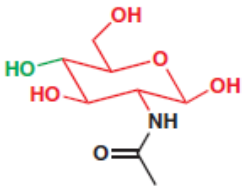
Deoxy sugars

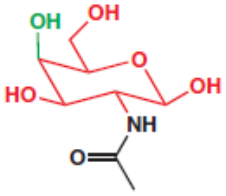
In these sugars one of the OH groups is replaced by a hydrogen. 2-Deoxyribose (oxygen missing at C-2 position) is an important example of a deoxy sugar. It is important component of DNA, and lack of C-2 hydroxyl provide additional stability to it as compared to RNA as no intramolecular nuclephilic attack on phosphate chain can occur.

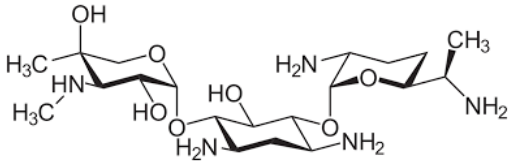
Amino sugars

In amino sugars one of the OH groups is replaced by an amino group. These molecules allow proteins and sugars to combine and produce structures of remarkable variety and beauty. The most common amino sugars are *N*-acetyl glucosamine and *N*-acetyl galactosamine, which differ only in stereochemistry. The hard outer skeletons of insects and crustaceans contain chitin, a polymer very like cellulose but made of *N*-acetyl glucosamine instead of glucose itself. It coils up in a similar way and provides the toughness of crab shells and beetle cases. Some important antibiotics contain amino sugars. For example, the three subunits of the antibiotic gentamicin are deoxyamino sugars (the middle subunit is missing the ring oxygen).

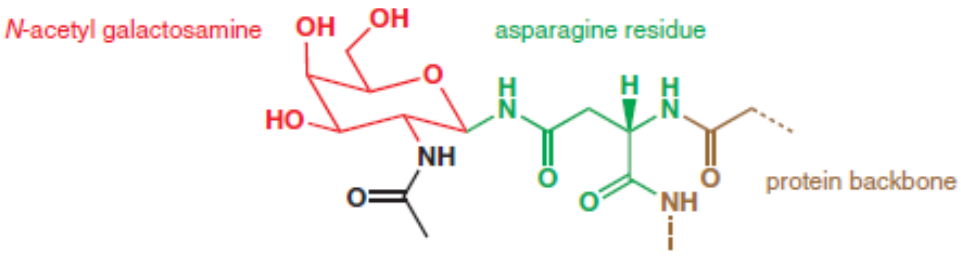
N-Acetyl glucosamine *N*-Acetyl galactosamine Gentamicin, an antibiotic







Cell membranes must not be so impermeable as they need to allow the passage of water and complex molecules. These membranes contain glycoproteins—proteins with amino sugar residues attached to asparagine, serine, or threonine in the protein. The attachment is at the anomeric position so that these compounds are *O*- or *N*-glycosides of the amino sugars. The structure below shows *N*-acetyl galactosamine attached to an asparagine residue as an *N*-glycoside.

