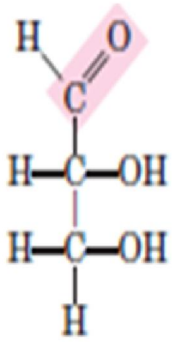
BCM 210 LECTURE

SALEMCITY, A.J

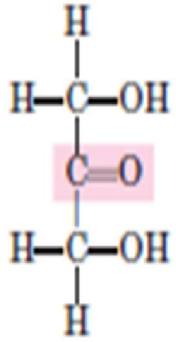
CARBOHYDRATE CHEMISTRY

- Carbohydrates (saccharides) are a large family of naturally occurring compounds including sugars, starches, and cellulose, as well as materials found in bacterial cell walls and insect exoskeletons.

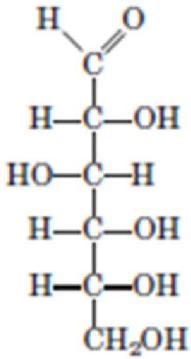
- Carbohydrates, in general, contain a C-C skeletal monomers bearing C=O and OH (and sometimes NH_2) functional groups.



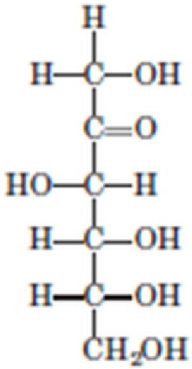
Glyceraldehyde, an aldotriose



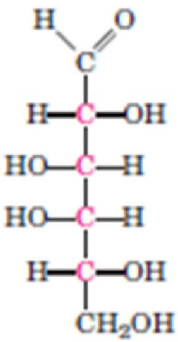
Dihydroxyacetone, a ketotriose



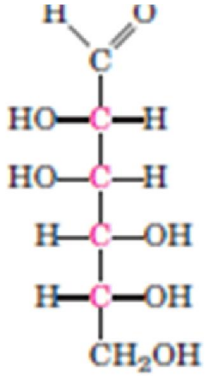
D-Glucose, an aldohexose



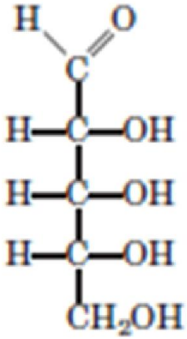
D-Fructose, a ketohexose



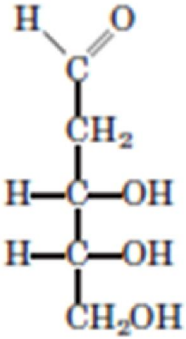
D-Galactose



D-Mannose



D-Ribose, an aldopentose



2-Deoxy-D-ribose, an aldopentose

SUGAR DERIVATIVES OF BIOLOGICAL IMPORTANCE

- Monosaccharides undergo various reactions to form biologically important derivatives.
- The important functional groups present in monosaccharides are hydroxyl and carbonyl groups.
- The hydroxyl group forms phosphodiester bond, usually with phosphoric acid or is replaced by a hydrogen or amino group.
- The carbonyl group undergoes reduction or oxidation to produce number of derived monosaccharides.

- These derivatives include amino sugar, sugar acids, sugar phosphates, deoxy sugars, and sugar amides etc.

➢ **Amino Sugars and N-acetylated sugars**

- The hydroxyl group, usually at C-2, is replaced by an amino group to produce amino sugars such as glucosamine, galactosamine and mannosamine.

- The amino group may be condensed with acetic acid to produce N-acetyl amino sugars, for example, N-acetyl glucosamine.
- This glucosamine derivative is important constituent of many structural polymers (chitin, bacterial cell wall polysaccharides etc.).

- **Glucosamine:** the systemic name is 2-Amino-2-deoxy-D-glucose.

- Glucosamine is an amino sugar derived from glucose, produced in the body from the sugar glucose and the amino acid glutamine through the action of the enzyme glucosamine synthetase.
- Glucosamine stimulates the synthesis of proteoglycans, glycosaminoglycans (also called mucopolysaccharides), and collagen.
- Glycosaminoglycans are a major component of joint cartilage, supplemental glucosamine may help to rebuild cartilage and treat arthritis.

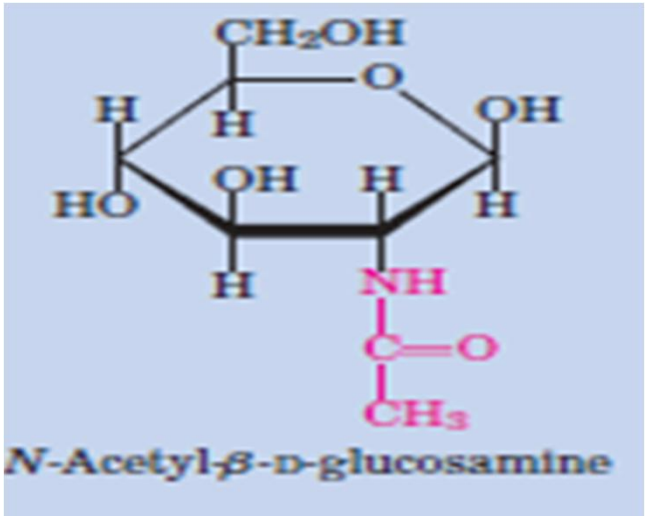
- It therefore plays a role in the formation of cartilage and the cushioning synovial fluid between the joints

- Glucosamine has been shown to help repair the mucosal-lining defensive barrier called the glycosaminoglycan layer (GAG).

