorial positions (less steric strain)
Carbohydrates- Chapter 8

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Derivatives of Monosaccharides

• Many sugar derivatives are found in biological systems
• Some are part of monosaccharides, oligosaccharides or polysaccharides
• These include sugar phosphates, deoxy and amino sugars, sugar alcohols and acids
Be sure to know these abbreviations

Abbreviations for some monosaccharides and their derivatives

<table>
<thead>
<tr>
<th>Monosaccharide or derivative</th>
<th>Abbreviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pentoses</td>
<td>Rib</td>
</tr>
<tr>
<td>Ribose</td>
<td>Rib</td>
</tr>
<tr>
<td>Xylose</td>
<td>Xyl</td>
</tr>
<tr>
<td>Hexoses</td>
<td>Fru</td>
</tr>
<tr>
<td>Fructose</td>
<td>Gal</td>
</tr>
<tr>
<td>Galactose</td>
<td>Gle</td>
</tr>
<tr>
<td>Glucose</td>
<td>Man</td>
</tr>
<tr>
<td>Manrose</td>
<td>Man</td>
</tr>
<tr>
<td>Deoxy sugars</td>
<td>Abe</td>
</tr>
<tr>
<td>Aboqueose</td>
<td>Abe</td>
</tr>
<tr>
<td>Fucose</td>
<td>Fuc</td>
</tr>
<tr>
<td>Amino sugars</td>
<td>GlcN</td>
</tr>
<tr>
<td>Glucosamine</td>
<td>GalN</td>
</tr>
<tr>
<td>Galactosamine</td>
<td>GlcNAc</td>
</tr>
<tr>
<td>N-Acetylgalactosamine</td>
<td>GalNAc</td>
</tr>
<tr>
<td>N-Acetylneuraminic acid</td>
<td>NeuNAc</td>
</tr>
<tr>
<td>N-Acetylmuramic acid</td>
<td>MurNAc</td>
</tr>
<tr>
<td>Sugar acids</td>
<td>GlcUA GlcA</td>
</tr>
<tr>
<td>Glucuronic acid</td>
<td>GlcUA GlcA</td>
</tr>
<tr>
<td>Idoxuronic acid</td>
<td>IdoA IdoA</td>
</tr>
<tr>
<td>Galacturonic acid</td>
<td>GalUA GalA</td>
</tr>
</tbody>
</table>

see Fig. 10.7
Some important sugar phosphates

- In deoxy sugars an H replaces an OH

Deoxy sugars
• An amino group replaces a monosaccharide OH
• Amino group is sometimes acetylated
• Amino sugars of glucose and galactose occur commonly in glycoconjugates

Several ________________

• Amino and acetylamino groups are shown in red

\[\alpha-D-\text{Glucosamine}\]

\[N-\text{Acetyl-}\alpha-D-\text{galactosamine}\]
Sialic acids (e.g. neuraminic acid) are important in animal glycoproteins (formed from ManNAc + pyruvate)

(polyhydroxy alcohols)

• Sugar alcohols: carbonyl oxygen is reduced

Several sugar alcohols
• Sugar acids are carboxylic acids
• Produced from aldoses by:
  (1) Oxidation of C-1 to yield an aldonic acid
  (2) Oxidation of the highest-numbered carbon to an alduronic acid

Sugar acids derived from glucose
(example of an aldonic acid)

A lactone is a cyclic ester in organic chemistry. It is the condensation product of an alcohol group and a carboxylic acid group in the same molecules.
(continued)
(example of an alduronic acid)

\[ \text{Carbohydrates- Chapter 10} \]

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- Proteoglycans
- Glycoproteins
Disaccharides and Other Glycosides

- Primary structural linkage in all polymers of monosaccharides
- Glucose provides the anomeric carbon
- A general term meaning that a carbohydrate provides the anomeric carbon

Glucopyranose + methanol yields a glycoside

Under acidic conditions, alcohols, amines or thiols can condense with the anomeric C to form a glycosidic bond
Carbohydrates - Chapter 8

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Structures of Disaccharides

Structures of (a) maltose, (b) cellobiose

(a) β-anomer of maltose
(α-D-Glucopyranosyl-(1→4)-β-D-glucopyranose)

(b) β-anomer of cellobiose
(β-D-Glucopyranosyl-(1→4)-β-D-glucopyranose)

___________ is a hydrolysis product of amylose (starch)

___________ is a degradation product of cellulose

see Fig. 10.10
Structures of Disaccharides (continued)

Structures of (c) lactose, (d) sucrose

(c) \[\beta-D-Galactopyranosyl-(1\rightarrow4)-D-glucopyranose\]

\[\text{\(\beta\)-anomer of lactose}\]