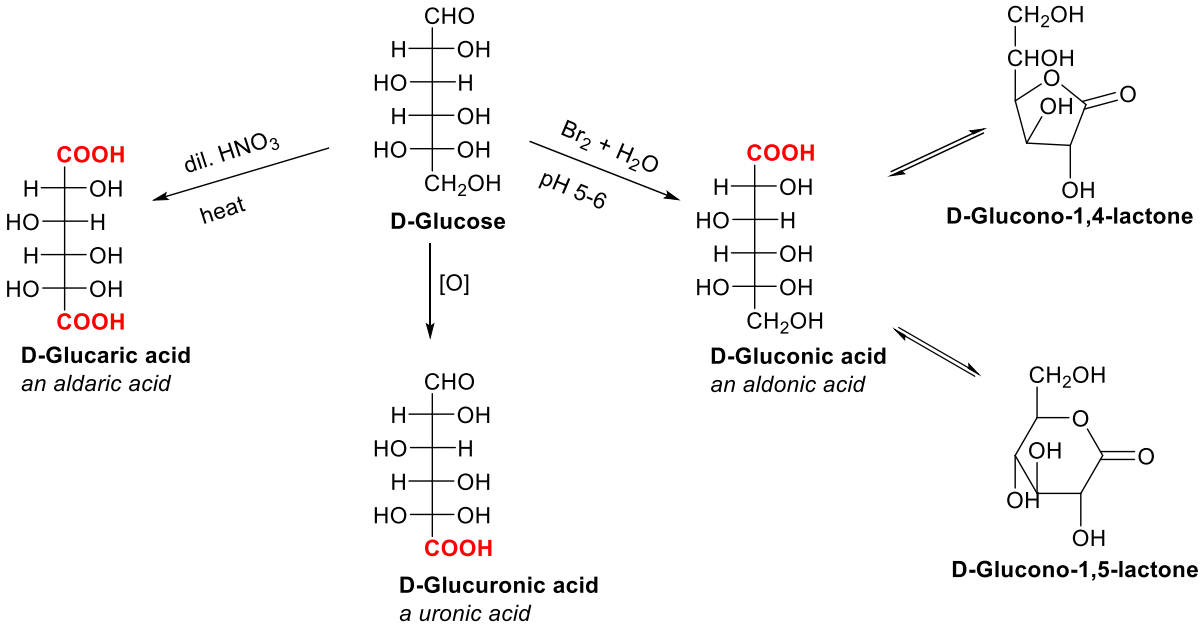


Acid derivatives of sugars

Aldonic acid

An aldehyde group is easily oxidized to a carboxyl group. The product of oxidation of the aldehyde group of an aldose is a polyhydroxy carboxylic acid called an aldonic acid. Although Tollens reagent can affect the conversion, a more convenient and less expensive reagent for the synthetic reaction is a buffered solution of bromine.

In alkaline solution, the aldonic acid exist as open chain carboxylate ions. Upon acidification, they form cyclic esters (lactones), just as any γ or δ-hydroxy acid would, forming five or six membered ring.



Aldaric acid

Vigorous oxidizing agents Ooxidize the aldehyde group and also the terminal hydroxyl group (a primary alcohol) of a monosaccharide. The product, a polyhydroxy dicarboxylic acid is called an aldaric acid. They also form lactones readily.

