UNIVERSITY OF MEDICAL SCIENCES (UNIMED), ONDO FACULTY OF BASIC MEDICAL SCIENCES DEPARTMENT OF BIOCHEMISTRY

BIOCHEMISTRY LECTURES BY RASAQ, N.O

LECTURE CONTENT

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- **POLYSACCHARIDES**
- **STRUCTURAL POLYSACCHARIDES: CELLULOSE AND CHITIN**
- **BACTERIA CELL WALLS**
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- **PENICILLIN AND β-LACTAM ANTIBIOTICS AND BACTERIAL CELL WALL**
- **GLYCOSAMINOGLYCANS**
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- **CHONDROITIN SULPHATE**
- **OLIGOSACCHARIDES:SUCROSE, LACTOSE AND MALTOSE**
- **QUESTIONS AND ANSWER**

INTRODUCTION

- **Carbohydrates are defined as polyhydroxyl aldehyde or ketone and compounds that can give same on hydrolysis**
- **Monosaccharides (simple sugars) cannot be broken down into simpler sugars under mild conditions**
- **Oligosaccharides = "a few" - usually 2 to 10**
- **Polysaccharides are polymers of the simple sugars**

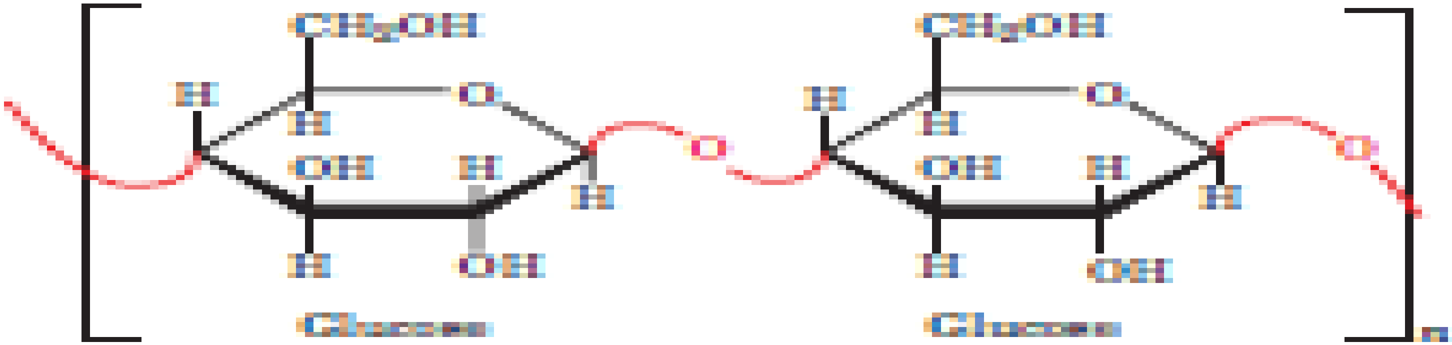
POLYSACCHARIDES

- **Nomenclature: homopolysaccharide vs. heteropolysaccharide**
- **Starch and glycogen are storage molecules**
- **Chitin and cellulose are structural molecules**
- **Cell surface polysaccharides are recognition molecules**