(d) \[\text{Sucrose}\]

\[\text{(n-D-Glucopyranosyl-(1\rightarrow2)-D-fructofuranoside)}\]

\[\text{see Fig. 10.10}\]

\[\text{\(\beta\)-anomer of sucrose}\]

\[\text{Fructose}\]

\[\text{(D-Fructofuranoside)}\]

__lactose__ is an abundant disaccharide in milk

__sucrose__ is table sugar, most abundant disaccharide in nature, synthesized only in plants

Reducing and Nonreducing Sugars

- Carbohydrates with a reactive carbonyl (i.e. aldoses with free C1) are called __reducing__ because they can reduce metal ions (e.g. Cu\(^{2+}\), Ag\(^{+}\))

- Carbohydrates with no free anomeric Carbon are called __nonreducing__ (e.g. sucrose)

See Pg. 161
Nucleosides and Other Glycosides

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

- ____________: nonsugar molecule attached to the anomeric sugar carbon

- ____________: compound containing glycosidic bonds

- _________ + ________ = _____________

Structures of three glycosides

(a) Guanosine

(b) Vanillin β-D-glucoside

(c) β-D-Galactosyl 1-glycerol

nucleoside flavor
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Polysaccharides

• __________ - homopolysaccharides containing only one type of monosaccharide

• __________ - heteropolysaccharides containing residues of more than one type of monosaccharide

• Lengths and compositions of a polysaccharide may vary within a population of these molecules
Starch and Glycogen

- D-Glucose is stored intracellularly in polymeric forms
- Plants and fungi - starch
- Animals - glycogen
- Starch is a mixture of amylose (unbranched) and amylopectin (branched)

Structure of amylose

(a) Amylose is a linear polymer of D-glucose in an $\alpha$-1,4-linkage; DP of 100-1000

(b) Assumes a left-handed helical conformation in water

DP: degree of polymerization

See Fig. 10.12
Structure of amylopectin

Amylopectin is amylose strands connected by an α-1,6-linkage; DP of 300-6000

Comparison of between amylopectic and glycogen

• Both are energy storage forms of glucose

• Both are strands of α-1,4-linked glucose connected by α-1,6-linkages

• Amylopectin: found in plants; DP 300-6000, crystallin, α-1,6-linkages branches occur 1/25 residues

• Glycogen: found in animals; DP ≤ 50,000, NOT crystallin, α-1,6-linkages branches occur 1/8 to 1/12 residues
Action of $\alpha$- and $\beta$-amylase on amylopectin (both cleave $\alpha$-1,4-glucan)

- $\alpha$-amylase cleaves random internal $\alpha$-(1-4) glucosidic bonds (endoglycanase)
- $\beta$-amylase acts on nonreducing ends, exoglycosidase, releases dimers

Cellulose: most abundant organic molecule on earth, DP 300 - $>$15,000, synthesized by plants & some bacteria, cell wall polysaccharide

Structure of cellulose ($\beta$-1,4-linked glucose homopolymer)

(a) Chair conformation

(b) Haworth projection

see Fig. 10.14
Stereo view of cellulose fibrils
Individual cellulose chains interact to give cellulose microfibrils and bundles
• Intra- and interchain H-bonding gives strength

Cellulose chains interact via H-bonds to form microfibrils and fibers.
In plants a cellulose synthase rosette complex of 6 X 6 cellulose synthase subunits synthesizes a cellulose microfibril of 36 individual cellulose molecules bound together by H-bonds.

Doblin et al., 2002, Plant Cell Physiol. 43:1407
**Structure of chitin:** exoskeleton of spiders & crustaceans, & in cell wall sf some fungi & algae

- Repeating units of $\beta$-(1-4)GlcNAc residues

![Structure of Chitin Diagram](image)

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  - Proteoglycans
  - Glycoproteins
Peptidoglycans

- **Peptidoglycans** - heteroglycan chains linked to peptides
- Major component of bacterial cell walls
- Heteroglycan composed of alternating GlcNAc and N-acetylmuramic acid (MurNAc)
- $\beta-(1 \rightarrow 4)$ linkages connect the units

Glycan moiety of peptidoglycan

MurNAc found only in bacteria and consists of GlcNAc connected at C-3 by an ether linkage to lactate.
Fig. 8.16 A schematic representation of the peptidoglycan in *Staphylococcus aureus*.

