Carbohydrates
Reading in Garrett & Grisham textbook

Chapter 7 pages 205-240 – (quite complete discourse on carbohydrate structure and function with some emphasis on cell surfaces)

several figures presented in these notes are taken from The G & G chapter
General characteristics

• the term carbohydrate is derived from the french: hydrate de carbone
• compounds composed of C, H, and O
• \((\text{CH}_2\text{O})_n\) when \(n = 5\) then \(\text{C}_5\text{H}_{10}\text{O}_5\)
• not all carbohydrates have this empirical formula: deoxysugars, aminosugars
• carbohydrates are the most abundant compounds found in nature (cellulose: 100 billion tons annually)
General characteristics

• Most carbohydrates are found naturally in bound form rather than as simple sugars
  • Polysaccharides (starch, cellulose, inulin, gums)
  • Glycoproteins and proteoglycans (hormones, blood group substances, antibodies)
  • Glycolipids (cerebrosides, gangliosides)
  • Glycosides
  • Mucopolysaccharides (hyaluronic acid)
  • Nucleic acids
Functions

• sources of energy
• intermediates in the biosynthesis of other basic biochemical entities (fats and proteins)
• associated with other entities such as glycosides, vitamins and antibiotics)
• form structural tissues in plants and in microorganisms (cellulose, lignin, murein)
• participate in biological transport, cell-cell recognition, activation of growth factors, modulation of the immune system
Classification of carbohydrates

- **Monosaccharides (monoses or glycoses)**
  - Trioses, tetroses, pentoses, hexoses

- **Oligosaccharides**
  - Di, tri, tetra, penta, up to 9 or 10
  - Most important are the disaccharides

- **Polysaccharides or glycans**
  - Homopolysaccharides
  - Heteropolysaccharides
  - Complex carbohydrates
Monosaccharides

• also known as simple sugars
• classified by 1. the number of carbons and 2. whether aldoses or ketoses
• most (99%) are straight chain compounds
• D-glyceraldehyde is the simplest of the aldoses (aldotriose)
• all other sugars have the ending ose (glucose, galactose, ribose, lactose, etc...)
Aldose sugars

- Aldose
- Aldotriose \( n = 1 \)
- Aldotetrose \( n = 2 \)
- Aldopentose \( n = 3 \)
- Aldohexose \( n = 4 \)
Ketose sugars
Structure of a simple aldose and a simple ketose

L-isomer  
\[
\begin{align*}
\text{HO} & - \text{C} - \text{H} \\
\text{CH}_2\text{OH} & \\
\text{or} & \\
\text{H} & - \text{C} - \text{OH} \\
\text{CH}_2\text{OH} &
\end{align*}
\]

Glyceraldehyde

D-isomer  
\[
\begin{align*}
\text{H} & - \text{C} - \text{OH} \\
\text{CH}_2\text{OH} & \\
\text{C} & = \text{O} \\
\text{CH}_2\text{OH} &
\end{align*}
\]

Dihydroxyacetone
these two aldotetroses are enantiomers. They are stereoisomers that are mirror images of each other.

these two aldohexoses are C-4 epimers. They differ only in the position of the hydroxyl group on one asymmetric carbon (carbon 4).
D-Fructose

L-Fructose

Enantiomers

Mirror image configurations
Properties

- Differences in structures of sugars are responsible for variations in properties
  - Physical
    - Crystalline form; solubility; rotatory power
  - Chemical
    - Reactions (oxidations, reductions, condensations)
  - Physiological
    - Nutritive value (human, bacterial); sweetness; absorption
Dihydroxyacetone