- Defects in the GAG layer have been implicated in Crohn's disease, ulcerative colitis, and interstitial cystitis.

➢ N-Acetylglucosamine (GlcNAc)

- GlcNAc is a crucial biopolymer component of the bacterial cell wall which alternates between monomeric chains of GlcNAc and N-acetyl muramic acid, cross-linked with oligopeptides at the lactic acid residue of MurNAc. This is called peptidoglycan.

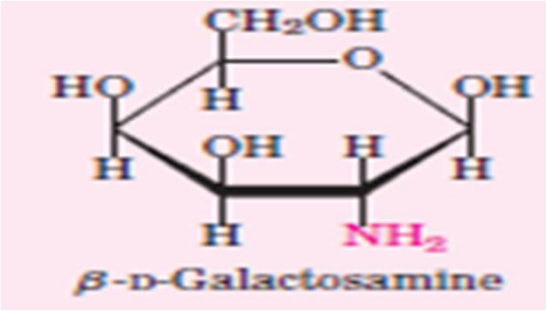


N-Acetyl-β-D-glucosamine

- GlcNAc is the monomeric unit of the polymer chitin found in insects and crustaceans.
- In bacteria, GlcNAc induces components that are important for colonization of human hosts, including fimbrins that mediate adhesion to host cells, multidrug exporter genes and Curli fibers that promote biofilm formation.
- In mammals, GlcNAc is a key sensor of nutrient status that is involved in insulin signaling, cell cycle control, and other essential processes.
- N-acetylglucosamine also play role in limiting cholesterol absorption and decreasing insulin secretion.

➢Galactosamine

Galactosamine is a hexosamine derived from galactose. This amino sugar is a constituent of some glycoprotein hormones such as follicle-stimulating hormone (FSH) and luteinizing hormone (LH).



β-D-Galactosamine

➢ N-Acetylgalactosamine

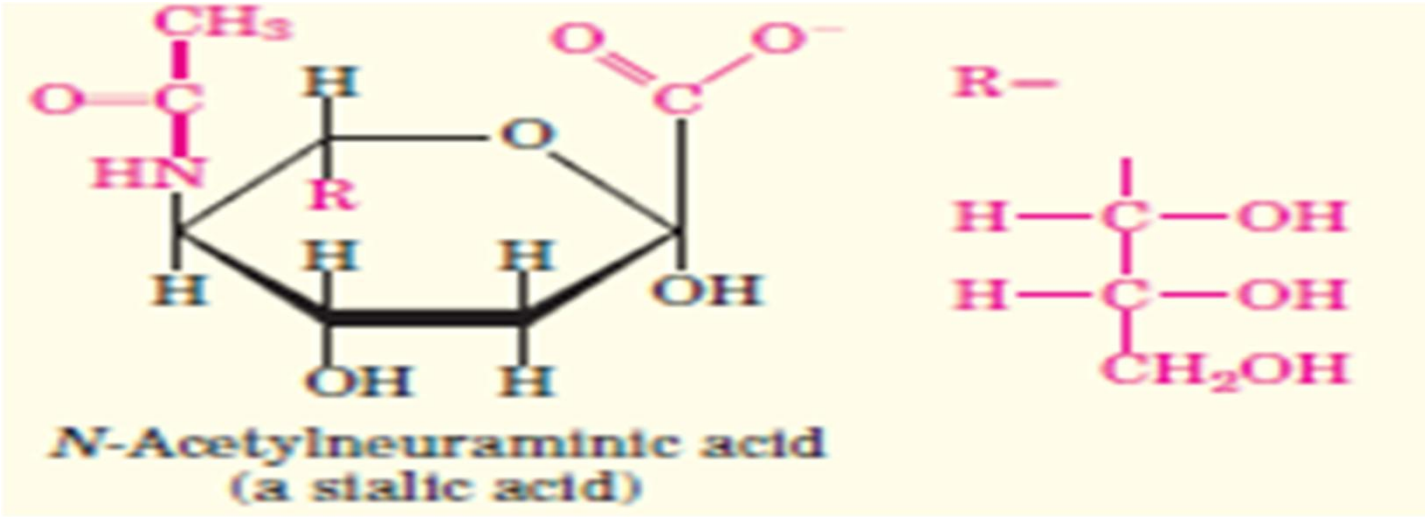
- Chemically, it is an amide between galactosamine and acetic acid.
- N-Acetylgalactosamine is necessary for intercellular communication, and is concentrated in sensory nerve structures of both humans and animals.

