

## AMINO SUGARS

Amino sugars are constituents of structures found in all tissues, mostly on the surface of cells and in the spaces between them, forming the substance that binds cells together, membranes that envelope them and protective layers that cover them (1, 2, 3, 4). Unlike most sugars, that are obtained in the diet and are oxidized for energy, amino sugars are formed in the body from glucose and are committed entirely to the formation of structural components. The “glue” that holds tissues together is a meshwork of fibers of the protein collagen together with giant molecular complexes of proteoglycans, where approximately half of the constituent molecules are amino sugars. These substances are in a constant state of formation, degradation, restructuring and recycling: the life of a constituent molecule is only a few days. Our diet may contain some amino sugars but it is not an important source. The need to replace those lost in the steady turnover of tissue components, i.e. their metabolism, is met by synthesis starting from glucose; about one fifth of the glucose is destined for amino sugar formation.

## INCORPORATION OF AMINO SUGARS INTO MACROMOLECULES

### Glycoproteins:

Glycoproteins are proteins containing a chain of sugars, usually a dozen or so sugars, called an oligosaccharide chain. This chain modifies the properties of the protein to which it is attached. The sugars are added to newly synthesized protein in the endoplasmic reticulum and Golgi regions of the cell<sup>5</sup>. Some will be extruded from the cell as secreted products, enzymes, hormones etc. while others will remain on the cell surface where the “antenna” of the oligosaccharides chains function in a specific manner, for example as recognition and binding sites for hormones. Some glycoproteins with higher sugar content have special functions. Mucus contains a glycoprotein with a relatively high content of sugar, giving it the property of forming a viscous solution.

The human body contains perhaps 100,000 different proteins, each composed of an assortment of 20 or so amino acids. The sequence of these 20 or so amino acids determines the unique properties of each protein, e.g. its role as an enzyme acting as a catalyst for a specific biochemical reaction. If even one of the essential amino acids is missing, the protein cannot be formed. This fact is well known to nutritionists since ensuring an adequate supply of essential amino acids is important in determining the nutritional value of proteins in the diet.

Amino sugars also confer specificity similar to that of amino acids. Many functions of proteins are dependent upon the structure of the oligosaccharide chain, including for example, their insertion on cell surfaces which govern the interaction with other cells and may determine the antigenic properties of the protein and the lifespan of the protein in the circulation.

### Glycolipids:

Lipids with an oligosaccharide chain are cell membrane constituents where the sugars are invariably located on the outer surface of the cell. An example is the glycolipid, called a ganglioside, which determines what blood group we belong. In blood group A there is a molecule of N-acetyl galactosamine in the chain, while in blood group B this is galactosamine<sup>6</sup>. In group O there is no sugar in that position

in the chain. This illustrates the great specificity that can be determined by a single constituent amino sugar.

### **Proteoglycans:**

Proteoglycans (PG) are giant molecular complexes where many molecules of glycosaminoglycans (GAG) or as they are more commonly known, mucopolysaccharides (MPS) are attached through their core proteins to a long strand of hyaluronate. Whereas glycoproteins are mostly protein with a minor quantity of carbohydrate, the PG is mostly CHO, 90% or more. The whole structure has a molecular weight of millions and is a major component of the extra cellular space (2, 7).

## **TISSUE STRUCTURES FORMED BY MACROMOLECULES CONTAINING AMINO SUGARS**

### **The Interstitium:**

The space between cells in a tissue is occupied by a meshwork of fibers of the protein collagen. Collagen is the most abundant protein in the body making up a quarter of the total protein. There are several types: Type 1, 11 and 111 vary somewhat in their structure. Interspersed in the network of collagen fibers are molecules of PG. The gel-like structures formed resist compression and limit the diffusion of molecules and the movement of cells. This matrix binds cells together and regulates what passes among them. The enzyme hyaluronidase, once called “spreading factor” depolymerizes hyaluronate, breaking down the structure and allowing for freer movement, e.g., of bacteria, in the interstitium<sup>2,7</sup>. The type of collagen and the types of PG vary in different tissues, as well as the presence of other proteins. Each tissue has features of its own but the general pattern of the matrix is common. The constituent sugars and amino sugars etc. that go into the structure of the matrix are synthesized in each tissue independently.

### **Basement Membranes:**

Basement membranes (BM) are structures composed of collagen and PG that surround blood vessels and tissues. The BM contains a special type of collagen, mostly type 1V and a glycoprotein called laminin. Under electron microscopy BM have 3 layers, the outer side bordering on the interstitium. APG containing GAG, heparan sulphate is important in determining the permeability of the BM and thus what passes between blood and tissues (7).