1. CH₂OH
2. C=O
3. CH₂OH

KETOTRIOSE

Carbon number

1. CH₂OH
2. C=O
3. HCOH
4. CH₂OH

KETOTETROSE

d-Erythulose

1. CH₂OH
2. C=O
3. HCOH
4. HCOH
5. CH₂OH

KETOPENTOSES

Carbon number

1. CH₂OH
2. C=O
3. HCOH
4. HCOH
5. HCOH
6. CH₂OH

KETOHEXOSES

d-Ribulose

1. CH₂OH
2. C=O
3. HCOH
4. HCOH
5. HCOH
6. CH₂OH

d-Xylulose

1. CH₂OH
2. C=O
3. HOCH
4. HCOH
5. HCOH
6. CH₂OH

d-Psicose

1. CH₂OH
2. C=O
3. HCOH
4. HCOH
5. HCOH
6. CH₂OH

d-Fructose

1. CH₂OH
2. C=O
3. HOCH
4. HCOH
5. HCOH
6. CH₂OH

d-Sorbose

1. CH₂OH
2. C=O
3. HCOH
4. HCOH
5. HCOH
6. CH₂OH

d-Tagatose
Structural representation of sugars

- Fisher projection: straight chain representation
- Haworth projection: simple ring in perspective
- Conformational representation: chair and boat configurations
Rules for drawing Haworth projections

- draw either a six or 5-membered ring including oxygen as one atom

- most aldohexoses are six-membered
- aldotetroses, aldopentoses, ketohexoses are 5-membered
Rules for drawing Haworth projections

• next number the ring clockwise starting next to the oxygen

• if the substituent is to the right in the Fisher projection, it will be drawn down in the Haworth projection (Down-Right Rule)
Rules for drawing Haworth projections

• for D-sugars the highest numbered carbon (furthest from the carbonyl) is drawn up. For L-sugars, it is drawn down.

• for D-sugars, the OH group at the anomeric position is drawn down for $\alpha$ and up for $\beta$. For L-sugars $\alpha$ is up and $\beta$ is down.
Optical isomerism

• A property exhibited by any compound whose mirror images are non-superimposable

• Asymmetric compounds rotate plane polarized light
POLARIMETRY

Measurement of optical activity in chiral or asymmetric molecules using plane polarized light

Molecules may be chiral because of certain atoms or because of chiral axes or chiral planes

Measurement uses an instrument called a polarimeter (Lippich type)

Rotation is either (+) dextrorotatory or (-) levorotatory
polarimetry

Magnitude of rotation depends upon:

1. the nature of the compound

2. the length of the tube (cell or sample container) usually expressed in decimeters (dm)

3. the wavelength of the light source employed; usually either sodium D line at 589.3 nm or mercury vapor lamp at 546.1 nm

4. temperature of sample

5. concentration of analyte in grams per 100 ml
\[ [\alpha]_D^T = \frac{\alpha \text{ observed} \times 100}{l \times c} \]

D = Na D line
T = temperature °C
\( \alpha_{\text{obs}} \): observed rotation in degree (specify solvent)
l = length of tube in decimeter
c = concentration in grams/100ml
\([\alpha] = \text{specific rotation}\)
Specific rotation of various carbohydrates at 20°C

- D-glucose +52.7
- D-fructose -92.4
- D-galactose +80.2
- L-arabinose +104.5
- D-mannose +14.2
- D-arabinose -105.0
- D-xylose +18.8
- Lactose +55.4
- Sucrose +66.5
- Maltose+ +130.4
- Invert sugar -19.8
- Dextrin +195
Reactions of monosaccharides

• Carbonyl reactions:
  • Osazone formation
  • Cyanohydrin reaction
  • Reduction
  • Oxidation
  • Action of base
  • Action of acid
  • Ring chain tautomerism

• Alcohol reactions
  • Glycoside formation
  • Ether formation
  • Ester formation
Formation of osazones

- once used for the identification of sugars
- consists of reacting the monosaccharide with phenylhydrazine
- a crystalline compound with a sharp melting point will be obtained
- D-fructose and D-mannose give the same osazone as D-glucose
- seldom used for identification; we now use HPLC or mass spectrometry
glucose, fructose, sucrose with phenylhydrazine after 9 minutes
Cyanohydrin formation

