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GLYCOBIOLOGY review

The Language of Life

an overview and history of the science of glycobiology

Antiquated Thinking

It is widely taught in educational institutions around the world that there are four major classes of biomolecules: proteins, fats, nucleic acids, and carbohydrates. These molecules have specific and limited uses in the body, and if the diet contains the correct proportions, coupled with minor amounts of vitamins and minerals, proper nutrition is achieved.

Research from the last few decades, however, has exposed limitations in this traditional view, particularly in the role of carbohydrates (sugars). It is almost universally accepted that carbohydrates play a role solely in the production of energy. It is becoming increasingly apparent that this theory is inaccurate, as sugars play a far more complex role than originally thought.[1] This expanded view has led to a new genre of science called Glycobiology, an area of research with exciting possibility.

History of Glycobiology

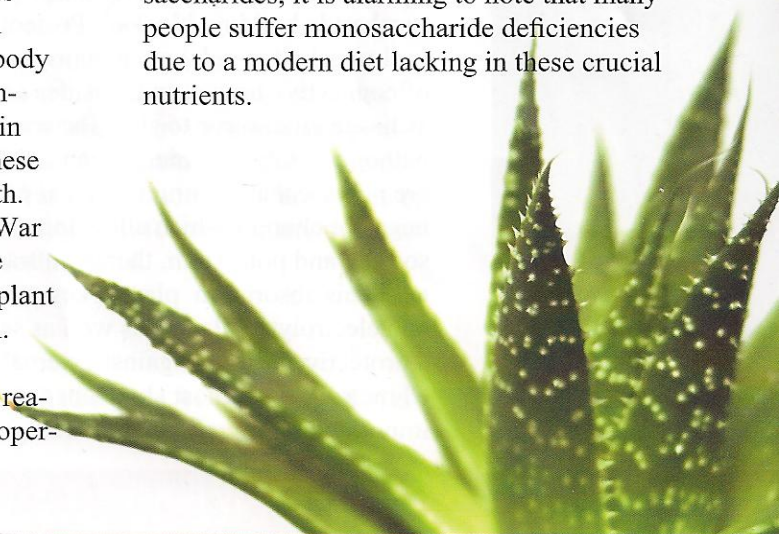
When the body is breached by microscopic invaders, how does the immune system know foreigners from healthy cells? What leads the digestive tract to absorb nutrients and repel bacteria? What changes when the body suddenly begins attacking itself in autoimmune disease or fails to defend the body in infections and cancer? The answers to these questions are critical to maintaining health.

In the Cold War era, following World War II, interest in the Aloe Vera plant became widespread as it was discovered that the plant had therapeutic value in its ability to heal. Despite its inclusion in a wide variety of products, it took 30 years to discover the reason why this plant had such beneficial properties. Researchers finally identified a single monosaccharide, Mannose,[2] as the therapeutic molecule in this plant and the science of Glycobiology gained momentum.

