

BE.342/442 Thursday, November 3, 2005
Topic: Polysaccharides and Oligosaccharides

Administrative:

Next Tuesday, Prof. Zhang will be out of town, but we'll play a movie about Francis Crick. Please come on time, because the movie is 2 hours long.

On November 15th, Prof. Zhang will be out of time, but we'll have a guest lecture about self-assembly.

At the end of this lecture, we'll look at Peter Seeberger's work, featured on the cover of last week's *Science*. He has synthesized sugars from scratch in his lab!

We've spent many lectures on proteins, and last time, we discussed lipids as a biomaterial. Today, we'll discuss another important class of materials built from sugars.

Polysaccharides and oligopolysaccharides can be divided into two classes:

Homopolysaccharides: cellulose (plant structures), starch (plant energy storage), chitin (exoskeletons of animals like lobsters)

Heteropolysaccharides: hemicellulose, hyaluronic acid, heparan sulfate, etc.

Their functions include:

Storage: starch, glycogen

Structural: cellulose, hemicellulose, chitin

Signaling: glycoproteins, lipopolysaccharides, glycolipids

Sugars are difficult to synthesize in the lab, can be obtained from organisms, which construct them by:

(1) Photosynthesis

(2) Gluconeogenesis

and are then chemically manipulated. Sugars serve as the building blocks of polysaccharides.

Starch is a mixture of glucans that plants synthesize as their principal food reserve. It is deposited as insoluble granules composed of alpha-amylose and amylopectin.

Glycogen is an "animal starch" used to store energy. It is present in all cells, but prevalent in skeletal muscle and in the liver, where it occurs as cytoplasmic granules. Its structure is similar to amylopectin, but is highly branched, with branching points every 8-12 residues.

Chitin is a homopolymer of N-acetyl-glucosamine and has a structure similar to cellulose. It can be found in fungi, algae, and the exoskeletons of invertebrates such as arthropods and mollusks.

Cellulose composes the plant cell wall.

Linkages between glucose residues

Special enzymes are required to break the beta (1 → 4) D-glucose linkages that hold together cellulose. Many herbivorous animals, such as cows, have specialized bacteria in their stomachs that produce the enzymes to break these bonds. Humans lack this enzyme, and can't digest grass!

In contrast, the glucose monomers in cellulose and starch are held together by alpha (1 → 4) D-glucose linkages.

Plant cell walls

(See figures from Chapter 24 of the course textbook.)

Cellulose is a linear polymer of several thousand residues of glucose. The (1 → 4) D-glucose linkages form cellulose chains, which assemble into bundles called microfibrils. Hemicellulose is a copolymer of glucose and galactose, with a branched structure that has different mechanical properties. The single hydrogen bonds between adjacent chains are weaker than cross-links, but collectively, they form a strong force holding the bundles together.

Cellulose chains can bundle into microfibrils, forming a nanoscale fibrous structure that provides the organism with mechanical support on both the cell and tissue level. On a cellular level, cellulose can maintain balance pressures inside the cell membrane. On a macroscopic level, of course, cellulose gives plants shape and rigidity.

The enzyme cellulose synthase (textbook Fig. 24-73) synthesizes cellulose in spirals going around an elongating cell.

Bacterial cell walls can contain chitin and peptidoglycans.

Monosaccharides

Single sugars can have between 4 and 8 carbons in a linear chain. Sugars, like amino acids, have handedness, or chirality. Typically, the D-form is prevalent in organisms and “fits” into biological enzymes, whereas the L-form cannot be processed by biological enzymes.

Some important sugars in our lives are:

ribose (5 carbons) forms the backbone of our DNA and RNA

Beta-ribose is found in RNA. With one –OH group removed, alpha-deoxyribose is found in DNA. The difference of that one –OH group in terms of stability is enormous! The additional –OH group allows ribose to make two more hydrogen bonds than deoxyribose, making it susceptible to self-hydrolysis and enzymatic degradation. This explains the stability of DNA as compared to RNA. Your body

uses the enzyme ribonuclease to defend itself from viruses. These 2 hydrogen bonds make all the difference in the world: experiments in which the –OH group was replaced with other chemical groups showed that the hydrogen bonding ability was the key to the relative instability of the modified ribose.

glucose (6 carbons) is found in our favorite sweets!

Glucose can be found as a straight chain, or as a ring. When a D-glucose chain reacts with itself to close into a ring, it can form either D-alpha-glucose or D-beta-glucose. This rotational difference in the closing process makes an enormous structural difference: the difference between cellulose and glycogen/starch!

Glucose typically assumes a “chair” conformation, but is sometimes found in a “boat” conformation, which is usually less stable.

galactose (6 carbons) differs from glucose only by one –OH group, and is found in milk.

In the textbook, review the structures of the common hexoses: glucopyranose, mannopyranose, galactopyranose, fructopyranose. The 6-carbon chains can occur in a furan form (a five-membered ring) or a pyran form (a six-membered ring).

Chitin

Found in the shells of lobsters, crabs, and squid, and the wings of butterflies and shells of beetles, these polysaccharides add an extra group to the base structure of glucose. Scanning electron micrographs of a beetle’s trachea shows a fibrous web-like structure. Mathematically, this structure has not yet been solved.

Proteoglycans

Sugars coupled to proteins provide important biochemical functions, such as blood type groups. People have learned how to cleave the identifying sugars from blood proteoglycans in order to turn blood into universal donor types!

An important proteoglycan found in humans is aggrecan, a brush-like molecule that is important for the load-bearing properties of cartilage.

Glycosaminoglycans, found in mucus and extracellular matrices, consist of three repeating units: chondroitin sulfate, keratan sulfate, and hyaluronic acid.

Peter Seeburger, OJ Plante, Michael Hewitt, and others learned to sequence and synthesize sugars. Through 9 steps of side group protection chemistry, each with a limited yield (and therefore a need to purify at each step!) he synthesized a 6-sugar oligosaccharide. Read about his work on the course website. Also, read more in the textbook about enzymatic degradation of

polysaccharides, and the biochemical roles of chitobiose, heparin, and other polysaccharides not discussed here.