- reaction of an aldose with HCN
- used to increase the chain length of monosaccharides
- results in a cyanohydrin which is then hydrolyzed to an acid and reduced to the aldehyde
- known as the Fischer-Kiliani synthesis
- can prepare all monosaccharides from D-glyceraldehyde
D-glucose can cyclize in two ways forming either furanose or pyranose structures.
D-ribose and other five-carbon saccharides can form either furanose or pyranose structures.
Chair and boat conformations of a pyranose sugar

Chair and boat conformations of β-D-glucose

a = axial bond
e = equatorial bond

2 possible chair conformations of β-D-glucose
Oxidation reactions

- Aldoses may be oxidized to 3 types of acids
  - **Aldonic acids**: aldehyde group is converted to a carboxyl group (glucose – gluconic acid)
  - **Uronic acids**: aldehyde is left intact and primary alcohol at the other end is oxidized to COOH
    - Glucose --- glucuronic acid
    - Galactose --- galacturonic acid
  - **Saccharic acids** (glycaric acids) – oxidation at both ends of monosaccharide
    - Glucose ---- saccharic acid
    - Galactose --- mucic acid
    - Mannose --- mannaric acid
Glucose oxidase

- glucose oxidase converts glucose to gluconic acid and hydrogen peroxide
- when the reaction is performed in the presence of peroxidase and o-dianisidine a yellow color is formed
- this forms the basis for the measurement of urinary and blood glucose
  - Testape, Clinistix, Diastix (urinary glucose)
  - Dextrostix (venous glucose)
d-Glucose

Oxidation at C-1

d-Gluconic acid

Oxidation at C-6

d-Glucuronic acid (GlcUA)

Oxidation at C-1 and C-6

d-Glucaric acid

d-Gluconic acid

d-δ-Gluconolactone

Note: d-Gluconic acid and other aldonic acids exist in equilibrium with lactone structures.

l-Iduronic acid (IdUA)
Reduction

• either done catalytically (hydrogen and a catalyst) or enzymatically
• the resultant product is a polyol or sugar alcohol (alditol)
• glucose form sorbitol (glucitol)
• mannose forms mannitol
• fructose forms a mixture of mannitol and sorbitol
• glyceraldehyde gives glycerol
Structures of some sugar alcohols

- d-Glucitol (sorbitol)
- d-Mannitol
- d-Xylitol
- d-Glycerol
- myo-Inositol
- d-Ribitol
Sugar alcohols are very useful intermediates

- Mannitol is used as an osmotic diuretic
- Glycerol is used as a humectant and can be nitrated to nitroglycerin
- Sorbitol can be dehydrated to tetrahydropyrans and tetrahydrofuran compounds (sorbitans)
- Sorbitans are converted to detergents known as spans and tweens (used in emulsification procedures)
- Sorbitol can also be dehydrated to 1,4,3,6-dianhydro-D-sorbitol (isosorbide) which is nitrated to ISDN and ISMN (both used in treatment of angina)
Formation of spans and tweens

SORBITOL → 1,4-SORBITAN → THF compound

SPANS (form W/O emulsions)

TWEENS (form O/W emulsions)
Action of strong acids on monosaccharides

- Monosaccharides are normally stable to dilute acids, but are dehydrated by strong acids.
- D-ribose when heated with concentrated HCl yields furfural (commercial route for the production of THF (tetrahydrofuran)).
- D-glucose under the same conditions yields 5-hydroxymethyl furfural.
Action of base on sugars

• Sugars are weak acids and can form salts at high pH
• A 1,2-enediol salt is formed as the result
• This allows the interconversion of D-mannose, D-fructose and D-glucose
• The reaction is known as the Lobry de Bruyn-Alberta von Eckenstein reaction
Action of base on sugars