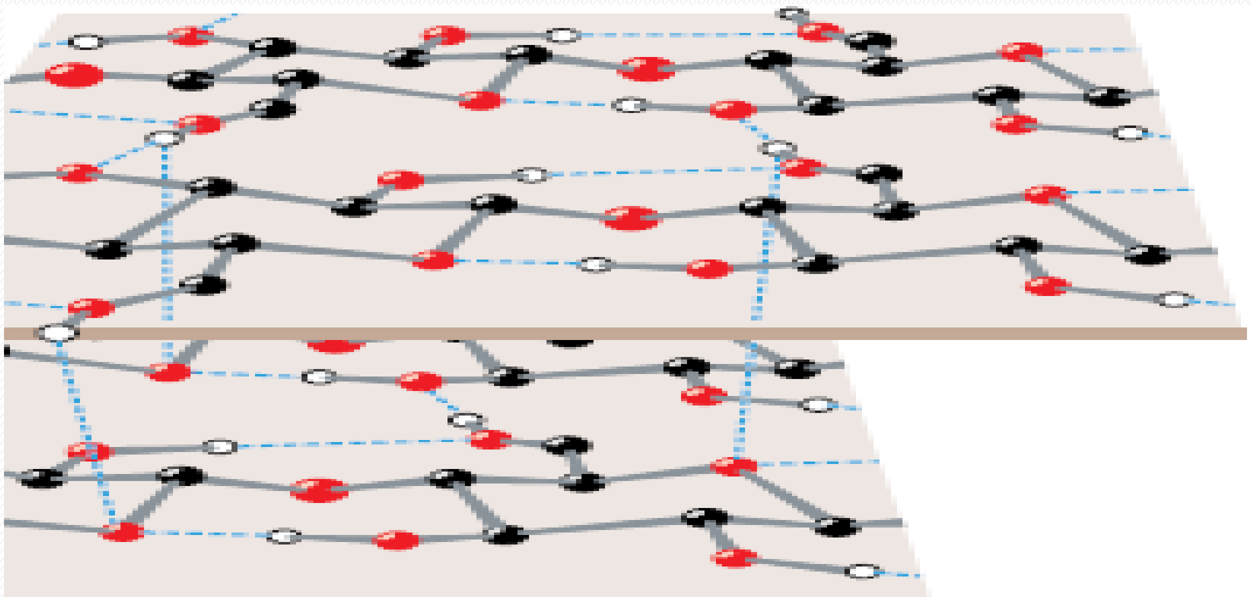
STRUCTURAL POLYSACHHARIDES:CELLULOSE

- **Cellulose is the most abundant natural polymer on earth**
- **Cellulose is the principal strength and support of trees and plants**
- **Cellulose is a linear polymer of up to 15000 D-glucose residues (a glucan) linked by β(1-4) glycosidic bonds in contrast to the α(1-4) bonds of amylose.**
- **This difference gives cellulose and amylose very different structural and physical properties**

