CARBOHYDRATES OR SUGARS

• A group of naturally occurring aldehydes / ketones, formally composed of C atoms and H₂O molecules in a ratio equal or close to 1 : 1

  general formula: (CH₂O)ₙ ... or close

• Immense biological importance of carbohydrates:
  - blood group determinants
  - antigens, immune responses
  - cancer cell markers
  - energy storage & generation
  - nucleic acids, glycoproteins
  - materials & fibers
  - extracellular support matrices
  - genetic disease
SIMPLE SUGARS OR MONOSACCHARIDES

• Carbohydrates of general formula \((\text{CH}_2\text{O})_n\) (3 ≤ n ≤ 9) that possess a structure based on a linear polyhydroxy aldehyde (aldoses) or polyhydroxy ketone (ketose)

\[
\text{HOCH}_2-(\text{CHOH})_x-\text{CHO} \quad \text{HOCH}_2-(\text{CHOH})_x-(\text{CO})-(\text{CHOH})_y-\text{CH}_2\text{OH}
\]

an aldose \quad \text{a ketose}

• Triose, tetrose, pentose, hexose, heptose, octose, nonose: a monosaccharide that incorporates a total of 3, 4, 5, 6, 7, 8 or 9 carbon atoms

Note: most monosaccharides of biological importance contain 5 or 6 C atoms. Monosaccharides incorporating more that 6 C atoms are known, but they are rare, and rarity increases with an increasing number of C atoms.
STEREOISOMERISM IN MONOSACCHARIDES

• Monosaccharides as chiral molecules due to the presence of multiple stereogenic centers

\[
\begin{align*}
\text{HOCH}_2\text{–(CHOH)}_x\text{–CHO} & \quad \text{HOCH}_2\text{–(CHOH)}_x\text{–(CO)–(CHOH)}_y\text{–CH}_2\text{OH} \\
\text{an aldose} & \quad \text{a ketose}
\end{align*}
\]

• Common ketoses of biological interest as compounds of the type \( \text{HOCH}_2\text{–(CHOH)}_x\text{–(CO)–CH}_2\text{OH} \)

• The vast majority of naturally occurring monosaccharides as chiral and enantiomerically pure substances
REPRESENTATION OF MONOSACCHARIDES

• Frequent use of Fischer projections to represent monosaccharides; e.g.:

\[\text{CHO} \quad \text{CHO} \quad \text{OH} \]
\[\text{H} \quad \text{H} \quad \text{OH} \]
\[\text{OH} \quad \text{OH} \quad \text{H} \]
\[\text{H} \quad \text{H} \quad \text{OH} \]
\[\text{H} \quad \text{OH} \quad \text{H} \]

- Ribose as a pentose; glucose and fructose as hexoses
- Ribose and glucose as aldoses; fructose as a ketose
GLYCERALDEHYDE: THE SIMPLEST ALDOPENTOSE

- D- and L-forms of glyceraldehyde:

\[
\begin{align*}
\text{CHO} & \quad \leftrightarrow \quad \text{enantiomers} \quad \rightarrow \\
\ast & \quad \text{D-(R)-(+)glyceraldehyde} \\
& \quad \text{(OH on the right)} \\
\ast & \quad \text{L-(S)-(−)glyceraldehyde} \\
& \quad \text{(OH on the left)}
\end{align*}
\]

- D-Glyceraldehyde as the formal progenitor of all common monosaccharides
STEREOCHEMICAL PROGENY OF COMMON ALDOSES

key stereogenic center

glyceraldehyde (aldotriose)

(aldotetroses)

threose

(aldopentoses)

xylose

(aldohexoses)

allose

altrose

glucose

mannose

gulose

idose

galactose

talose
Most natural monosaccharides belong to the D-stereochemical series. The much rarer L-sugars are produced primarily by fungal or microbial organisms for specialized purposes.
STRUCTURE OF MONOSACCHARIDES: FORMATION OF HEMIACETALS

• Molecules incorporating both an alcohol and an aldehyde or ketone functionality tend to exist as cyclic hemiacetals — if a 5- or 6-membered ring can thus be formed; e.g.:
HEMIACETAL FORMS OF D-RIbose AND D-GLUCOSE