- N-acetylgalactosamine is also concentrated in other sensory nerve structures especially in the retina, photoreceptors, optic nerve, and the epithelial pigment of the eyes of both humans and animals.
- Thus, suggesting it may be extremely important for optimal vision.

➢ **Neuraminic acid and Sialic acid**

- Neuraminic acid ($\mathbf{C_9H_{17}NO_8}$) is a nine carbon monosaccharide. It may be theoretically visualized as the aldol-condensation product of pyruvic acid and D-mannosamine .
- The N- or O-substituted derivatives of neuraminic acid are collectively and commonly known as sialic acids, with N-acetylneuraminic acid as the predominant .

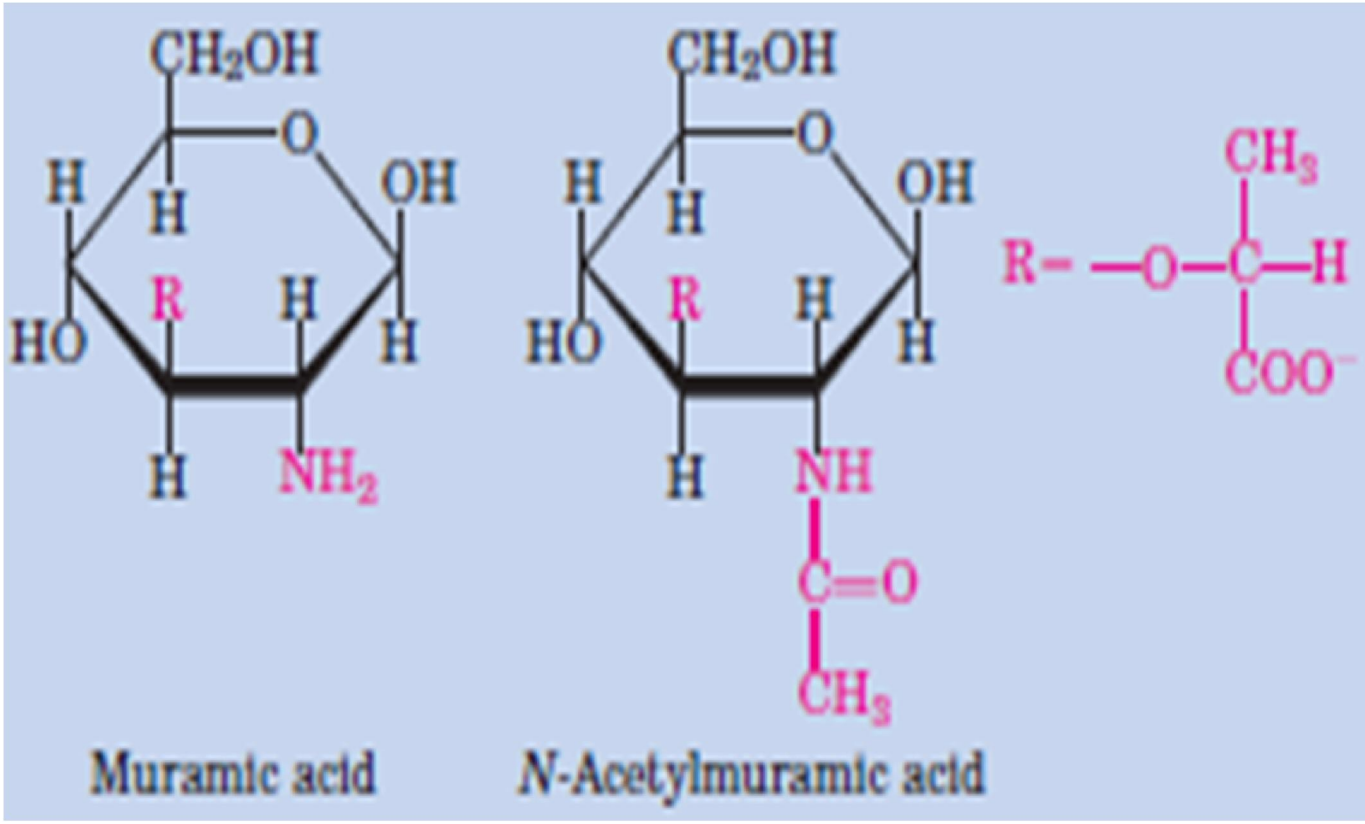
- Neuraminic acid does not occur naturally, but its derivatives are widely distributed in animals tissues such as brain, heart etc and in the body fluids like amniotic fluid, saliva and breast milk.
- It is important for brain development, learning, memory and cognitive performance.
- N-acetylneuraminic acid is important for cellular communication and is an immune system modulator.
- As an immune modulator, N-acetylneuraminic acid affects the viscosity of mucus, which in turn repels viruses, bacteria and other pathogens.