- Enediols obtained by the action of base are quite susceptible to oxidation when heated in the presence of an oxidizing agent.
- Copper sulfate is frequently used as the oxidizing agent and a red precipitate of Cu$_2$O is obtained.
- Sugars which give this reaction are known as reducing sugars.
- Fehling’s solution: KOH or NaOH and CuSO$_4$.
- Benedict’s solution: Na$_2$CO$_3$ and CuSO$_4$.
- Clinitest tablets are used to detect urinary glucose in diabetics.
Glucose measurement methods

• Most methods are enzymatic methods
  – 3 enzyme systems are currently used to measure glucose:
    • Glucose oxidase
    • Glucose dehydrogenase
    • Hexokinase

• These reactions produce either a product that can be measured photometrically or an electrical current that is proportional to the initial glucose concentration
Glucose dehydrogenase methods

\[ \alpha-D\text{-glucose} \xrightarrow{\text{mutarotase}} \beta-D\text{-glucose} \]

\[ \beta-D\text{-glucose} + \text{NAD} \xrightarrow{\text{glucose dehydrogenase}} \text{D-gluconolactone} + \text{NADH} \]

\[ \text{MTT} + \text{NADH} \xrightarrow{\text{diaphorase}} \text{MTTH} \text{ (blue color)} + \text{NAD} \]

\[ \text{glucose} + \text{pyrroloquinoline quinone (PQQ)} \xrightarrow{\text{glucose dehydrogenase}} \text{Gluconolactone} + \text{PQQH} \]

\[ \text{PQQH}_2 + 2\text{[Fe(CN)}_6\text{]}^{-3} \xrightarrow{} \text{PQQ} + 2\text{[Fe(CN)}_6\text{]}^{-4} + 2\text{H}^+ \]

\[ 2\text{[Fe(CN)}_6\text{]}^{-4} \xrightarrow{} 2\text{[Fe(CN)}_6\text{]}^{-3} + 2\text{e}^- \]
Glucose oxidase methods: colorimetric method

\[
\begin{align*}
\beta-D-glucose + O_2 & \xrightarrow{\text{glucose oxidase}} D-gluconolactone + H_2O_2 \\
D-gluconolactone + H_2O & \rightarrow \text{gluconic acid} \\
H_2O_2 + \text{chromogenic oxygen acceptor (ortho-dianisidine, 4 aminophenazone, ortho-tolidine)} & \xrightarrow{\text{peroxidase}} \text{colored chromogen} + H_2O
\end{align*}
\]
Glucose oxidase methods: electronic sensing method

\[ \beta-D-\text{glucose} + 2[\text{Fe(CN)}_6]^{3-} + \text{H}_2\text{O} \xrightarrow{\text{glucose oxidase}} \text{D-gluconic acid} + 2[\text{Fe(CN)}_6]^{4-} + 2\text{H}^+ \]

\[ 2[\text{Fe(CN)}_6]^{4-} \xrightarrow{} 2[\text{Fe(CN)}_6]^{3-} + 2e^- \]

\[ \beta-D-\text{glucose} + \text{O}_2 \xrightarrow{\text{glucose oxidase}} \text{D-gluconolactone} + \text{H}_2\text{O}_2 \]

\[ \text{H}_2\text{O}_2 \xrightarrow{} 2\text{H}^+ + \text{O}_2 + 2e^- \]
A blood test for glucose levels

D-Glucose

H
C=O
H
HO
H
HO
H
HO
CH₂OH

D-Gluconic Acid (An Aldonic Acid)

H
C=O
H
HO
H
HO
H
HO
CH₂OH

O₂ → H₂O₂

Glucose Oxidase

Dye

Colored Dye
Special monosaccharides: deoxy sugars

• These are monosaccharides which lack one or more hydroxyl groups on the molecule

• one quite ubiquitous deoxy sugar is 2’-deoxy ribose which is the sugar found in DNA