STRUCTURE OF CELLULOSE

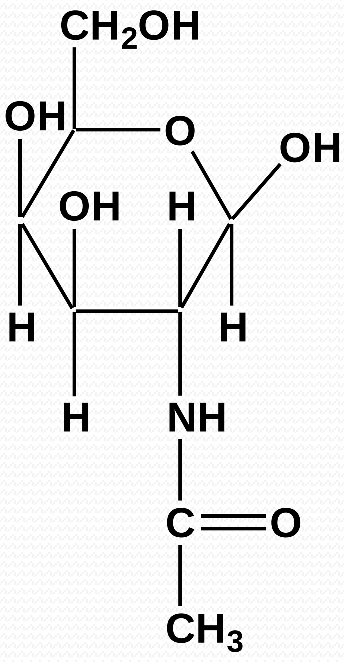


Cellulose

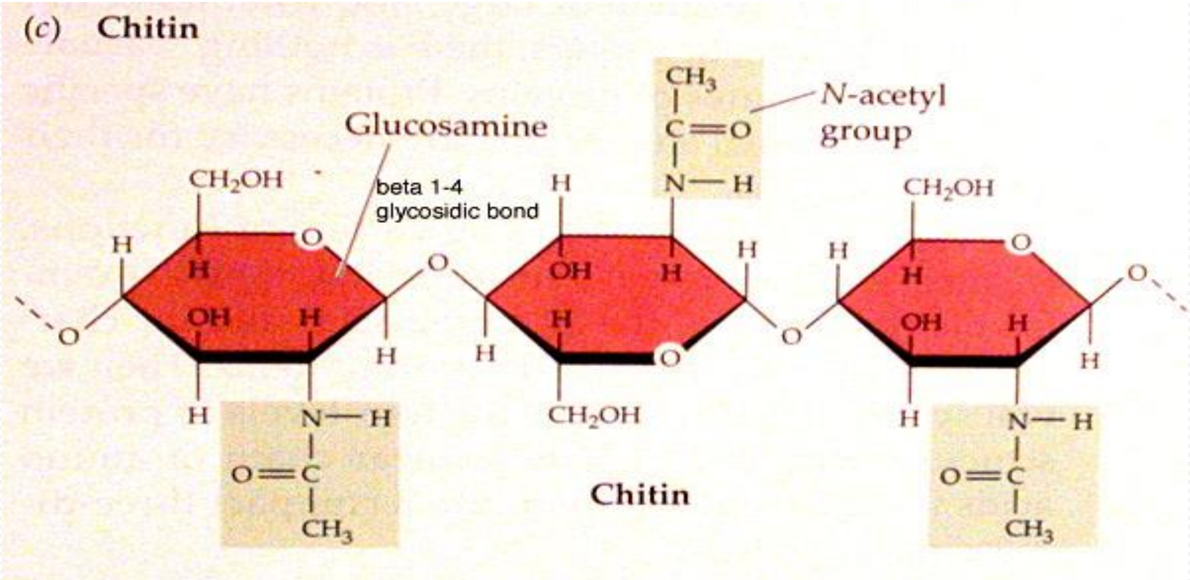


STUCTURAL POLYSACCHARIDE: CHITIN

- Chitin is the principal structural component of invertebrates such as crustaceans, insects and is also a major cell wall constituent of most fungi and many algae
- Chitin is a linear homopolysaccharide composed of N-acetylglucosamine residues in β (1-4) linkages
- similar to cellulose, but instead of glucose uses N-acetyl glucosamine (C-2s are N-acetyl instead of –OH)
- cellulose strands are parallel, chitins can be parallel or anti-parallel