Yellow: polysaccharide
Red: tetrapeptide
Blue: pentaglycine

Structure of the peptidoglycan of *Staphylococcus aureus* (gram positive bacteria cell wall peptidoglycan)

(a) Repeating disaccharide unit, (b) Cross-linking of the peptidoglycan macromolecule

(to tetrapeptide, next slide)

Review section pgs. 132-134, Chapter 8
Transpeptidase acts here

Penicillin inhibits a transpeptidase involved in bacterial cell wall formation

- Structures of penicillin and -D-Ala-D-Ala
- Penicillin structure resembling -D-Ala-D-Ala is shown in red
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- Lipo-oligosaccharides
- Glycoproteins

Proteoglycans

- ___________________ – glycosaminoglycan (~95%)-carbohydrate-protein conjugates. Often found in ECM. Function as lubricants, cell-cell adhesion, messengers, & give tensile strength & elasticity to soft tissues

- ___________________ (GAGs)- unbranched heteroglycans of repeating disaccharides (many sulfated hydroxyl and amino groups)

- Disaccharide components include: (1) amino sugar (D-galactosamine or D-glucosamine), (2) an alduronic acid
Repeating disaccharide of hyaluronic acid

- GlcUA = D-glucuronate
- GlcNAc = N-acetylglucosamine

Hyaluronic acid is GAG not attached to protein
Types of GAGs

1. Not covalently attached to protein
   * Hyaluronic acid

2. Covalently attached to proteins (i.e. present in proteoglycans)
   * Heparin (and heparan sulfate)
   * Keratan sulfate
   * Chondroitin sulfate
   * Dermatan sulfate

Proteoglycan aggregate in cartilage

～150 GAGs:protein

Proteoglycans
(core proteins with glycosaminoglycan chains attached)

Central strand of hyaluronic acid

Noncovalent attachment

Core protein

Keratan sulfate

2 other GAGs not in this aggregate: heparan sulfate; heparin

Chondroitin sulfate

Link proteins
Lipo-oligosaccharides and oligosaccharides can serve as signal molecules

Specific lipo-oligosaccharides are produced by nitrogen-fixing bacteria that interact specifically with certain plants (i.e. legumes) to form root nodules. These lipo-oligosaccharides resemble chitin oligomers with specific modifications.

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Glycoproteins

• Proteins that contain covalently-bound oligosaccharides
• O-Glycosidic and N-glycosidic linkages
• Oligosaccharide chains exhibit great variability in sugar sequence and composition
• _______________ - proteins with identical amino acid sequences but different oligosaccharide chain composition

Four subclasses of _______________ linkages

(1) GalNAc-Ser/Thr (most common)
(2) 5-Hydroxylysine (Hyl) to D-galactose (unique to collagen)
(3) Gal-Gal-Xyl-Ser-core protein (in proteoglycans)
(4) GlcNAc to a single serine or threonine
**O-Glycosidic and N-glycosidic linkages**

Consensus sequence for N-glycosylation: Asn-X-Ser/Thr

See Fig. 10.15

**Four subclasses of O-glycosidic linkages**

(a) NeupNAc α-(2 → 3) GalNAc β-(1 → 3) GalNAc — Ser/Thr

(b) — Gal — Hyl

(c) — Gal — Gal — Xyl — Ser

(d) GlcNAc — Ser/Thr

See Fig. 10.23
Structures of N-linked oligosaccharides

(a) Man \(\alpha(1 \rightarrow 2)\) Man \(\alpha(1 \rightarrow 6)\) \(\alpha(1 \rightarrow 3)\) \(\beta(1 \rightarrow 4)\) GlcNAc \(\beta(1 \rightarrow 4)\) GlcNAc \(\rightarrow\) Asn

(b) SA \(\alpha(2 \rightarrow 3,6)\) Gal \(\beta(1 \rightarrow 4)\) GlcNAc \(\beta(1 \rightarrow 2)\) Man \(\alpha(1 \rightarrow 3)\) \(\beta(1 \rightarrow 4)\) GlcNAc \(\beta(1 \rightarrow 4)\) GlcNAc \(\rightarrow\) Asn

SA \(\alpha(2 \rightarrow 3,6)\) Gal \(\beta(1 \rightarrow 4)\) GlcNAc \(\beta(1 \rightarrow 2)\) Man \(\alpha(1 \rightarrow 6)\)

(continued)

(c) Gal \(\beta(1 \rightarrow 4)\) GlcNAc \(\beta(1 \rightarrow 2)\) Man \(\alpha(1 \rightarrow 3)\) \(\beta(1 \rightarrow 4)\) GlcNAc \(\beta(1 \rightarrow 4)\) GlcNAc \(\rightarrow\) Asn

Man \(\alpha(1 \rightarrow 3)\) \(\beta(1 \rightarrow 4)\) GlcNAc \(\beta(1 \rightarrow 4)\) GlcNAc \(\rightarrow\) Asn

Man \(\alpha(1 \rightarrow 6)\)

The oligosaccharides attached to proteins may alter physical properties such as size, shape, solubility, or stability, may effect folding, and/or may have biological roles

see Fig. 10.16
Why do blood transfusions sometimes cause death?

Reason discovered by Karl Landsteiner at University of Vienna in 1901.

All humans and many primates have **A, B, AB or O types** of oligosaccharides on the $N$-linked and $O$-linked oligosaccharides on the surface of their red blood cells (includes glycoproteins and glycolipids).

see Fig. 10.24

http://www.steve.gb.com/images/science/abo_glycolipids.png