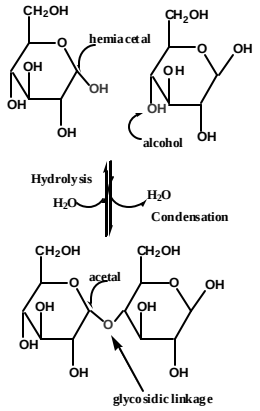
Chapter 8 (part2)

Carbohydrates: oligo- and polysaccharides

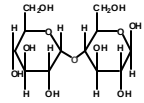
Carbohydrates

- 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

Glycosidic Linkage

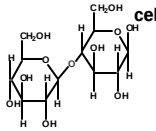


Disaccharides



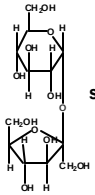
maltose

(a -D-glucosyl-(1->4)-b -D-glucopyranose)



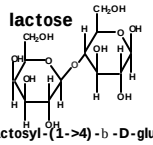
cellobiose

(b -D-glucosyl-(1->4)-b -D-glucopyranose)



sucrose

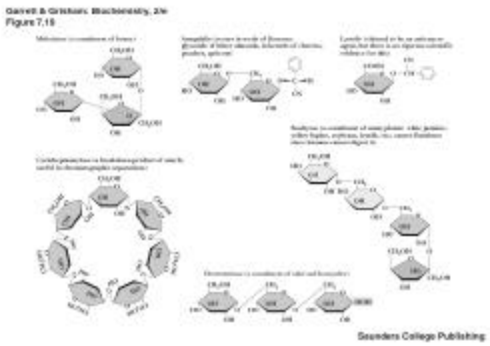
(a -D-glucosyl-(1->2)-b -D-fructofuranose)



lactose

(b -D-galactosyl-(1->4)-b -D-glucopyranose)

Higher Oligosaccharides



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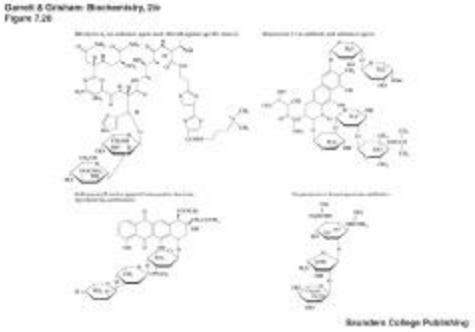
Oligosaccharide groups are incorporated in to many drug structures



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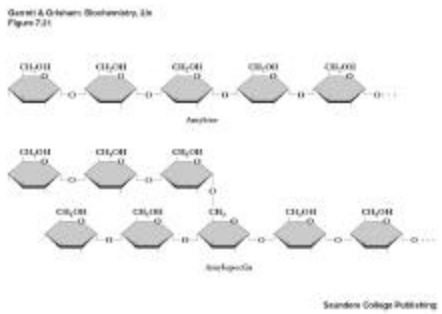
Polysaccharides

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

Starch

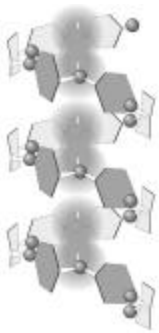
- **A plant storage polysaccharide**
- **Two forms: amylose and amylopectin**
- **Most starch is 10-30% amylose and 70-90% amylopectin**
- **Average amylose chain length 100 to 1000 residues**
- **Branches in amylopectin every 25 residues (15-25 residues) a-1->6 linkages**
- **Amylose has a-1->4 links, one reducing end**

Amylose and Amylopectin



Starch

- Amylose is poorly soluble in water, but forms micellar suspensions
- In these suspensions, amylose is helical



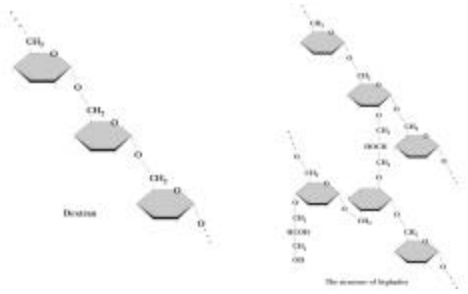
Glycogen

- Storage polysaccharide in animals
- Glycogen constitutes up to 10% of liver mass and 1-2% of muscle mass
- Glycogen is stored energy for the organism
- Only difference from starch: number of branches
- Alpha(1,6) branches every 8-12 residues
- Like amylopectin, glycogen gives a red-violet color with iodine

Dextrans

- If you change the main linkages between glucose from alpha(1,4) to alpha(1,6), you get a new family of polysaccharides - dextrans
- Branches can be (1,2), (1,3), or (1,4)
- Dextrans formed by bacteria are components of dental plaque
- Cross-linked dextrans are used as "Sephadex" gels in column chromatography
- These gels are up to 98% water!