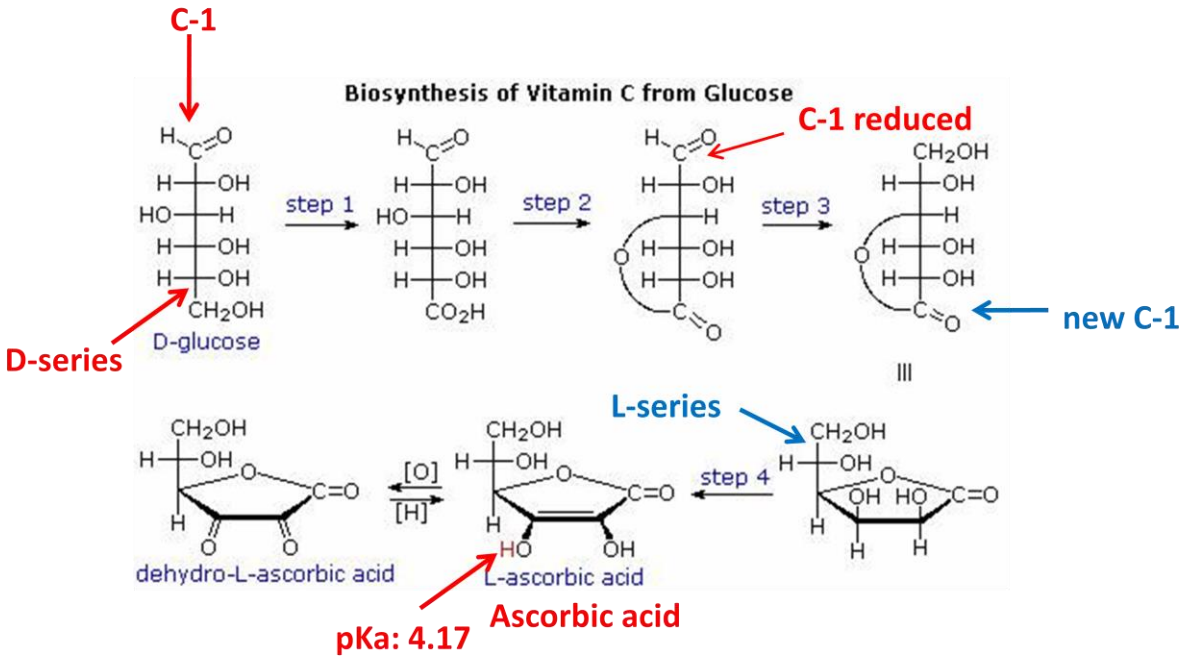
Uronic acids

Although it is not easy to do in laboratory, in biological systems the terminal CH_2OH group can be oxidized enzymatically without oxidation of the aldehyde group. The product is called Uronic acid.

Glucuronic acid is important in animal dietary systems because many toxic substances are excreted in the urine as glucuronides, derivatives of this acid.

Ascorbic acid (vitamin C)

D-glucuronic acid can be converted to L-gulonic acid, which is used to biosynthesize L-ascorbic acid (vitamin C). L-gulonic acid is converted into a γ-lactone by enzyme lactonase, and then an enzyme called oxidase oxidise the lactone to ascorbic acid. This last conversion does not take place in primates or guinea pigs, which require a source of vitamin C. The fact that a compound of D-series becomes a compound of the L-series is not due to biochemical change in configuration; rather, the change arises from the change in the numbering of the carbons, as shown below. The L-configuration refers to the configuration at C-5, which was C-2 in D-Glucose.

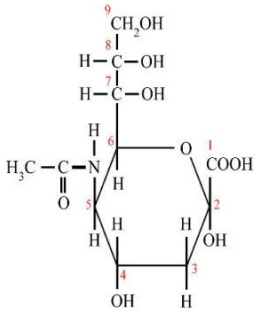


Although L-ascorbic does not have a carboxylic group, it is an acidic compound because the pKa of the C-3 OH group is 4.17. L-ascorbic acid is readily oxidized to L-dehydroascorbic acid, which is also physiologically active. If the lactone ring is opened by hydrolysis, all vitamin C activity is lost. Not much intact vitamin C survives in food that has been thoroughly cooked. And if the food is cooked in water, the water soluble vitamin is thrown out with the water.

Vitamin C traps radicals formed in aqueous environments. It is an antioxidant because it prevents oxidation reactions by radicals. Also, vitamin C is required for the synthesis of collagen, which is structural protein of skin, tendons, connective tissue and bone. Deficiency of vitamin C, known as scurvy, led to lesions appear on the skin, severe bleeding about gums, in the joints, and under the skin, and wounds heal slowly.

Sialic acid

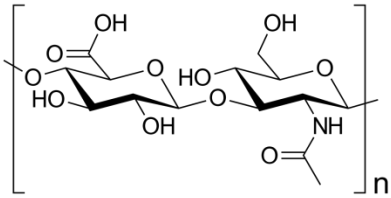
In addition to acidic hexose derivatives i.e. aldonic and uronic acids discussed above, one nine-carbon acidic sugar deserves mention: often referred to simply as “sialic acid”. In fact the ‘Sialic acid’ is a generic term for a family of derivatives of neuraminic acid. It is also the name for the most common member of this group, *N*-acetylneuraminic acid (Neu5Ac), a derivative of *N*-acetylmannosamine, is a component of many glycoproteins and glycolipids in animals. They occur at the end of sugar chains connected to the surfaces of cells and soluble proteins. In humans the brain has the highest sialic acid concentration, where these acids play an important role in neural transmission and ganglioside structure (discussed later).