N-Acetylneuraminic acid
(a sialic acid)

➢ N-Acetylmuramic acid, or MurNAc

- Molecular formula: $\mathbf{C_{11}H_{19}NO_8}$
- It is the ether of lactic acid and N-acetylglucosamine.
- It is part of a biopolymer in the bacterial cell wall, built from alternating units of N-acetylglucosamine (GlcNAc) and N-acetylmuramic acid (MurNAc) linked by β(1→4) glycosidic bonds, cross-linked with oligopeptides at the lactic acid residue of MurNAc.
- This layered structure is called peptidoglycan.


CH2OH
O
OH
H
H
R
H
HO
H
H
NH2
CH2OH
O
OH
H
H
R
H
HO
H
H
NH
C=O
CH3
CH3
R–
O
C
H
COO⁻
Muramic acid
N-Acetylmuramic acid

➢ Polyols

- Both aldoses and ketoses are reduced to polyhydric alcohols (polyols) when treated with enzymes, sodium amalgam, and hydrogen under high pressure with catalyst or sodium borohydride.

➢ Ethylene glycol

- In its pure form, it is an odourless, colourless, syrupy liquid with a sweet taste.
- Ethylene glycol is toxic, and its ingestion should be considered a medical emergency.

• Glucose	Sorbitol
• Fructose	Sorbitol and mannitol
• Mannose	Mannitol
• Glyceraldehyde	Glycerol
• Erythrose	Erythritol
• Ribose	Ribitol
• Galactose	Dulcitol

- **Glycerol**

- Glycerol is a precursor for synthesis of triacylglycerols and of phospholipids in the liver and adipose tissue.
- The glycerol component can be converted to glucose by the liver and provides energy for cellular metabolism.

- **Erythritol**

- Erythritol is a natural sugar alcohol. It occurs naturally in fruits and fermented foods.

- **Xylitol**

- It naturally occurs in the fibers of many fruits and vegetables, including various berries, cornhusks, oats, and mushrooms. Xylitol is roughly as sweet as sucrose but with only two-thirds the food energy.

- Xylitol is a low-calorie alternative to table sugar.

➢ **Mannitol**

- Mannitol is used clinically to reduce acutely raised intracranial pressure, until more definitive treatment can be given, and to treat patients with oliguric renal failure.
- Mannitol can also be used to open the blood-brain barrier by temporarily shrinking the tightly coupled endothelial cells that make up the barrier.
- This makes mannitol indispensable for delivering various drugs directly to the brain (e.g. in the treatment of Alzheimer's disease)

➢ Sorbitol

- As a food additive it is categorized as a sweetener, emulsifier and humectant.
- Ingesting excess sorbitol can lead to some abdominal pain, gas, and mild to severe diarrhea.
- Diabetic retinopathy and neuropathy may be related to excess sorbitol in the cells of the eyes and nerves.

➢ Carboxylic acid sugars

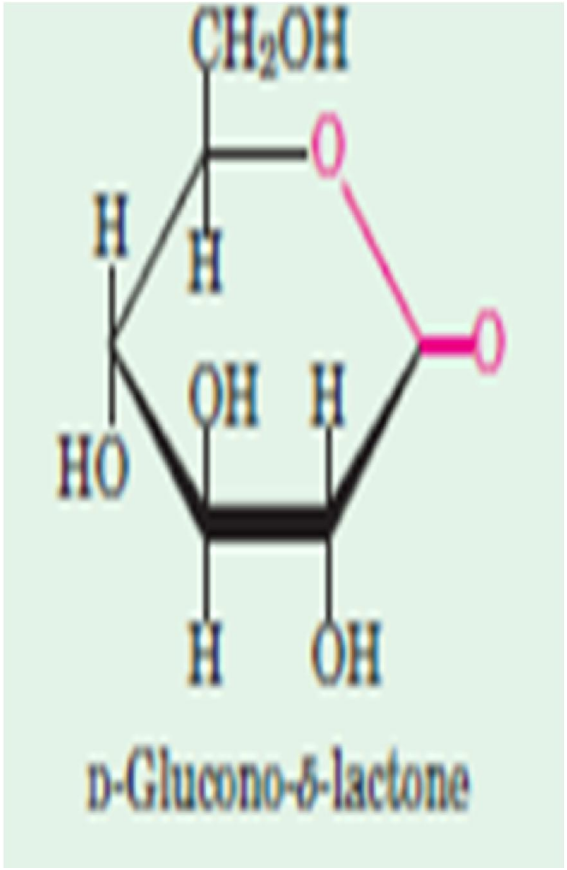
- The carbonyl group at C1 of monosaccharides may be oxidized to generate aldonic acids while C-6 oxidation results in uronic acids.