Dextrans



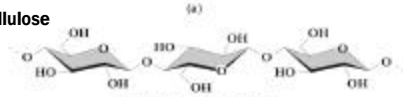
Cellulose

- Cellulose is the most abundant natural polymer on earth
- Cellulose is the principal strength and support of trees and plants
- Cellulose can also be soft and fuzzy - in cotton

Cellulose vs Amylose

amylose

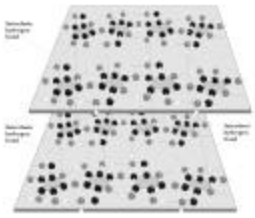
cellulose



Glucose units rotated 180° relative to next residue

Cellulose

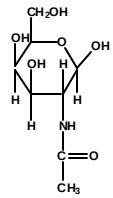
- **Beta(1,4) linkages make all the difference!**
- **Strands of cellulose form extended ribbons**
- **Interchain H-bonding allows multi-chain interactions. Forms cable like structures.**



Chitin

- **exoskeletons of crustaceans, insects and spiders, and cell walls of fungi**
- **similar to cellulose, but instead of glucose uses N-acetyl glucosamine (C-2s are N-acetyl instead of –OH)**

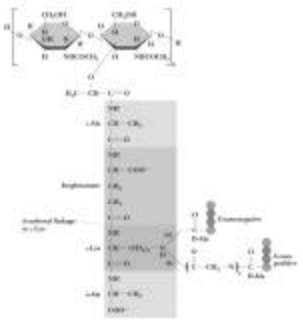
  b-1->4 linked N-acetylglucosamine units
- **cellulose strands are parallel, chitins can be parallell or antiparallel**



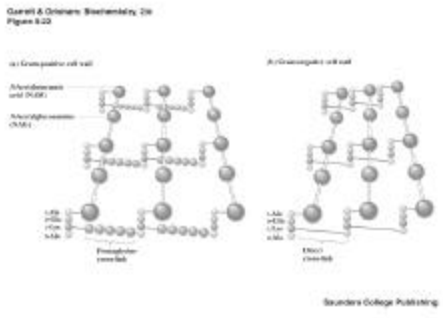
Chitin vs Cellulose

Peptidoglycan

- N-acetylglucosamine and N-acetylmuramic acid groups linked b-1->4
- Heteroglycan linked to a tetrtapeptide (Ala-IsoGlu-Lys-Ala)
- Gram (-) have petanta-glycine linker to next strand
- Gram (+) have directly cross links to next strand



Peptidoglycan



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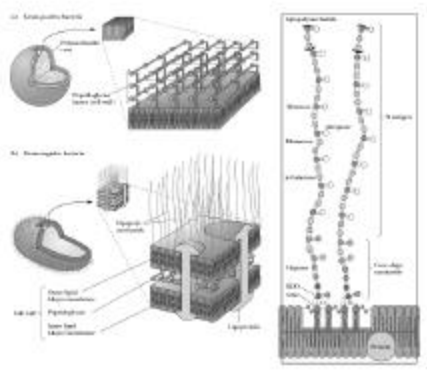
Peptidoglycan is target of antibacterial agents

- Lysozyme = enzyme that cleaves polysaccharide chain of peptidoglycan
- Penicillin = inhibits linking of peptidoglycan chains.
- Inhibits bond formation between terminal alanine and pentaglycine linker
- Penicillian looks like an Ala-Ala

Peptidoglycan and Bacterial Cell Walls

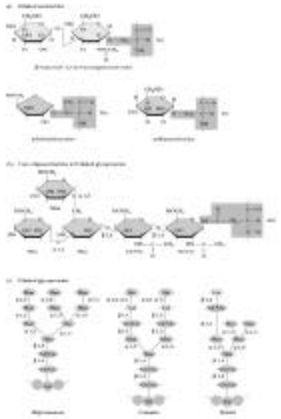
Composed of 1 or 2 bilayers and peptidoglycan shell

- **Gram-positive: One bilayer and thick peptidoglycan outer shell**
- **Gram-negative: Two bilayers with thin peptidoglycan shell in between**
- **Gram-positive: pentaglycine bridge connects tetrapeptides**
- **Gram-negative: direct amide bond between tetrapeptides**



Glycoproteins

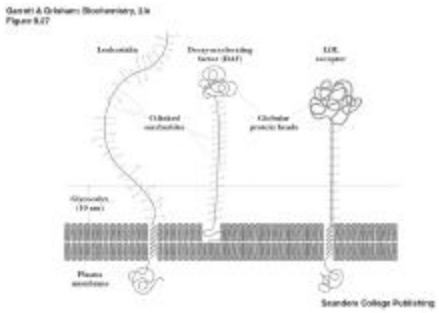
- **May be N-linked or O-linked**
- **N-linked saccharides are attached via the amide nitrogens of asparagine residues**
- **O-linked saccharides are attached to hydroxyl groups of serine, threonine or hydroxylysine**



O-linked Glycoproteins

- Function in many cases is to adopt an extended conformation
- These extended conformations resemble "bristle brushes"
- Bristle brush structure extends functional domains up from membrane surface

O-linked Glycoproteins



N-linked Glycoproteins

- **Oligosaccharides can alter the chemical and physical properties of proteins**
- **Oligosaccharides can stabilize protein conformations and/or protect against proteolysis**
- **Cleavage of monosaccharide units from N-linked glycoproteins in blood targets them for degradation in the liver**
- **Involved in targeting proteins to specific subcellular compartments**