• 6-deoxy-L-mannose (L-rhamnose) is used as a fermentative reagent in bacteriology
examples of deoxysugars

2-Deoxy-α-D-Ribose

α-L-Rhamnose (Rha)

α-L-Fucose (Fuc)

Ouabain
Several sugar esters important in metabolism
Special monosaccharides: amino sugars

Constituents of mucopolysaccharides

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

\[ \beta-D-\text{Galactosamine} \]
Muramic acid

Pyruvic acid

$N$-Acetylmannosamine

$N$-Acetyl-$\alpha$-neuraminic acid (NeuNAc)

Fischer projection

Haworth projection

Chair conformation

$N$-Acetyl-$\alpha$-neuraminic acid (NeuNAc), a sialic acid
Condensation reactions: acetal and ketal formation
The anomeric forms of methyl-D-glucoside
Examples of glycosides

**Amygdalin** (occurs in seeds of *Rosaceae*, glycoside of bitter almonds, in kernels of cherries, peaches, apricots)

**Laetrile** (claimed to be an anticancer agent, but there is no scientific evidence for this)
Oligosaccharides

- Most common are the disaccharides
  - Sucrose, lactose, and maltose
  - Maltose hydrolyzes to 2 molecules of D-glucose
  - Lactose hydrolyzes to a molecule of glucose and a molecule of galactose
  - Sucrose hydrolyzes to a molecule of glucose and a molecule of fructose
Sucrose

- α-D-glucopyranosido-β-D-fructofuranoside
- β-D-fructofuranosido-α-D-glucopyranoside
  - also known as tablet sugar
  - commercially obtained from sugar cane or sugar beet
  - hydrolysis yield glucose and fructose (invert sugar) (sucrose: +66.5°; glucose +52.5°; fructose –92°)
  - used pharmaceutically to make syrups, troches
Sugar cane

Sugar beet
Sucralfate (Carafate)

\[ R = \text{OSO}_3\text{Al}_2(\text{OH})_5 \]
Lactose

- β-D-galactose joined to α-D-glucose via β (1,4) linkage
- milk contains the α and β-anomers in a 2:3 ratio
- β-lactose is sweeter and more soluble than ordinary α- lactose
- used in infant formulations, medium for penicillin production and as a diluent in pharmaceuticals
The good news is that you don't have mad cow's disease. The bad news is you're lactose intolerant.
Maltose

- 2-glucose molecules joined via $\alpha(1,4)$ linkage
- known as malt sugar
- produced by the partial hydrolysis of starch (either salivary amylase or pancreatic amylase)
- used as a nutrient (malt extract; *Hordeum vulgare*); as a sweetener and as a fermentative reagent
Lactulose

- galactose-β-(1,4)-fructose
- a semi-synthetic disaccharide (not naturally occurring)
- not absorbed in the GI tract
- used either as a laxative (Chronulac) or in the management of portal systemic encephalopathy (Cephulac)
- metabolized in distal ileum and colon by bacteria to lactic acid, formic acid and acetic acid (remove ammonia)
Oligosaccharides

• Trisaccharide: raffinose (glucose, galactose and fructose)
• Tetrasaccharide: stachyose (2 galactoses, glucose and fructose)
• Pentasaccharide: verbascose (3 galactoses, glucose and fructose)
• Hexasaccharide: ajugose (4 galactoses, glucose and fructose)
Honey also contains glucose and fructose along with some volatile oils
Structures of some oligosaccharides

Cycloheptaamylose (a breakdown product of starch useful in chromatographic separations)
Structures of some oligosaccharides

Dextrantriose (a constituent of saké and honeydew)
Structures of some oligosaccharides

**Stachyose** (a constituent of many plants: white jasmine, yellow lupine, soybeans, lentils, etc.; causes flatulence since humans cannot digest it)

An enzymatic product (Beano) can be used to prevent the flatulence
Oligosaccharides occur widely as components of antibiotics derived from various sources.