STRUCTURE OF CHITIN



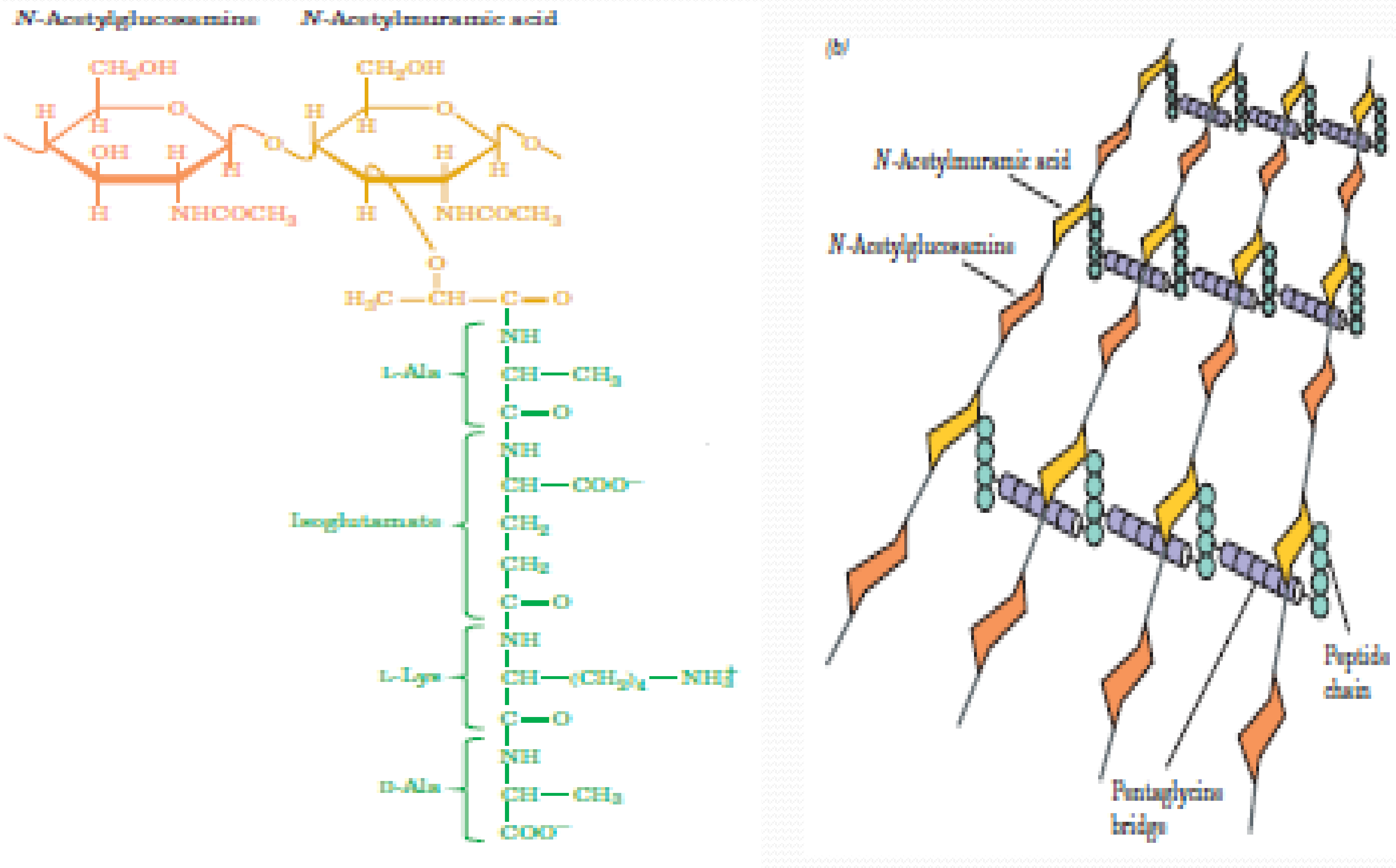
BACTERIAL CELL WALLS

- **Bacteria are surrounded by rigid cell walls that give them their characteristics shapes and permit them to live in hypotonic environments that would otherwise cause them to swell osmotically until their plasma (cell)membranes lysed (burst)**
- **Bacterial cell walls are of considerable medical significance because they are responsible for bacterial virulence (disease-evoking power)**
- **Bacteria are classified as gram-positive or gram-negative depending on whether or not they take up gram stain**

PEPTIDOGLYCAN

- **The cell walls of both gram-positive and gram-negative bacteria consist of covalently linked polysaccharide and polypeptide chains which form a bag-like molecule that completely encases the cell**
- **This framework, whose structure was elucidated by Jack Strominger is known as PEPTIDOGLYCAN or MUREIN**
- **Peptidoglycan is a heteropolymer of alternating β(1-4) linked N-acetylglucosamine (NAG) and N-acetylmuramic acid (NAM)**
- **The NAM's lactic acid residue forms an amide bond with a D-amino acid containing tetrapeptide to form the Peptidoglycan repeating Units**
- **Neighbouring parallel Peptidoglycan chains are covalently cross-linked through their tetrapeptide side chains**
- **The peptide cross-links weld the polysaccharide chains into a strong sheath that envelopes the entire cell and prevents cellular swelling and lysis due to the osmotic entry of water**