Ribose (building block of RNA):

Fischer projection of D-ribose

\[
\text{CHO} \\
\text{H} \quad \text{OH} \\
\text{H} \quad \text{OH} \\
\text{H} \quad \text{OH} \\
\text{OH}
\]

aldehyde (carbonyl) form of D-ribose

common hemiacetal form of D-ribose (preferred)

Glucose:

Fischer projection of D-glucose

\[
\text{CHO} \\
\text{H} \quad \text{OH} \\
\text{H} \quad \text{OH} \\
\text{H} \quad \text{OH} \\
\text{OH}
\]

aldehyde (carbonyl) form of D-glucose

common hemiacetal form of D-glucose (preferred)

wavy line means that either configuration is possible
FURANOSE AND PYRANOSE FORMS OF MONOSACCHARIDES

Anomeric position or anomeric carbon: the one sustaining the hemiacetal function (arrows above)
POSSIBLE EXISTENCE OF TWO DIASTEREOISOMERS OF
THE HEMIACETAL FORM OF A MONOSACCHARIDE

alpha- and beta-anomers of a monosaccharide

\[ \alpha\text{-anomer of D-ribofuranose (} \alpha\text{-D-ribofuranose)} \]
\[ \beta\text{-anomer of D-ribofuranose (} \beta\text{-D-ribofuranose)} \]
\[ \alpha\text{-anomer of D-glucopyranose (} \alpha\text{-D-glucopyranose)} \]
\[ \beta\text{-anomer of D-glucopyranose (} \beta\text{-D-glucopyranose)} \]

alpha-anomer: the OH group of the hemiacetal moiety is \textit{trans} relative to
the CH\textsubscript{2}OH group on the carbon that defines the D / L series

beta-anomer: the OH group of the hemiacetal moiety is \textit{cis} relative to
the CH\textsubscript{2}OH group on the carbon that defines the D / L series
**CONFORMATIONS OF PYRANOSES; e.g., GLUCOSE**

under appropriate conditions, it is possible to obtain pure \( \alpha \)-D-glucopyranose or pure \( \beta \)-D-glucopyranose (crystallization). These two anomeric forms of glucopyranose, being diastereomeric, differ in solubility, melting point (146 °C for the \( \alpha \)-anomer, 150 °C for the \( \beta \)-anomer), and optical rotation (\([\alpha]_D^{25} = +112^\circ\) for the \( \alpha \)-anomer, + 19° for the \( \beta \)-anomer).
all forms will be present at equilibrium in a solution of ribose, although one especially thermodynamically favorable form may be the dominant (or even the exclusive) species (β-D-ribofuranose in this case)
INTERCONVERSION OF PYRANOSE AND FURANOSE FORMS AND OF α- and β-ANOMERS: GLUCOSE

at equilibrium in H₂O: 1 ≈ 64%; 2 ≈ 36%; 3 + 4 < 1%
MUTAROTATION OF MONOSACCHARIDES:
THE CASE OF GLUCOSE

if one prepares an aqueous solution of either pure anomer of glucose, and one measures the specific optical rotation of the solution over time, one observes that the rotation of a solution of pure \( \alpha \)-anomer, initially equal to +112°, drops to a final value of ca. +53°, while that of a solution of pure \( \beta \)-anomer, initially equal to +19°, increases to a final value of ca. +53°.

This phenomenon is termed mutarotation (="rotation change") and it is due to equilibration of the anomers. At equilibrium, the solution contains a mixture of ca. 64% of \( \beta \)-anomer (all equatorial, more stable) and ca. 36% of \( \alpha \)-anomer:

\[
(0.64 \times 19°) + (0.36 \times 112°) = 12.2° + 40.3° = +52.5°
\]
carbohydrates contain both OH and C=O groups (often “masked” as hemiacetals); therefore, their reactivity will parallel that of alcohols, hemiacetals, and C=O compounds:
much like a hemiacetal will react with an alcohol under acidic conditions to form an acetal, so a monosaccharide will react under the same conditions to form an acetal termed a glycoside (riboside, glucoside, ....)