❖ Glucuronic acid

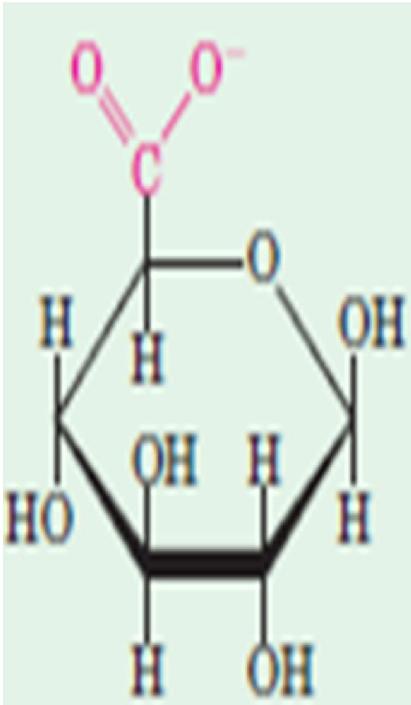
- Glucuronic acid is a carboxylic acid. It occurs by C-6 oxidation.
- In the animal body, glucuronic acid is often linked to poisonous substances, mainly in the liver, to allow for subsequent elimination, and to hormones to allow for easier transport.
- These linkages involve O-glycosidic bonds. The process is known as glucuronidation.

➢ Gluconic acid

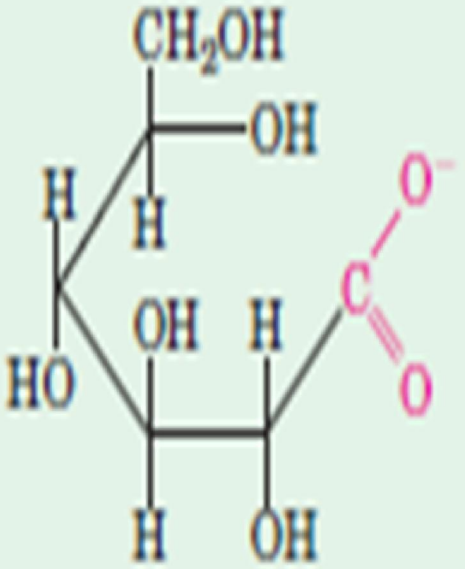
- Gluconic acid is the carboxylic acid formed by the oxidation of the C-1 of glucose.
- In aqueous solution, some gluconic acid molecules will convert to the cyclic ester Glucono delta lactone, and the two exist in equilibrium.
- Gluconic acid occurs naturally in fruit, honey, and wine; and is used as a food additive, an acidity regulator. It is a strong chelating agent, especially in alkaline solution.



D-Glucono-δ-lactone



β-D-Glucuronate



D-Gluconate

➢ Sugar phosphates

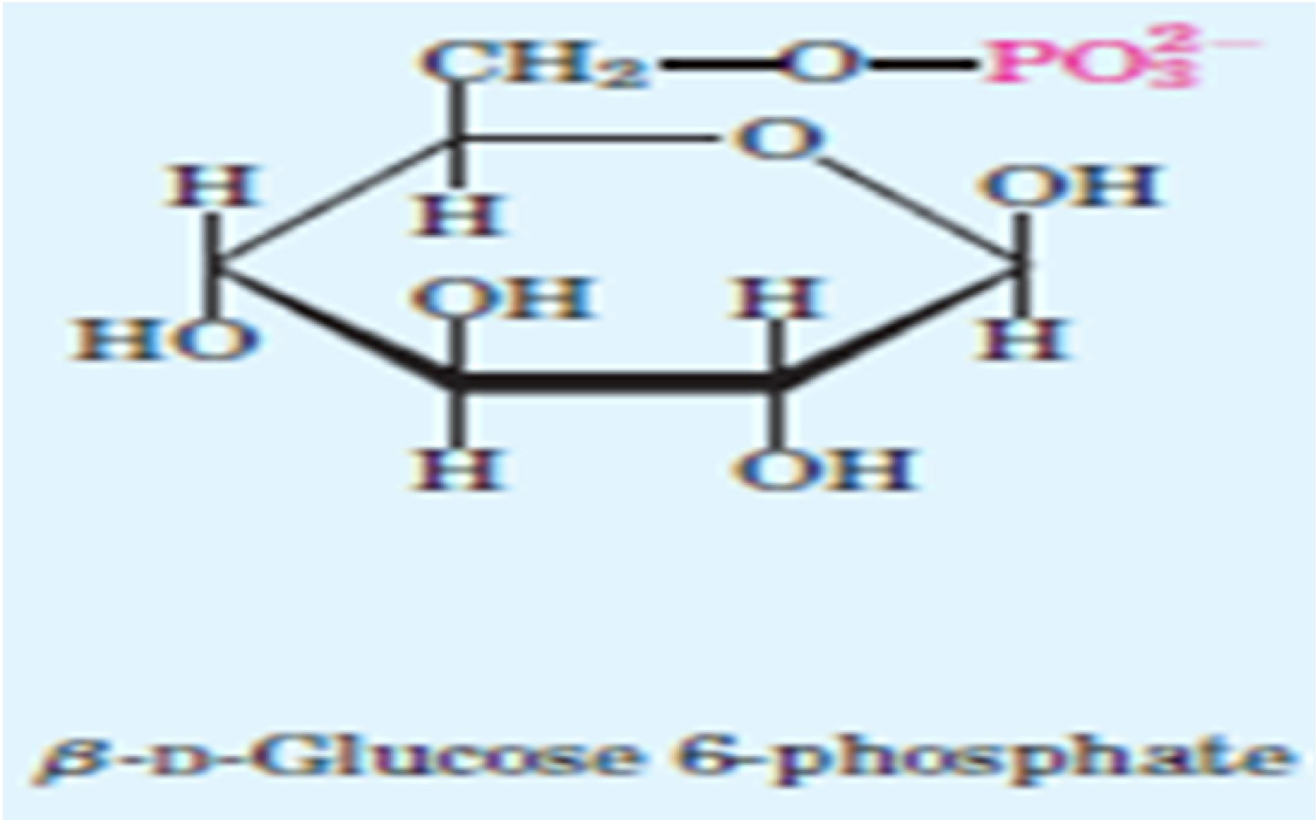
- Phosphorylated sugars are another important class of derivatives of sugars. At the normal pH of a cell, most of the hydroxyl groups (OH) on the phosphates are ionized (O-).
- The hydroxyl group of sugars form ester bond with phosphates.

