

Carbohydrates

- General formula $C_n(H_2O)_n$ (carbon-hydrates)
- Also known as saccharides or sugars
- They serve as energy stores or fuel
- They are components of DNA and RNA
- They are the primary component of cell walls of bacteria and plants
- They are linked to proteins and lipids to form key intermediates and regulators of physiological processes

Monosaccharides

- They are polyhydroxy aldehydes (aldose) or ketones (ketose).
- Carbon chain from 3 to 9 with general name of triose, hexose etc or aldohexose, ketohexose etc.
- Fischer projection formulas are written as linear C chains with the aldehyde numbered as C1 in aldoses and ketone as C2 in ketoses.
- Each monosaccharide (except dihydroxyacetone) has at least one chiral carbon. The highest numbered C is generally achiral
- The orientation of the $-OH$ around the chiral carbons determines the identity of the sugar.

Stereoisomers

- The (n-1) C determines the enantiomeric form of the sugar. If the hydroxyl on C_{n-1} is to the left, it is the L-isoform; if the n-1 hydroxyl is to the right, it is the D isoform. Enantiomers are mirror-images of each other. All sugars in biomolecules are in the D-form
- All of the aldoses that possess the same number of C atoms are called as diastereomers. They are not mirror images of each other.
- Usually there is n-2 chiral carbons in hexoaldoses. And there are 2⁽ⁿ⁻²⁾ possible hexoaldose stereoisomers (enantiomers + diastereoisomers)
- Two sugars that differ in the orientation of only one hydroxyl are called as epimers of each other. Eg: glucose and galactose

Haworth Projections

- Alcohols react with aldehydes to form hemiacetals and with ketones to form hemiketals
- Most long-chain aldoses and ketoses form intramolecular hemiacetals / hemiketals to form 5-(furanose) or 6- (pyranose) membered ring structures.
- The ring-form depictions of monosaccharide structures are called Haworth projections. When converting Fischer to Haworth formulas follow the rule: right down
- Ring formation results in C1 becoming achiral. The α-anomer is when -OH is below and β-anomer is when -OH is above the plane of the ring
- Complete name of sugar includes: anomer, enantiomer, sugar identity and ring type. Eg: α-D-Glucopyranose

Reactions of monosaccharides

- Monosaccharides have a free carbonyl group which is prone to oxidation. Thus, monosaccharides reduce other compounds. Any sugar with a 'free' carbonyl C is called a reducing sugar
- A acetal can react with an alcohol or an amine to form an adduct with the removal of H₂O. The resulting bond with an alcohol results in an O-glycosidic linkage. Reaction with an amine results in a N-glycosidic bond
- O-glycosidic linkages can join one monosaccharide to another to form polymers. These are called as disaccharides, oligosaccharides or polysaccharides.
- Polysaccharides may be linear or branched. The repeating unit may be a monosaccharide or a disaccharide.

Structures to Memorize

- *Glyceraldehyde *Ribose *Glucose
- *Galactose *Dihydroxyacetone *Fructose
- *Lactose: galactose $\beta(1 \rightarrow 4)$ glucose
- *Sucrose: glucose $\alpha, \beta(1 \rightarrow 2)$ fructose (non-reducing sugar)
- *Amylose: glucose $\alpha(1 \rightarrow 4)$ glucose
- *Starch / Glycogen: glucose $\alpha(1 \rightarrow 4)$ glucose; branches by $\alpha(1 \rightarrow 6)$ linkages
- *Cellulose: glucose $\beta(1 \rightarrow 4)$ glucose

Important Modified Monosaccharides

- Glucosamine/Galactosamine: -OH on C2 is replaced by $-\text{NH}_2$
- The amines are usually esterified with methanol to form N-acetylglucosamine and N-acetylgalactosamine
- Glucuronic / galactouronic acid: C6 is oxidized to $-\text{COOH}$.
- These modified monosaccharides are abundantly found in mucopolysaccharides and glycosaminoglycans
- Neuraminose is a 9 C ketose. In sialic acid (N-acetylneuraminic acid) C1 is oxidized to COOH and C4 has a N-acetyl group. Sialic acid is the terminal sugar of oligosaccharides found on glycoproteins
- Sulfated polysaccharides: The $-\text{OH}$ on C4 or C6 may be sulfated ($-\text{OH}$ to $-\text{OSO}_3^-$) on several glycosaminoglycans. The degree of sulfation is variable