N-Acetylneuraminic acid (Neu5Ac: a sialic acid)

Hyaluronic acid

Hyaluronic acid is naturally produced by our body and the largest amounts of it is found in skin, connective tissue and eyes. Its main function is to retain water to keep tissues well lubricated and moist. The average 70 kg person has roughly 15 grams of hyaluronan in the body, one-third of which is turned over (degraded and synthesized) every day. The glycosaminoglycan hyaluronic acid contains alternating residues of D-glucuronic acid and *N*-acetylglucosamine. With up to 50,000 repeats of the basic disaccharide unit, hyaluronates have molecular weights greater than 1 million; they form clear, highly viscous solutions that serve as lubricants and shock absorbant in the joints of animals. Hyaluronates give the vitreous humor of the vertebrate eye its jellylike consistency (a glassy or translucent appearance).

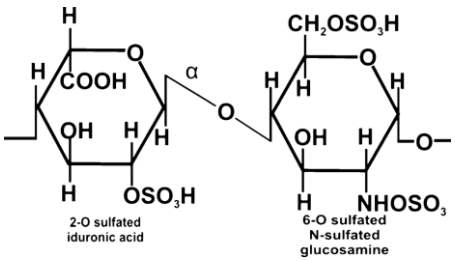


Hyaluronate is also an essential component of the extracellular matrix of cartilage and tendons, to which it contributes tensile strength and elasticity as a result of its strong interactions with other components of the matrix. Hyaluronidase, an enzyme secreted by some pathogenic bacteria, can hydrolyze the glycosidic linkages of hyaluronate, rendering tissues more susceptible to bacterial invasion. In many organisms, a similar enzyme in sperm hydrolyzes an outer glycosaminoglycan coat around the ovum, allowing sperm penetration.

Heparin

Heparin is a medication and naturally occurring glycosaminoglycan. It is a natural anticoagulant (blood thinner) made in mast cells (a type of leukocyte) and released into the blood, where it inhibits blood coagulation by binding to the protein antithrombin. Heparin binding causes antithrombin to bind to and inhibit thrombin, a protease essential to blood clotting. The interaction of heparin is strongly electrostatic; heparin has the highest negative charge density of any known biological macromolecule. It consists of a variably sulfated repeating disaccharide unit. The most common disaccharide unit is composed of a 2-*O*-sulfated iduronic acid and 6-*O*-sulfated, *N*-sulfated glucosamine.

It is used to treat and prevent blood clots caused by certain medical conditions or medical procedures. It is also used before surgery to reduce the risk of blood clots. Purified heparin is routinely added to blood samples obtained for clinical analysis, and to blood donated for transfusion, to prevent clotting.



Glycobiology: Carbohydrates as Informational Molecules

In addition to their important roles as stored fuels (starch, glycogen, dextran) and as structural materials (cellulose, chitin, peptidoglycans), polysaccharides and oligosaccharides are information carriers: they serve as destination labels for some proteins and as mediators of specific cellular interactions. The surfaces of many cells contain short polysaccharide chains that allow the cells to interact with each other, as well as to interact with invading viruses and bacteria. Also, the polysaccharide chain can act as a receptor site on the cell surface in order to transmit signals from hormones and other molecules across the cell membrane into the cell.

Glycoconjugates

The study of the structure and function of glycoconjugates, is one of the most active and exciting areas of biochemistry and cell biology. Cells use specific oligosaccharides to encode important information about intracellular targeting of proteins, cell-cell interaction, tissue development, extracellular signals, blood clotting, the immune response, and wound healing, to name but a few of their many roles. In most of these cases, the informational carbohydrate is covalently joined to a protein or a lipid to form a glycoconjugate**,** which is the biologically active molecule.