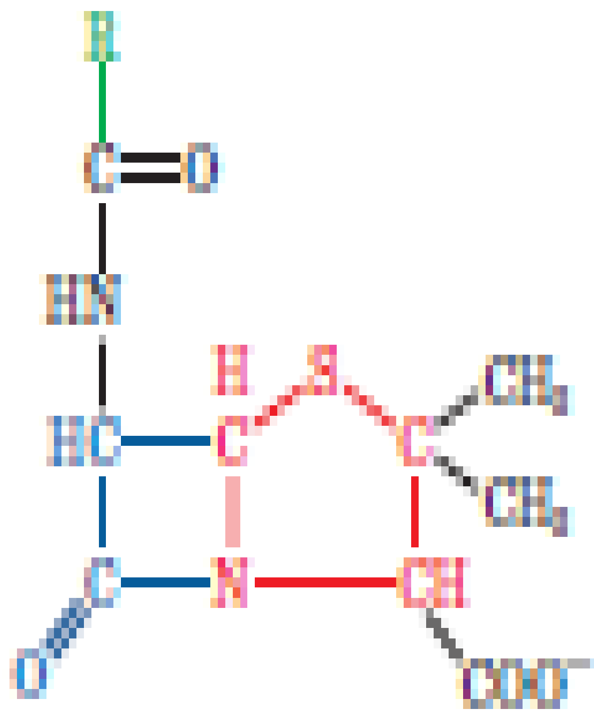
PEPTIDOGLYCAN STRUCTURE



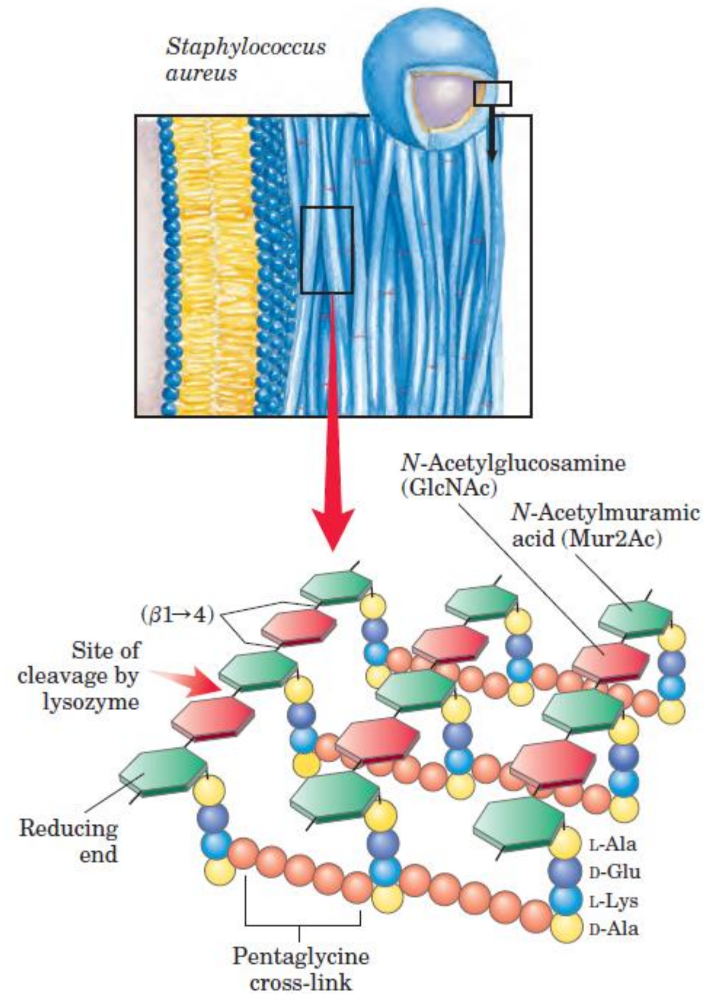
PENICILLIN AND β-LACTAM ANTIBIOTICS AND BACTERIAL CELLWALL

- **Penicillin and related antibiotics kill bacteria by preventing synthesis of the cross-links leaving the cell wall too weak to resist osmolytic lysis**
- **Penicillin specifically binds to and inactivates enzymes (transpeptidase)that function to cross-link the peptidoglycan strands of bacterial cell walls**
- **It is this reaction that is inhibited by penicillin and related compounds all of which mimic one conformation of the D-ala-D-ala segment of the peptidoglycan precursor**
- **The peptide bond in the precursor is replaced by a highly reactive β-lactam ring of the penicillin .**
- **The β-lactam ring of the penicillin forms an adduct(complex) with the transpeptidase enzyme thereby inactivating it. This in turn blocks synthesis of the bacterial cell wall and most bacteria die as the fragile innermembrane burst under osmotic presuure**
- **Human use of penicillin and its derivates has lead to the evolution of strains of pathogenic bacteria that express β-lactamases (penicillinase), enzymes that cleave β-lactam antiboitics, rendering them inactive. The bacteria thereby become resistant to the antibiotics**
- **This has led to improvement and modification in the initial structure of penicillin to produce antibiotics such as penicillin V, Amoxicillin and Ampicillin but certain strains of bacteria have developed resistance to them**