❖ Glucose 6 phosphate

❖ Adenosine triphosphate (ATP)

- It is produced as an energy source during the processes of photosynthesis and cellular respiration and consumed by many enzymes and various cellular processes including biosynthetic reactions, motility and cell division.

- In signal transduction pathways, ATP is used by kinases that phosphorylate proteins and lipids, as well as by adenylate cyclase, which uses ATP to produce the second messenger molecule cyclic AMP.



β-D-Glucose 6-phosphate

❖ Cyclic Adenosine MonoPhosphate (cAMP)

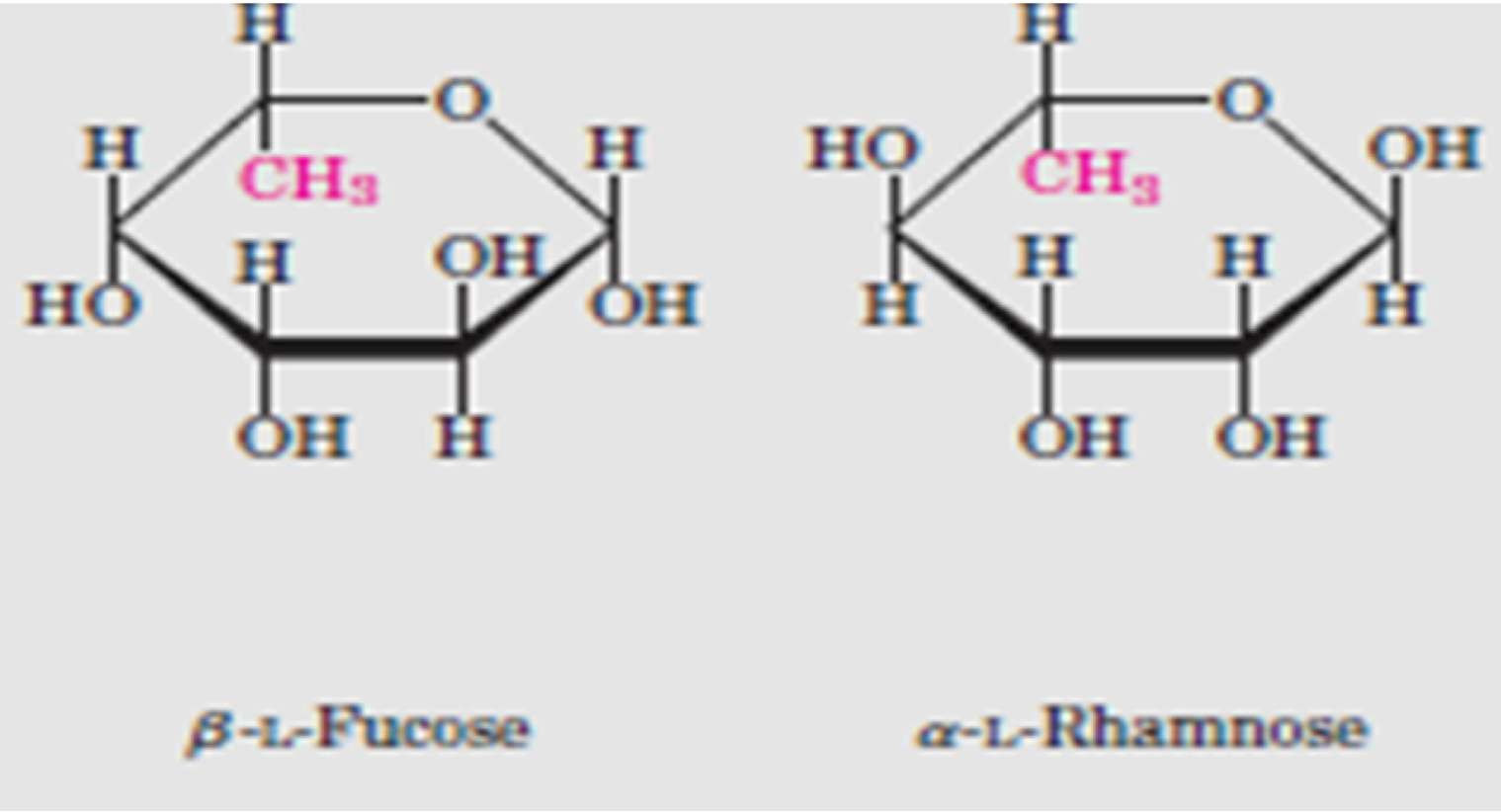
- It is derived from adenosine triphosphate (ATP) by the action of adenylyl cyclase.