**Bleomycin A₂** (an antitumor agent used clinically against specific tumors)

**Streptomycin** (a broad spectrum antibiotic)
Polysaccharides or glycans

- homoglycans (starch, cellulose, glycogen, inulin)
- heteroglycans (gums, mucopolysaccharides)

Characteristics:
- polymers (MW from 200,000)
- White and amorphous products (glassy)
- not sweet
- not reducing; do not give the typical aldose or ketose reactions
- form colloidal solutions or suspensions
Starch

- most common storage polysaccharide in plants
- composed of 10 – 30% $\alpha$–amylose and 70-90% amylopectin depending on the source
- the chains are of varying length, having molecular weights from several thousands to half a million
Amylose and amylopectin are the 2 forms of starch. Amylopectin is a highly branched structure, with branches occurring every 12 to 30 residues.
suspensions of amylose in water adopt a helical conformation

iodine ($I_2$) can insert in the middle of the amylose helix to give a blue color that is characteristic and diagnostic for starch
\[\alpha-1,4\text{-Linked } \delta\text{-glucose units (in starch)}\]

\[\beta-1,4\text{-Linked } \delta\text{-glucose units (in cellulose)}\]
Cellulose

• Polymer of β-D-glucose attached by β(1,4) linkages
• Yields glucose upon complete hydrolysis
• Partial hydrolysis yields cellobiose
• Most abundant of all carbohydrates
  • Cotton flax: 97-99% cellulose
  • Wood: ~ 50% cellulose
• Gives no color with iodine
• Held together with lignin in woody plant tissues
Linear structures of cellulose and chitin
(2 most abundant polysaccharides)

**Cellulose**

**Chitin**

N-Acetylglucosamine units
Products obtained from cellulose

- Microcrystalline cellulose: used as binder-disintegrant in tablets
- Methylcellulose: suspending agent and bulk laxative
- Oxidized cellulose: hemostat
- Sodium carboxymethyl cellulose: laxative
- Cellulose acetate: rayon; photographic film; plastics
- Cellulose acetate phthalate: enteric coating
- Nitrocellulose: explosives; collodion (pyroxylin)
Glycogen

- also known as animal starch
- stored in muscle and liver
- present in cells as granules (high MW)
- contains both $\alpha(1,4)$ links and $\alpha(1,6)$ branches at every 8 to 12 glucose unit
- complete hydrolysis yields glucose
- glycogen and iodine gives a red-violet color
- hydrolyzed by both $\alpha$ and $\beta$-amylases and by glycogen phosphorylase
Inulin

- $\beta$-(1,2) linked fructofuranoses
  - linear only; no branching
  - lower molecular weight than starch
  - colors yellow with iodine
  - hydrolysis yields fructose
  - sources include onions, garlic, dandelions and jerusalem artichokes
  - used as diagnostic agent for the evaluation of glomerular filtration rate (renal function test)
Chitin

- chitin is the second most abundant carbohydrate polymer
- present in the cell wall of fungi and in the exoskeletons of crustaceans, insects and spiders
- chitin is used commercially in coatings (extends the shelf life of fruits and meats)
Chitin

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Dextran

- products of the reaction of glucose and the enzyme transglucosidase from *Leuconostoc mesenteroides*
- contains α (1,4), α (1,6) and α (1,3) linkages
- MW: 40,000; 70,000; 75,000
- used as plasma extenders (treatment of shock)
- also used as molecular sieves to separate proteins and other large molecules (gel filtration chromatography)
- components of dental plaques
Dextrins

- produced by the partial hydrolysis of starch along with maltose and glucose
- dextrins are often referred to as either amylodextrins, erythrodextrins or achrodextrins
- used as mucilages (glues)
- also used in infant formulas (prevent the curdling of milk in baby’s stomach)
Glycosaminoglycans