ANTIBIOTICS AND THEIR EFFECTS ON BACTERIAL CELLWALL



Penicillin

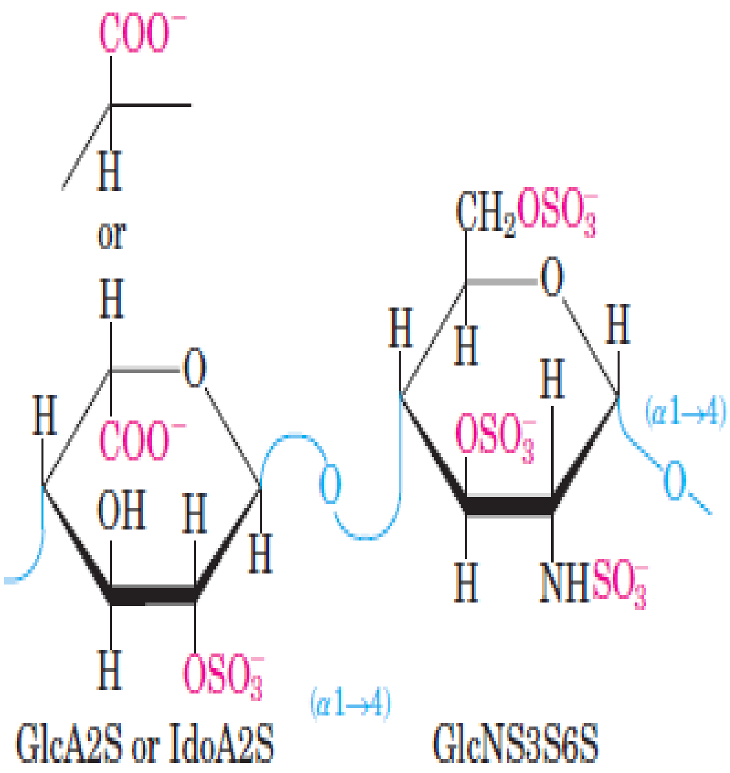


GLYCOSAMINOGLYCANS

- **The extracellular spaces, particularly those of connective tissues such as cartilage, tendon, skin and blood vessel walls, consist of collagen and elastin fibres embedded in a gel-like matrix known as GRUOND SUBSTANCE.**
- **Ground substance is composed largely of glycosaminoglycans (alternatively, MUCOPOLYSACCHARIDES**
- **They are polysaccharides of alternating Uronic and hexasamine residues.**
- **Solutions of glycosaminoglycans have a slimy, Mucus like consistency that results from their high viscosity and elasticity**
- **Heparin and chondroitin sulphates are popular examples of glycosaminoglycans**

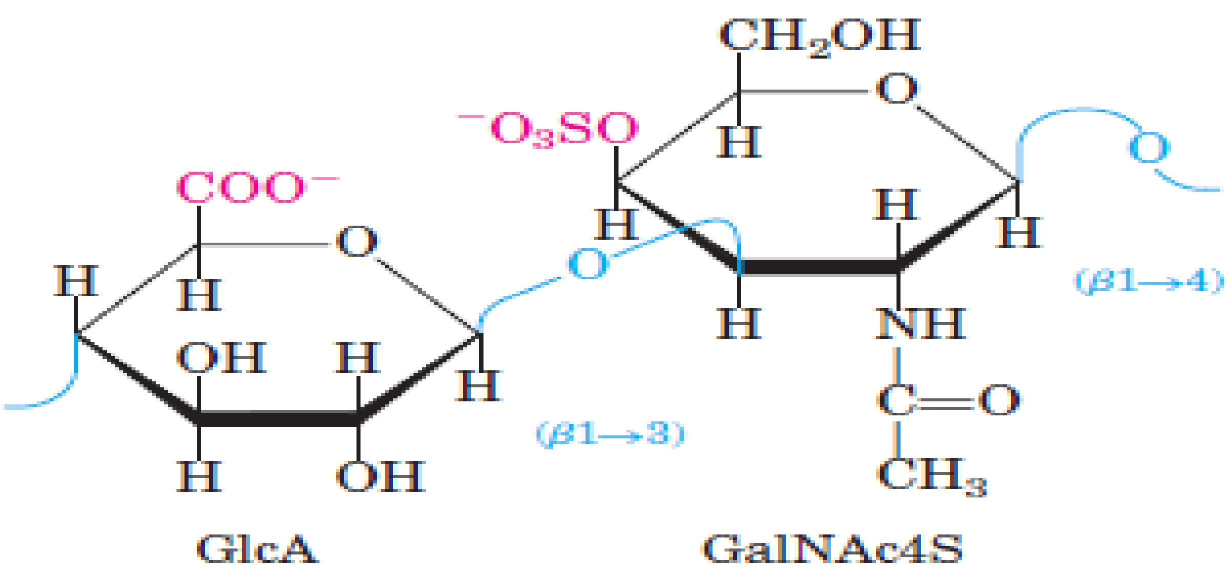
HEPARIN AS ANTICOAGULANT

- Heparin is a variably sulfated glycosaminoglycan that consist predominantly of alternating α(1-4) linked residues of D-iduronate-2-sulfate and N-sulfo-D-glucosamine 6 sulphate
- It has an average of 2.5 sulfate residues per disaccharide unit, which makes it the most negatively charged polyelectrolyte in mammalian tissues
- It inhibits the clotting of blood, its release through injury is thought to prevent runaway clot formation
- Heparin is a therapeutic agent used to inhibit coagulation through its capacity to bind the protease inhibitor, **anti-thrombin**
- Heparin binding causes anti-thrombin to bind to and inhibit thrombin, a **protease** essential to blood clothing. The interaction is strongly electrostatic. Heparin has the highest negative density of any known biological macromolecules