- Adenylyl cyclase is activated by the hormones glucagon and epinephrine. cAMP is a second messenger, used for intracellular signal transduction, such as transferring the effects of hormones like glucagon and adrenaline, which cannot get through the cell membrane.

- Its purposes include the activation of protein kinases and regulating the effects of adrenaline and glucagon. It is also used to regulate the passage of Ca^{2+} through ion channels.

➢ Deoxy Sugars

- In sugars, the hydroxyl group is replaced by a hydrogen to produce deoxy sugars. The important deoxy sugar is 2-deoxy ribose that occurs in deoxy ribonucleic acid.
- Other important deoxy sugars are L-fucose and L-rhamnose. The substitution of the hydroxyl group at C-6 of L-galactose or L-mannose with hydrogen produces fucose or rhamnose respectively.
- L-fucose occurs in the cell wall polysaccharides namely hemicelluloses and L-rhamnose occurs in pectic polysaccharides namely rhamnogalacturonan. These deoxy sugars are also found in the complex oligosaccharide components of glycoproteins and glycolipids.


H
O
H
CH3
H
H
HO
H
OH
OH
OH
H
β-L-Fucose
H
O
HO
CH3
OH
H
H
H
H
OH
OH
α-L-Rhamnose

ABO Blood group system

- The associated anti-A antibodies and anti-B antibodies are usually IgM antibodies.
- The corresponding blood group carbohydrate structures, are found at the termini of oligosaccharide chains on glycoproteins and glycolipids on the surface of RBC and endothelial and most epithelial cells.
- The immunodominant monosaccharide that determines blood group A, is a terminal α-1,3-linked N-acetylgalactosamine (GalNAc), whereas the corresponding monosaccharide of blood group B specificity is an α-1,3-linked galactose. Group O cells lack chains, which instead are terminated with α-1,2-linked-fucose.

- The majority of the ABO determinants are expressed on the ends of long polylactosamine chains attached mainly to Band 3 protein, the anion exchange protein of the red cell membrane.
- While few are expressed on the neutral glycosphingolipid.
- In blood group O, the H antigen remains unchanged and consists of a chain of beta-D-galactose, beta-D-N-Acetylglucosamine, beta-D-galactose, and 2-linked, alpha-L-fucose, the chain being attached to the protein or ceramide.

- H antigens can be changed into A or B antigens by enzymes coded by the blood group A or B genes, which are sugar (glycosyl) tranferases.
- Type A has an extra alpha-N-Acetyl-D-galactosamine bonded to the D-galactose at the end, while type B has an extra alpha-D-galactose bonded to the D-galactose at the end.

- Individuals with Type A blood can receive blood from donors of type A and type O blood.

- Individuals with type B blood can receive blood from donors of type B and type O blood.