- they are the polysaccharide chains of proteoglycans
- they are linked to the protein core via a serine or threonine (O-linked)
- the chains are linear (unbranched)
- the glycosaminoglycan chains are long (over 100 monosaccharides)
- they are composed of repeating disaccharides
Glycosaminoglycans

Involved in a variety of extracellular functions; chondroitin is found in tendons, cartilage and other connective tissues
Glycosaminoglycans

A characteristic of glycosaminoglycans is the presence of acidic functionalities (carboxylate and/or sulfates)
Hyaluronic acid derivatives

• several products are used in the management of osteoarthritis symptoms
  – Hyalagan and Synvisc

• others are used as ophthalmic surgical adjuncts in cataract extractions, intraocular lens implantation, corneal transplant and retinal attachment surgery (Healon, Amvisc, AMO Vitrax)
Glycosaminoglycans

<table>
<thead>
<tr>
<th>Dermatan sulfate</th>
<th>Keratan sulfate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-Iduronate</td>
<td>N-Acetyl-d-glucosamine-6-sulfate</td>
</tr>
<tr>
<td>N-Acetyl-d-galactosamine-4-sulfate</td>
<td>d-Galactose</td>
</tr>
</tbody>
</table>
Pectins

• pectins are heteropolysaccharides found in the pulp of fruits (citrus, apples)
• on hydrolysis pectins yield galacturonic acid, galactose, arabinose, methanol and acetic acid
• pectins are composed of galactans and arabans
• used as gelling agents (to make jellies)
Ball Fruit Jell Pectin

100% Natural

Easy Recipes Inside

Net Wt. 1.75 OZ (49g)
Gums

• widely used in the food and pharmaceutical industry

• used as: suspending agents, gelling agents, thickening agents, emulsifiers, foam stabilizers, crystallization inhibitors, adhesives, binding agents

• agar, tragacanth, karaya, carrageenan, guar gum, gum arabic (acacia), furcellaran, sodium alginate, locust bean gum
Gum tragacanth
Bacterial cell wall

- provide strength and rigidity for the organism
- consists of a polypeptide-polysaccharide known as peptidoglycan or murein
- determines the Gram staining characteristic of the bacteria
Structure of peptidoglycan
(a) Gram-positive cell wall

\[ N\text{-AcetylMuramic acid (NAM)} \]

\[ N\text{-Acetylg glucosamine (NAG)} \]

\[ \text{l-Ala} \]
\[ \text{d-Glu} \]
\[ \text{l-Lys} \]
\[ \text{d-Ala} \]

Pentaglycine cross-link

(b) Gram-negative cell wall

\[ \text{l-Ala} \]
\[ \text{d-Glu} \]
\[ \text{l-Lys} \]
\[ \text{d-Ala} \]

Direct cross-link
Cell wall of Gram-positive bacteria

(a) Gram-positive bacteria

- Polysaccharide coat
- Peptidoglycan layers (cell wall)
Gram-negative bacteria
Cross-section of the cell wall of a gram-negative organism such as E.coli.
Lipopolysaccharide (LPS) coats the outer membrane of Gram-negative bacteria. The lipid portion of the LPS is embedded in the outer membrane and is linked to a complex polysaccharide.
Teichoic acids are covalently linked to the peptidoglycan of gram-positive bacteria. These polymers of glycerol phosphate (a and b) or ribitol phosphate (c) are linked by phosphodiester bonds.
Mycobacterial cell wall
Glycosylated proteins

• Usually done as a post-translational process
• Proteins can contain either O-linked oligosaccharides or N-linked oligosaccharides
Serine or threonine O-linked saccharides