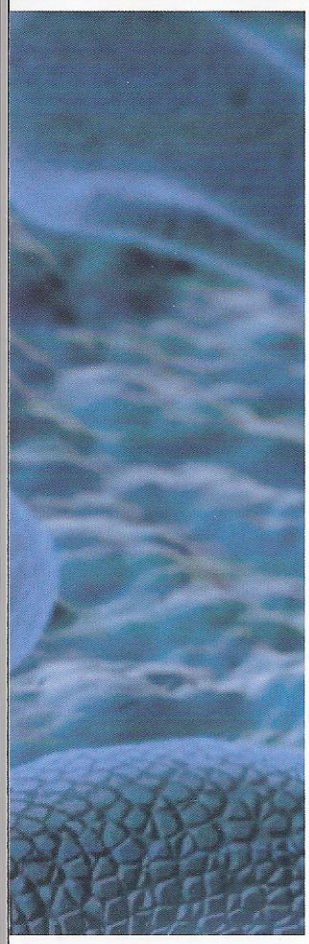
The Discovery

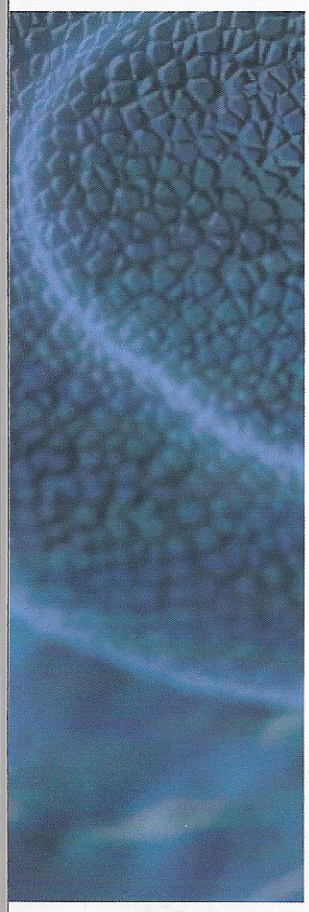
This discovery of health benefits from a little known monosaccharide led to the search for other sugars of potential value. What was eventually discovered was the fact that eight individual sugars are utilized by the body for the synthesis of glycoconjugates, molecules imperative to the health of many body systems.[3]

The magnitude of this discovery was not immediately recognized due to the persistent belief that saccharides are used only for energy production. This limited view still persists today despite a growing body of contradictory evidence. Multiple studies have determined that each of the saccharides have specific roles in the body beyond mere energy production.[4] These tasks include, but are not limited to, cellular communication, structural integrity, physical protection, and cellular adhesion. Because of the critical nature of these saccharides, it is alarming to note that many people suffer monosaccharide deficiencies due to a modern diet lacking in these crucial nutrients.



An Overview and Review of





Cellular Communication

Monosaccharides are utilized by the body for cell to cell communication. These sugars are arranged in various combinations and serve as an intercellular Braille. Healthy cells exhibit specific combinations that are recognized by other body cells, while foreign combinations of saccharides are not recognized and are tagged for elimination.[5] Correct configurations of monosaccharides are especially vital for immune system cellular communication, as it is the job of these specialty cells to recognize and eliminate foreign invaders.[6, 25]

> *"An inability to generate even one monosaccharide is fatal..."*

Communication is also vital for proper nerve transmission since receptors in the synaptic cleft have specific sugar configurations that are only activated by neurotransmitters when constructed properly.[7]

Red blood cells are coated in glycoproteins with specific sugar configurations as well. In fact, exact sugar combinations are so vital that changing a single sugar means the difference between Type-A and Type-B blood.[8]

Other examples that illustrate the importance of these saccharides to intercellular communication are insulin receptors,[9] antibodies recognizing and binding with pathogens,[10] and the joining of a sperm cell and the ovum in fertilization.[11]

Structure

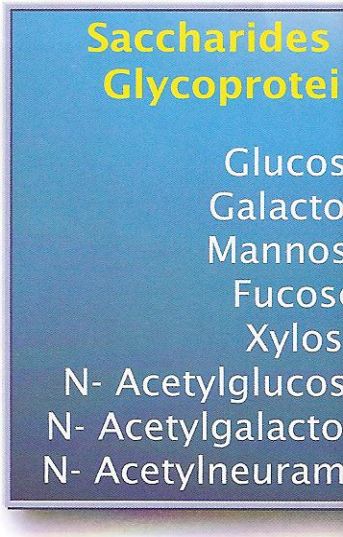
Sugar conjugates not only assist the cell in communication but are also integral to the stability of many body components. Connective tissue is highly dependent upon various saccharide building blocks.[8] Proteoglycans (polysaccharide gels) are a major component of connective tissues and, besides acting as tissue glue, serve to slow the spread of pathogens. Glycosaminoglycans (GAGs) are polysaccharide structures that possess negative charges which allow them to attract sodium and potassium, thereby attracting water. This absorption plays a key role in water and electrolyte balance, as well as serving as a protective cushion against external forces. Chondroitin, the most abundant GAG, is an important building block of cartilage and is highly dependent upon dietary saccharides for proper construction.[12]

The breakdown of nutrients and exposure to the environment causes the production of free radicals that can damage healthy tissue and genetic material. These free radicals are combated by antioxidants, the most important being glutathione. This molecule is constructed and utilized more effectively in the presence of certain saccharides.[13]

The delivery of many components depends upon transport proteins, and it is the saccharide portion of these trafficking proteins that both binds the package and determines its destination.[8]

Protection

The location of carbohydrates as the outer molecule on cell surfaces allows them to act as a cellular barrier from the environment. This role is seen in the mucosal lining of the gastrointestinal tract, where saccharide molecules block the adhesion of toxins and foreign matter while allowing nutrients and harmless molecules to bind and absorb.[14]



When properly constructed, cell membrane saccharides can competitively block virus and bacteria from binding and penetrating the cell.[15] These saccharides are also utilized in the circulatory system where they bind directly to foreign pathogens, preventing the penetration of these foreigners.