- Individuals with type AB blood can receive blood from donors of type A, type B, type AB, or type O blood.
- Type AB blood is referred to as the universal recipient.
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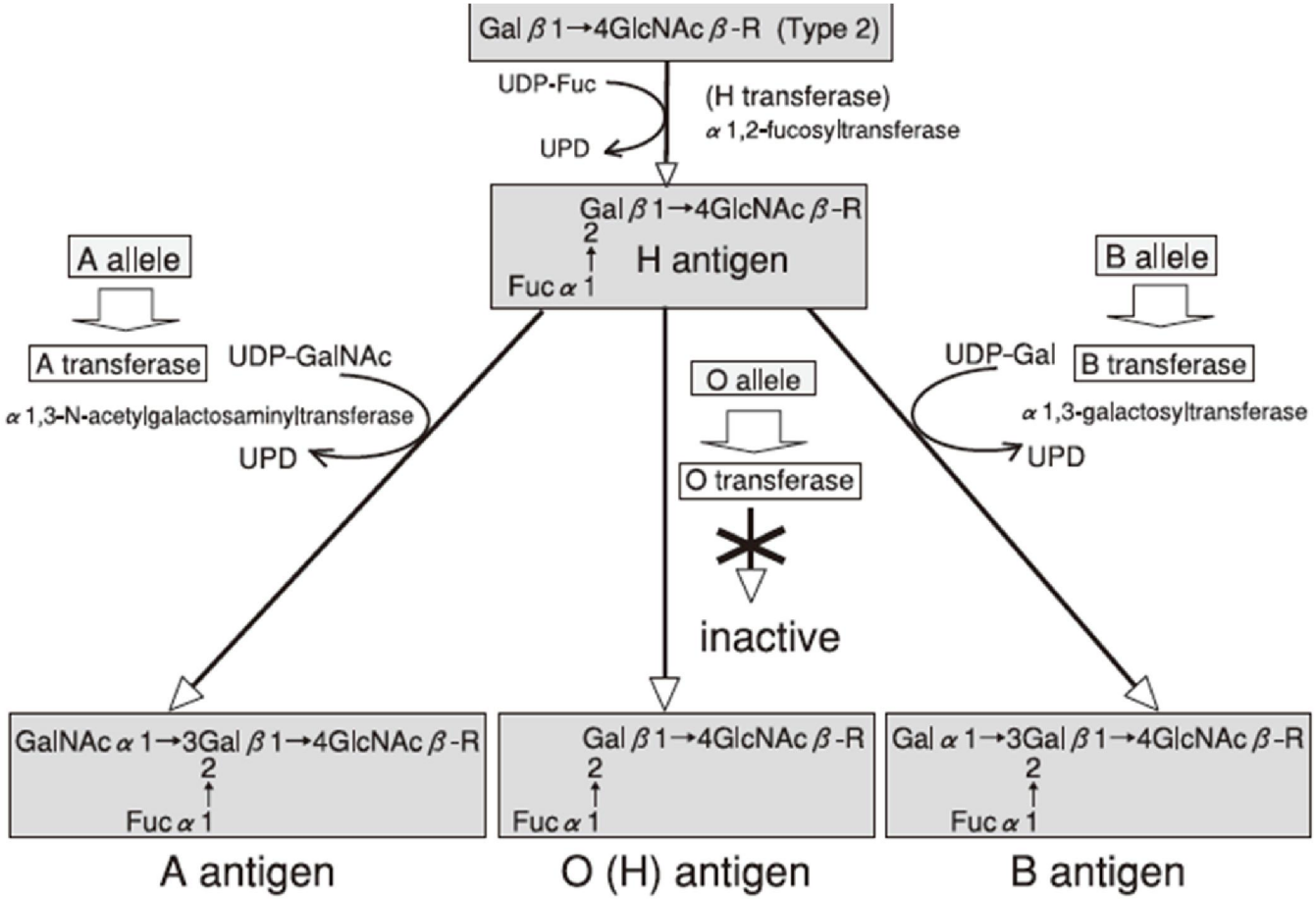
- Individuals with of O blood can receive blood from donors of only type O.

- Individuals of type A, B, AB and O blood can receive blood from donors of type O blood. Type O blood is called the universal donor.


Gal β 1→4GlcNAc β -R (Type 2)
UDP-Fuc
UPD
(H transferase)
α 1,2-fucosyltransferase
Gal β 1→4GlcNAc β -R
2
↑
Fuc α 1
H antigen
A allele
A transferase
UDP-GalNAc
α 1,3-N-acetylgalactosaminyltransferase
UPD
O allele
O transferase
inactive
B allele
B transferase
UDP-Gal
α 1,3-galactosyltransferase
UPD
GalNAc α 1→3Gal β 1→4GlcNAc β -R
2
↑
Fuc α 1
A antigen
Gal β 1→4GlcNAc β -R
2
↑
Fuc α 1
O (H) antigen
Gal α 1→3Gal β 1→4GlcNAc β -R
2
↑
Fuc α 1
B antigen

❖ *The Rh System*

- Rh antigens are transmembrane proteins with loops exposed at the surface of red blood cells. They appear to be used for the transport of carbon dioxide and/or ammonia across the plasma membrane.
- Red cells that are "Rh positive" are designated as D.
- About 15% of the population have no RhD antigens and thus are "Rh negative".
- The major importance of the Rh system for human health is to avoid the danger of RhD incompatibility between mother and fetus.