CHONDROITIN SULPHATES

- From the greek word (chondros which means cartilage)
- Chondroitin contributes to the tensile strength of cartilage, tendons, ligaments and the walls of the aorta
- There are 2 types of chondoitin sulphates: chondoitin 6 sulphate and chondroitin 4 sulphate depending on the position of the sulphate group
- It is made up of D-glucuronate and N-acetyl D-galactosamine 6 or 4 sulphate

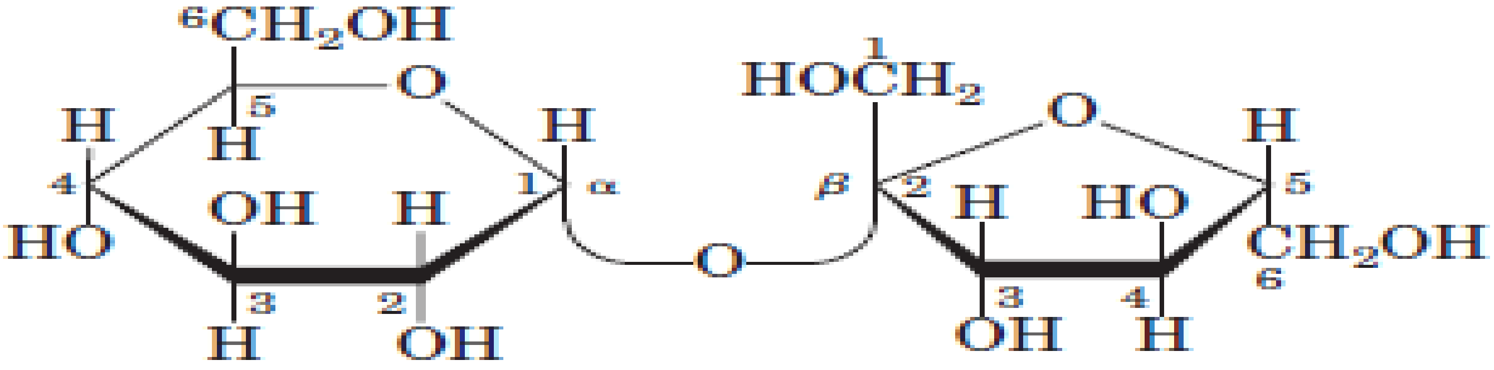


OLIGOSACCHARIDES

- **Oligosaccharides consist of short chain monosaccharide units or residues joined by characteristic linkages called glycosidic bonds**
- **The most abundant are the disaccharides with two monosaccharide units**
- **Sucrose, maltose and lactose are examples**

SUCROSE

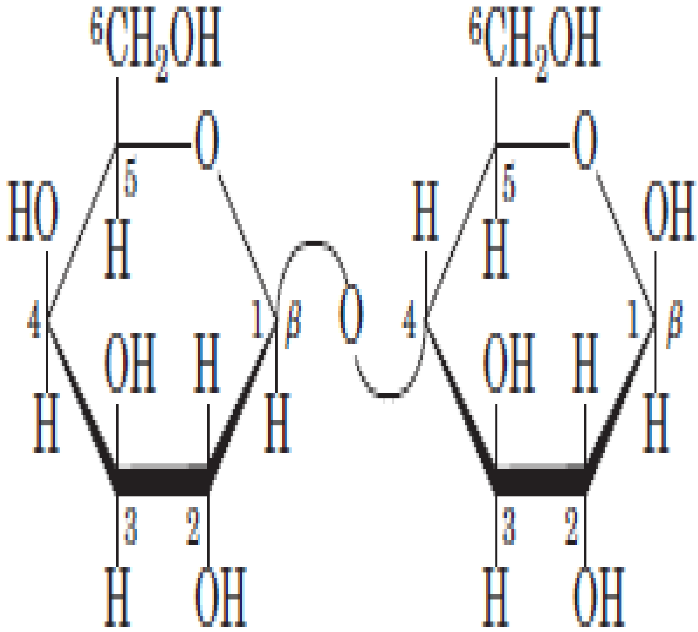
- Sucrose is the most abundant disaccharide and occurs throughout the plant kingdom and is familiar to us as common table sugar
- It is composed of o-α-D- (1-2)-β-D- fructo-furanoside where the symbol (1-2) indicates that the glycosidic bond links C1 of the glucose to the C2 of the fructose residue. Note that since these two positions are the anomeric carbon atoms of their respective monosaccharide sucrose is not a reducing sugar
- The hydrolysis of sucrose to D-glucose and D-fructose is catalyzed by α-D-GLUCOSIDASE also called invertase