### **Glycocalyx:**

A thin coat of glycoprotein called the glycocalyx<sup>(3, 8)</sup> covers the mucus membranes that line the digestive, respiratory and genitourinary tracts. Unlike mucus that is secreted over the surface of the cells the glycocalyx is an integral part of the cell membrane. Although it is very thin and can only be seen under the electron microscope, it is the ultimate barrier between the underlying cells of the intestinal mucosa, for example and the contents of the intestine – digestive juices, bacteria etc. It is also a filter through which all digested food must diffuse in order to be absorbed by the mucosal cells.

## TISSUE COMPONENTS CONTAINING PROTEOGLYCANS AND GLYCOPROTEINS

- **Tendons and ligaments** are rich in chondroitins.
- **Cartilage** contains these and keratan sulphates as well as a protein, elastin.
- **Synovial fluid**, which occurs in joints: hip, knee, elbow, etc, is rich in hyaluronate that is not associated with protein but provides lubrication for the smooth movement of cartilaginous surfaces.
- **Mucus** is a solution, the main constituent being a glycoprotein with a relatively high CHO content. This gives the solution high viscosity that provides lubrication and protection for the mucus membranes.
- **Skin** contains chondroitins and hyaluronate.
- **The eye** has several structures containing PG and GP. The aqueous humour is a solution of virtually only hyaluronate.
- **Blood vessels:** The Basement Membranes (BM) of all blood vessels contain collagen Type 1V, a glycoprotein laminin and a heparan sulphate PG.
- **Heart** valves are rich in hyaluronate and chondroitins.
- **Sexual organs** are influenced by hormones that elicit profound morphological and functional changes, many involving component PG. A striking example is the rooster's comb that is largely hyaluronate whose synthesis is stimulated by androgens. The growth of a capon's comb is an old assay for male hormones.
- **The placenta** is an extension of the blood vessels of the fetus. Here BM of syncytial cells and fetal capillaries as well as intervening supporting material constitute a major part of the barrier between the maternal and fetal circulations. Wharton's jelly in the umbilical cord is almost entirely hyaluronate; in fact the best source for its preparation.
- **Chitin** is a polymer of just N-acetyl glucosamine (NAG), analogous to cellulose, which is a polymer of glucose. Cellulose, the main constituent of plants, is the most abundant organic matter on earth; chitin, in shellfish and insects, is the second most abundant. In our bodies chitin is found in fingernails and toenails, which are almost entirely made of chitin.

## AMINO SUGARS, CELL PROLIFERATION AND THE AUTO IMMUNE THEORY

A widely held theory of the cause of many diseases is from the formation of antibodies to the body's own tissues, which then attack those tissues and cause damage. Such antibodies can frequently be found in the circulation and there is evidence for their formation in a number of situations (9).

Treatment of many conditions thought to be "auto-immune" in nature has been with drugs (immunosuppressive agents) known to suppress antibody formation. Such treatment is often successful in the short term, but there are serious side effects.

Cells of each tissue have their own characteristic life span and rate of replacement. Some, like certain nervous tissues are never replaced, although the cellular constituents do turn over. Cells that line the digestive tract have the highest rate of turnover; being replaced every 2 or 3 days. As a result of infection, injury or other disturbances, the lifespan of cells can be shortened, leading to an increased rate of turnover. This is a common to many disorders of diverse origin.

Increased cell turnover can impose a strain on the biosynthetic capabilities of cells, resulting in inadequate formation of some essential components of the cellular matrix. This would result in derangement of tissue architecture that would impair the integrity of the tissues and its functions. The leakage of proteins from damaged tissue could result in the formation of antibodies that might in turn react against the tissue.

There is much evidence that the intestinal tract with its large area for absorption is a major portal of entry for substances that cause immunological reactions, generally referred to as food allergies <sup>(10)</sup>.

The intestinal mucosa in such cases has been shown to be more permeable than normal allowing offending substances to be absorbed that are normally excluded <sup>(11)</sup>. Glycoproteins and proteoglycans play a key role in determining what passes into cells and thus in restricting the entry of injurious agents.

The amino sugars that make up these various tissue constituents are normally made in the cells where they are required. Each tissue has its own enzymes for the necessary processes. Unlike the deficiency of an essential amino acid, that would affect all cells in the body, a deficient process involving amino sugars could be restricted to one or a few types of cells.

In cases of a deficiency of amino sugars due to the body's inability to manufacture adequate amounts to satisfy the cells metabolic needs, dietary supplementation with amino sugars has proven beneficial. Dietary amino sugars can provide the needed material to allow the synthetic processes to continue, since amino sugars are readily absorbed and utilized. Amino sugars are normal, physiological substances with no known undesirable properties. N-acetyl glucosamine (NAG) and glucosamine sulphate (GLS) are examples of dietary amino sugars. They are soluble, stable and can be converted into other needed amino sugars. They circulate in the blood for several hours, very little is excreted and they are used exclusively for the formation of the substances described.

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