(a) O-linked saccharides

\[ \beta\text{-Galactosyl-1,3-} \alpha\text{-N-acetylgalactosyl-serine} \]

\[ \alpha\text{-Xylosyl-threonine} \]

\[ \alpha\text{-Mannosyl-serine} \]
Asparagine N-linked glycoproteins

(b) Core oligosaccharides in N-linked glycoproteins
(c) N-linked glycoproteins

- **High mannose**
  - Man \(\alpha 1,2\)
  - Man \(\alpha 1,3\)
  - Man \(\alpha 1,6\)
  - Man \(\alpha 1,3\)
  - Man \(\alpha 1,6\)
  - β 1,4
  - GlcNAc
  - β 1,4
  - GlcNAc
  - Asn

- **Complex**
  - Sia \(\alpha 2,3 \text{ or } 6\)
  - Gal
  - β 1,4
  - GlcNAc
  - β 1,2
  - Man \(\alpha 1,3\)
  - Man \(\alpha 1,6\)
  - Man
  - Asn

- **Hybrid**
  - Gal \(\beta 1,4\)
  - GlcNAc
  - β 1,2
  - Man
  - α 1,3
  - Man
  - α 1,6
  - Asn

---
These glycoproteins are found in the blood of Arctic and Antarctic fish enabling these to live at sub-zero water temperatures.

\[
\begin{align*}
\beta\text{-Galactosyl-1,3-}\alpha\text{-N-acetylglactosamine} \\
\text{Repeating unit of antifreeze glycoproteins}
\end{align*}
\]
Some of the oligosaccharides found in N-linked glycoproteins
Some of the oligosaccharides found in N-linked glycoproteins

One of several from ovalbumin

Various serum glycoproteins

Porcine thyroglobulin Soybean agglutinin
Proteoglycans are a family of glycoproteins whose carbohydrate moieties are predominantly glycosaminoglycans. Structures are quite diverse as are sizes. Examples: versican, serglycin, decorin, syndecan.

Functions:
- Modulate cell growth processes
- Provide flexibility and resiliency to cartilage
Heparin is a carbohydrate with anticoagulant properties. It is used in blood banks to prevent clotting and in the prevention of blood clots in patients recovering from serious injury or surgery.

Numerous derivatives of heparin have been made (LMWH, Fondaparinux)
Hyaluronate: material used to cement the cells into a tissue
GLYCOLIPIDS

• **Cerebrosides**
  • One sugar molecule
    – Galactocerebroside – in neuronal membranes
    – Glucocerebrosides – elsewhere in the body

• **Sulfatides or sulfogalactocerebrosides**
  • A sulfuric acid ester of galactocerebroside

• **Globosides: ceramide oligosaccharides**
  • Lactosylceramide
    – 2 sugars (e.g. lactose)

• **Gangliosides**
  • Have a more complex oligosaccharide attached
  • Biological functions: cell-cell recognition; receptors for hormones
glycolipids

There are different types of glycolipids: cerebrosides, gangliosides, lactosylceramides
GLYCOLIPIDS

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Gangliosides

• complex glycosphingolipids that consist of a ceramide backbone with 3 or more sugars esterified, one of these being a sialic acid such as N-acetylneuraminic acid

• common gangliosides: $G_{M1}$, $G_{M2}$, $G_{M3}$, $G_{D1a}$, $G_{D1b}$, $G_{T1a}$, $GT_{1b}$, $G_{q1b}$
Ganglioside nomenclature

• letter G refers to the name ganglioside

• the subscripts M, D, T and Q indicate mono-, di-, tri, and quatra(tetra)-sialic-containing gangliosides

• the numerical subscripts 1, 2, and 3 designate the carbohydrate sequence attached to ceramide
Ganglioside nomenclature

- Numerical subscripts:
  - 2. GalNAc-Gal-Glc-ceramide
  - 3. Gal-Glc-ceramide
A ganglioside (G_{M1})
Lipid storage diseases

• also known as sphingolipidoses
• genetically acquired
• due to the deficiency or absence of a catabolic enzyme
• examples:
  • Tay Sachs disease
  • Gaucher’s disease
  • Niemann-Pick disease
  • Fabry’s disease
The end of this lecture