Sucrose
α-D-glucopyranosyl β-D-fructofuranoside
Glc(α1↔2β)Fru

LACTOSE

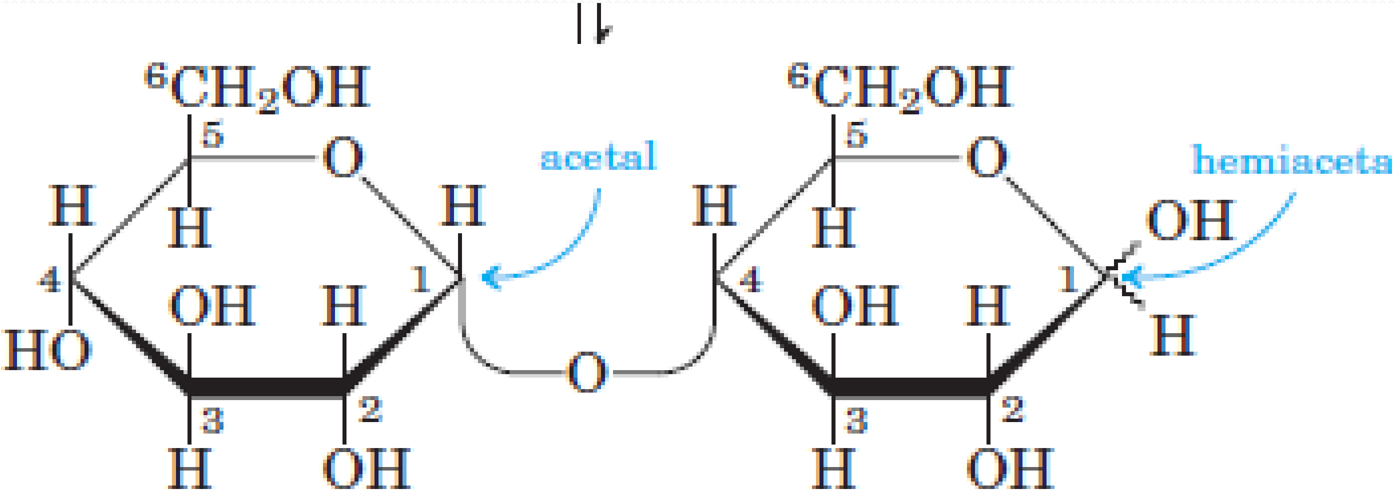
- **Lactose is O-β-D-galactopyranosyl-(1-4)-D-glucopyranose or milk sugar occurs naturally only in milk**
- **The free anomeric carbon of its glucose residue makes lactose a reducing sugar**
- **Infants normally have the intestinal enzyme β-D-galactosidase or lactase that catalyzes the hydrolysis of lactose to its component monosaccharides for absorption into the bloodstream**
- **Many adults suffer from LACTOSE INTOLERANCE because they lack lactase and as such experience painful digestive upset when they ingest milk**



Lactose (β form)
β-D-galactopyranosyl-(1→4)-β-D-glucopyranose
Gal(β1→4)Glc

MALTOSE

- Maltose contains two D-glucose residues joined by a glycosidic linkage between the C-1 (the anomeric carbon) of one glucose residue and C4 of the other
- Because the disaccharide retains a free anomeric carbon C1 of the glucose residue on the right
- Maltose is a reducing sugar



Maltose
α-D-glucopyranosyl-(1→4)-D-glucopyranose

QUESTIONS AND COMMENTS