Complex Carbohydrates

- Disaccharides and polysaccharides formed by O-glycosidic linkages between monosaccharides are called complex carbohydrates
- In sucrose, the carbonyl carbons of both glucose and fructose participate in the O-glycosidic linkage, so it is a non-reducing sugar.
- Lactose formed from glucose and galactose is the disaccharide of milk.
- Polysaccharides contain more than 2 monomeric sugars
- Homopolysaccharides are repeats of the same monomer, heteropolysaccharides contain a disaccharide repeating unit

Polysaccharides

- Storage polysaccharides: Starch and glycogen are polymers of glucose in α (1 \rightarrow 4) linkages with α (1 \rightarrow 6) branches. Starch is a mixture of amylose (linear) and amylopectin (branched). Glycogen is highly branched
- Structural polysaccharides: Cellulose makes up the cell wall of plant cells. It is a polymer of glucose in β (1 \rightarrow 4) linkages. Other eg: chitin, pectin.
- Mucopolysaccharides/glycosaminoglycans: Very viscous heteropolysaccharides found in extracellular cavities and connective tissue. Hyaluronic acid and chondroitin sulfate serve as lubricants for joints. Heparin is an anticoagulant.
- Glycosaminoglycans attach to proteins to form proteoglycans. Carbohydrates, rather than protein are the main component

Dietary Carbohydrates

- Digestion begins in the mouth: Saliva contains amylase which is specific for α (1 \rightarrow 4) glycosidic linkages.
- Complex carbohydrates are hydrolysed to their component monosaccharides in the small intestine by specific glycosidases on the epithelial cell lining.
- Deficiency of glycosidases results in reduced capacity to digest certain carbohydrates. Instead, gut bacteria metabolize the sugars liberating CO₂ and H₂ that cause gas and bloating. Eg: Lactose-intolerant people have lost the ability to synthesize lactase. One can rectify the problem by consuming glycosidase in the form of pills before a meal.
- Mammals lack cellulase and cannot digest vegetable fiber

Oligosaccharide Assembly

- Oligosaccharides are synthesized by the action of enzymes called glycosyl transferases.
- Many different glycosyl transferases, each specific for formation of a specific O-glycosidic linkage
- The monomeric sugar has to be activated in the form of a sugar nucleotide prior to attachment to the growing oligosaccharide
- Specificity of glycosyl transferases is demonstrated by human ABO blood groups. The basic O-type oligosaccharide antigen on RBC membranes is substituted with galNac by the action of N-acetylgalactosamine transferase to form A antigen. In individuals with the B antigen, galactosyl transferase adds on galactose to the oligosaccharide. The two enzymes differ by only 4 aa are absent in O-type individuals due to premature termination of polypeptide synthesis

Glycoproteins

- Glycoproteins are proteins with covalently attached oligosaccharide groups
- Most cell surface proteins as well as secreted proteins are glycoproteins with the oligosaccharide component essential for protein activity and function.
- Carbohydrates are linked to proteins by O-glycosidic linkages with ser or thr. They also form N-glycosidic linkages with Asn. Asn has to be in the seq NXS or NXT. No specific motif requirement for O-linked Ser / Thr.
- All N-linked oligosaccharides have a pentasaccharide core that grows to various oligosaccharide patterns. Two most common ones are the high-mannose type and complex type. The first sugar in O-linked oligosaccharides is usually glcNac.

Protein Glycosylation

- Specific glycosyltransferases are responsible for the glycosylation of proteins. Monomers are activated in the form of UDP- or GDP-sugar.
- **O-linked glycosylation:** Takes place in the golgi apparatus by the serial addition of monosaccharide units to a completed polypeptide chain
- **N-linked glycosylation:** Starts co-translationally in the ER lumen and processing continues in the golgi complex.
- A 14-unit oligosaccharide complex is first assembled on dolichol phosphate, a lipid present in the ER membrane

N-linked glycosylation (continued)

- The 14-unit oligosaccharide is transferred from dolichol phosphate to an acceptor Asn on the nascent protein in the ER
- The oligosaccharide is trimmed before the protein leaves the ER
- As the proteins traverse the different compartments of the golgi, their oligosaccharides are further processed to their final version.
- Oligosaccharide composition is important in protein targeting and protein folding