\[
\begin{align*}
\text{HO} & \quad \text{CH}_3\text{OH} & \quad \text{CH}_3\text{OH} \\
\text{HO} & \quad \text{HCl} & \quad \text{HCl} \\
\text{HO} & \quad \text{H}_2\text{O} & \quad \text{H}_2\text{O} \\
\text{alpha- or beta-d-ribofuranose} & & \alpha\text{-methyl-d-ribofuranoside} \\
\text{alpha- or beta-d-glucopyranose} & & \beta\text{-methyl-d-glucopyranoside}
\end{align*}
\]

\[
\begin{align*}
\text{HO} & \quad \text{CH}_3\text{OH} & \quad \text{CH}_3\text{OH} \\
\text{HO} & \quad \text{HCl} & \quad \text{HCl} \\
\text{HO} & \quad \text{H}_2\text{O} & \quad \text{H}_2\text{O} \\
\text{alpha- or beta-d-glucopyranose} & & \alpha\text{-methyl-d-glucopyranoside} \\
\text{alpha- or beta-d-glucopyranose} & & \beta\text{-methyl-d-glucopyranoside}
\end{align*}
\]

Note: the mechanism of these reactions is analogous to that seen earlier for simpler hemiacetals.
HYDROLYSIS OF GLYCOSIDES IN AQUEOUS ACID

much like an acetal undergoes hydrolysis in aqueous acid, so a glycoside can be hydrolyzed back to a “free” sugar under aqueous acidic conditions

\[
\begin{align*}
\text{a- or } \beta\text{-methyl-}D\text{-glucopyranoside} & \quad \xrightarrow{\text{aqueous } HCl} \quad \alpha\text{- and } \beta\text{-}D\text{-glucopyranoses}
\end{align*}
\]

\[\text{note: the mechanism of this reaction is analogous to that seen earlier for simpler acetals}\]
REDDUCING AND NON-REDDUCING SUGARS: THE TOLLENS TEST

Reminder: an acetal is stable in the presence of bases, even strong ones like carbanions

Note: the mechanism of the Tollens reaction is complex and will not be discussed in CHEM 203

Importance of the Tollens test in the structural elucidation of naturally occurring carbohydrates
• Oxidation to aldonic or aldaric acids

\[ \text{CHO} \quad \text{H} \quad \text{OH} \quad \text{HO} \quad \text{H} \quad \text{OH} \quad \text{COOH} \quad \text{HNO}_3 \quad \text{H}_2\text{O} \quad \text{CHO} \quad \text{H} \quad \text{OH} \quad \text{HO} \quad \text{H} \quad \text{OH} \quad \text{OH} \quad \text{Br}_2 \quad \text{H}_2\text{O} \]

D-glucaric acid: an aldaric acid
D-glucose
D-gluconic acid: an aldonic acid

• Reductions to alditols

\[ \alpha- \text{ or } \beta-\text{D-glucopyranose} \quad \leftrightarrow \quad \text{CHO} \quad \text{H} \quad \text{OH} \quad \text{HO} \quad \text{H} \quad \text{OH} \quad \text{COOH} \quad \text{HNO}_3 \quad \text{H}_2\text{O} \quad \text{CHO} \quad \text{H} \quad \text{OH} \quad \text{HO} \quad \text{H} \quad \text{OH} \quad \text{OH} \quad \text{NaBH}_4 \]

\( \alpha- \text{ or } \beta-\text{D-glucopyranose} \quad \leftrightarrow \quad \text{CHO} \quad \text{H} \quad \text{OH} \quad \text{HO} \quad \text{H} \quad \text{OH} \quad \text{COOH} \quad \text{HNO}_3 \quad \text{H}_2\text{O} \quad \text{CHO} \quad \text{H} \quad \text{OH} \quad \text{HO} \quad \text{H} \quad \text{OH} \quad \text{OH} \quad \text{NaBH}_4 \]

\( \text{CHO} \quad \text{H} \quad \text{OH} \quad \text{HO} \quad \text{H} \quad \text{OH} \quad \text{COOH} \quad \text{HNO}_3 \quad \text{H}_2\text{O} \quad \text{CHO} \quad \text{H} \quad \text{OH} \quad \text{HO} \quad \text{H} \quad \text{OH} \quad \text{OH} \quad \text{NaBH}_4 \]