Sialic acid containing glycoconjugates

Sialic acid-rich oligosaccharides on the glycoconjugates (glycolipids, glycoproteins, proteoglycans) found on surface membranes help keep water at the surface of cells. The sialic acid-rich regions contribute to creating a negative charge on the cells' surfaces. Since water is a polar molecule with partial positive charges on both hydrogen atoms, it is attracted to cell surfaces and membranes. This also contributes to cellular fluid uptake.

Sialic acid-rich glycoproteins (sialoglycoproteins) bind selectin in humans and other organisms. Metastatic cancer cells often express a high density of sialic acid-rich glycoproteins. This overexpression of sialic acid on surfaces creates a negative charge on cell membranes. This creates repulsion between cells (cell opposition) and helps these late-stage cancer cells enter the blood stream.

Gangliosides**,** the most complex sphingolipids, have oligosaccharides as their polar head groups and one or more residues of *N*-acetylneuraminic acid (Neu5Ac, a sialic acid), at the termini. Sialic acid gives gangliosides the negative charge at pH 7. Sphingolipids at cell surfaces are sites of biological recognition. The carbohydrate moieties of certain sphingolipids define the human blood groups and therefore determine the type of blood that individuals can safely receive in blood transfusions.

Furthermore, the residues of sialic acid situated at the ends of the oligosaccharide chains of many plasma glycoproteins protect those proteins from uptake and degradation in the liver. Removal of the sialic acid residues by the enzyme sialidase (also called neuraminidase) is one way in which the body marks “old” proteins for destruction and replacement.

A similar mechanism is apparently responsible for removing old erythrocytes from the mammalian bloodstream. Newly synthesized erythrocytes have several membrane glycoproteins with oligosaccharide chains that end in sialic acid (Neu5Ac). When the sialic acid residues are removed by withdrawing a sample of blood, treating it with sialidase *in vitro*, and reintroducing it into the circulation, the treated erythrocytes disappear from the bloodstream within a few hours; those with intact oligosaccharides (erythrocytes withdrawn and reintroduced without sialidase treatment) continue to circulate for days.

Several animal viruses, including the influenza virus, attach to their host cells through interactions with oligosaccharides displayed on the host cell surface. The lectin of the influenza virus, the HA protein, is essential for viral entry and infection. After initial binding of the virus to a sialic acid–containing oligosaccharide on the host surface, a viral sialidase removes the terminal sialic acid residue, triggering the entry of the virus into the cell. Inhibitors of this enzyme are used clinically in the treatment of influenza.