Adhesion

Saccharide conjugates are utilized in cellular adhesion. This has direct implications for platelet aggregation and tissue stability. A certain saccharide conjugate called heparin is an important molecule for halting the clotting cascade.[16] Deficiencies in construction of this molecule can lead to hypercoagulation, which

the Science of Glycobiology

in turn can result in heart attack or stroke.

As previously discussed, tissue stability is mainly a component of the saccharide glue and intercellular saccharide molecule linkages. Defects in this area are being investigated as a possible source of cancer metastasis, since malignant tumors often lose their adhesive properties and migrate to other parts of the body.[15, 17]

Saccharide Deficiencies

Almost every cell of the body depends upon these saccharides to function properly, and yet the modern diet is woefully deficient in these vital molecules. To counteract this lack of access to dietary saccharides, the body utilizes a backup system to generate any of the saccharides from glucose. This process depends upon multiple enzymatic steps and excess energy to occur.

A growing body of research suggests that a breakdown in this process is the cause of many common pathologies.[1] If a breakdown does occur, and dietary saccharides are not available, deficiencies will occur.

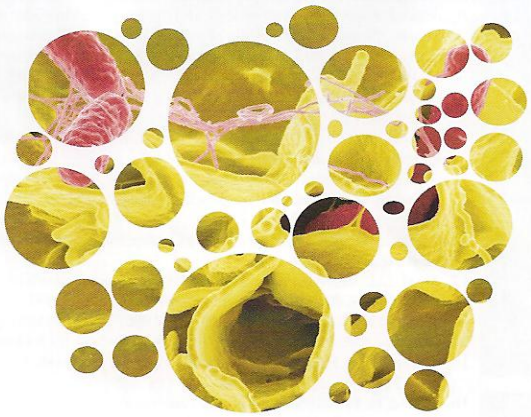
Required for Synthesis:

- e (Glu)
- se (Gal)
- e (Man)
- (Fuc)
- e (Xy)
- amine (GlcNAc)
- amine (GalNAc)
- nic Acid (NANA)

The most common causes of breakdowns in enzymatically constructing monosaccharides are vitamin deficiencies, stress, illness and aging. Also, genetic errors of saccharide metabolism result in the deficiency of at least one of the monosaccharides. It is important to note that being born with an inability to generate even one monosaccharide is fatal, unless prompt supplementation of that missing nutrient is supplied.[18] This illustrates the importance of these saccharides and the dire consequences of even minor deficiencies.

Disease Implications

Deficiencies or alterations in monosaccharide conjugates are the suspected culprits in a large number of pathologies, including some of the top killers in America.



Various inflammation disorders have been studied in relation to saccharides, including Rheumatoid Arthritis and Lupus. The sugars are imperative in their role as communication molecules on the binding end of the antibody IgG, which may signal false and prolonged inflammation of connective tissues.[19, 20]

Certain autoimmune diseases are believed to be linked to saccharides, including Diabetes Mellitus Type-1 and Multiple Sclerosis. The common factor in these conditions is an error in glycosylation, or the construction of glycoconjugates, which can lead to an attack of healthy tissue by immune cells.[21]

Saccharides may also play a key role in the pathology of certain cancers. Even a healthy human body can produce numerous cancerous cells on a daily basis, but these are typically disposed of by the immune system. Only when immune system fails to recognize the mutated cells do cancers begin their relentless growth to mature tumors. Improper saccharide construction has been investigated as a possible cause of the failure of immune cells to recognize cancer.[10]

Other pathologic conditions that have been studied in connection with saccharide deficiencies or alterations include cardiovascular disease[22], hypersensitivity, allergies[23], ulcerations of the gastrointestinal and genitourinary tract[24], infertility[11], neurological and psychiatric conditions.[7] Future issues of this publication will focus on many of these pathologies in detail.

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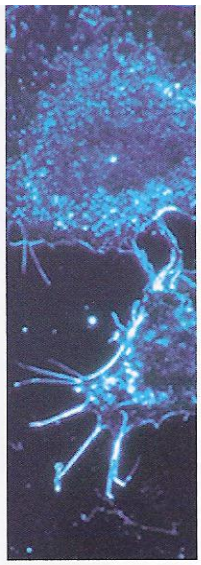

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