\( \alpha- \text{ or } \beta-\text{D-glucopyranose} \quad \leftrightarrow \quad \text{CHO} \quad \text{H} \quad \text{OH} \quad \text{HO} \quad \text{H} \quad \text{OH} \quad \text{COOH} \quad \text{HNO}_3 \quad \text{H}_2\text{O} \quad \text{CHO} \quad \text{H} \quad \text{OH} \quad \text{HO} \quad \text{H} \quad \text{OH} \quad \text{OH} \quad \text{NaBH}_4 \]

D-glucitol, a.k.a. D-sorbitol (noncaloric sweetener)
REDUCTION OF KETOSES: FORMATION OF DIASTEREOMERIC ALDITOLS

\[ \alpha \text{- or } \beta \text{-d-fructofuranose} \leftrightarrow \text{free ketone} \]

\[ \text{NaBH}_4 \]

\[ \text{D-glucitol (D-sorbitol)} \]

\[ \text{D-mannitol} \]
FORMATION OF ETHERS BY WILLIAMSON REACTION

• Reducing sugars are generally poor substrates for the Williamson reaction and must first be converted into glycosides:

\[ \text{Reducing sugars} \rightarrow \text{glycosides} \]

- Mild modification of the Williamson reaction:

\[ \text{Reducing sugars} \rightarrow \text{glycosides} \]
POLYSACCHARIDES OR COMPLEX SUGARS

- Polysaccharides or complex sugars are polymers of monosaccharides arising through glycosylation of a monosaccharide with another monosaccharide.

- Disaccharides, trisaccharides, ... oligosaccharides (“a few” saccharides, typically 2-10 saccharide units), polysaccharides (more than ≈ 10 saccharide units).

- Important disaccharides: sucrose, lactose, maltose:

  ![Chemical structure of sucrose](image)

  **α-D-glucopyranose**  
  **β-D-fructofuranose**

  **Glycosylation**

  **Sucrose (table sugar):**
  A disaccharide
  
  **Note:** No hemiacetals; non-reducing.
IMPORTANT DISACCHARIDES: LACTOSE & MALTOSE

Lactose (found in milk): a disaccharide

Maltose: a disaccharide

Glycosylation

Hemiacetal: reducing
A TRISACCHARIDE: RAFFINOSE

- abundant in beans, broccoli, cabbage,…
- indigestible to humans
- readily fermented by microorganism colonizing the human intestine

yes, raffinose is the culprit
KEY POLYSACCHARIDES: AMYLOSE AND CELLULOSE

Amylose: a major component of starch

Cellulose: key structural material in plants (cotton ≈ 90%; wood ≈ 50%)
ACIDIC HYDROLYSIS OF POLYSACCHARIDES

Sucrose and lactose can be hydrolyzed to simpler carbohydrates (ultimately, to free monosaccharides) with dilute aqueous acid (hydrolysis of the acetal functions), while a monosaccharide cannot be converted to simpler sugars under the same conditions.
FORMATION OF GLYCOSYLAMINES

- a free monosaccharide reacts with aqueous ammonia to yield a glycosylamine

D-glucopyranose

\[ \text{NH}_3 \]

\[ \text{Schiff base form.} \]

\[ \text{glucosylamine: a glycosylamine} \]

likewise:

D-ribofuranose

\[ \text{NH}_3 \]

\[ \text{ribosylamine: a glycosylamine} \]

- relevance of glycosylamines to nucleic acid chemistry . . .
PYRIMIDINE AND PURINE: HETEROCYCLES OF LIFE

pyrimidine

uracil

thymine

cytosine

purine

adenine

guanine
RIBONUCLEOTIDES: COMPONENTS OF RNA

uracil → uridine

adenine → adenosine

cytosine → cytidine

guanine → guanosine
2-DESOXYRIBONUCLEOTIDES: COMPONENTS OF DNA

2-desoxycytidine

2-desoxyadenosine

2-desoxyguanosine

thymine → 2-desoxythymidine

2-desoxycytidine

2-desoxyguanosine