Carbohydrates on Cell Surfaces

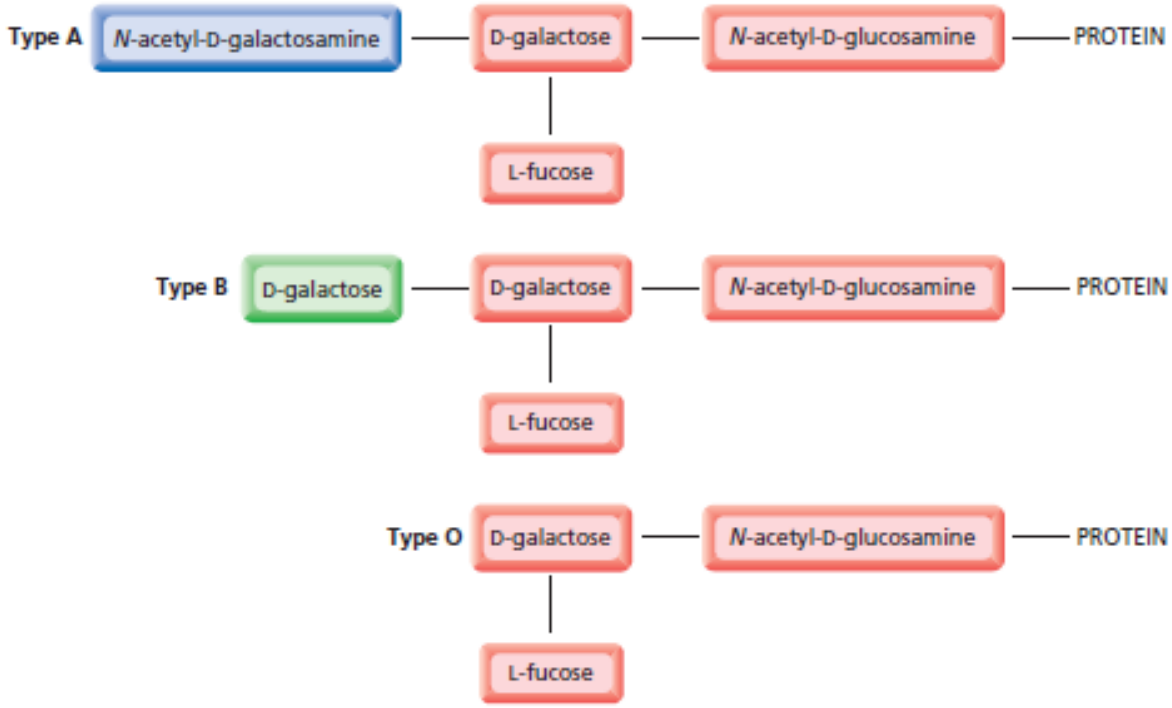
Carbohydrates on the surfaces of cells provide a way for cells to recognize one another. The interaction between surface carbohydrates has been found to play a role in many diverse activities, such as infection, the prevention of infection, fertilization, inflammatory diseases like rheumatoid arthritis and septic shock, and blood clotting. For example, the goal of the HIV protease inhibitor drugs is to prevent HIV from recognizing and penetrating cells. The fact that several known antibiotics contain amino sugars suggests that they function by recognizing target cells. Carbohydrate interactions also are involved in the regulation of cell growth, so changes in membrane glycoproteins are thought to be correlated with malignant transformations.

ABO blood type system

One well known example of cell-cell recognition mediated by carbohydrates is the ABO blood type system. The A, B, and O blood groups were first identified by Austrian immunologist Karl Landsteiner in 1901.The **ABO blood group system** is used to denote the presence of one, both, or neither of the A and B antigens on erythrocytes. All people synthesize a precursor carbohydrate, called the H-antigen, which is attached to lipids or proteins on the outer surface of red blood cells. Specific enzymes synthesized by ABO genes attach additional monosaccharides to the H-antigen and the completed carbohydrate determines person's blood type (A, B, AB, or O). Each type of blood is associated with a different carbohydrate structure. Blood containing red cells with type A antigen on their surface has in its serum (fluid) Antibodies* against type B red cells. If, in transfusion, type B blood is injected into persons with type A blood, the red cells in the injected blood will be destroyed by the antibodies in the recipient's blood. In the same way, type A red cells will be destroyed by anti-A antibodies in type B blood.

***Antibodies** are proteins that are synthesized by the body in response to a foreign substance, called an **antigen**. Interaction with the antibody either causes the antigen to

precipitate or flags it for destruction by immune system cells. This is why, for example, blood cannot be transferred from one person to another unless the carbohydrate portions of the donor and acceptor are compatible. Otherwise the donated blood will be considered a foreign substance.



Looking at Figure above, we can see why the immune system of type A people recognizes type B blood as foreign and vice versa. Type AB blood has the carbohydrate structure of both type A and type B. The immune system of people with type A, B, or AB blood does not, however, recognize type O blood as foreign, because the carbohydrate in type O blood is also a component of types A, B, and AB blood. Thus, anyone can accept type O blood, so people with type O blood are called universal donors. Type AB people can accept types AB, A, B, and O blood, so people with type AB blood are referred to as universal acceptors.