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Review Paper

Carbohydrates

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Carbohydrates are the major energy source in the body. In this review article, monosaccharides, disaccharides, sucrose, maltose, lactose, starch, dextrin, glycogen, cellulose, glycosaminoglycan, sialic acid and previous research study on carbohydrates has been given herewith

Keywords: Monosaccharides, disaccharides, polysaccharides, research study.

INTRODUCTION

Carbohydrates are the main source of energy that is ingested by the human body (Caffall et al., 2009). Brain mainly utilizes the glucose. Red blood cells also use glucose only. Fiber in the diet is not digested by human body due to lack of cellulase enzyme. Glucose is the major enegy source in the body. Glycogen is the storage form of glucose and glycogen is stored in skeletal muscles and liver. If glucose intake exceeds than it is utilized in the body it is converted into fat. Riboses are utilized in formation of deoxyribonucleic acid (Hou et al., 2009). Carbohydrates are polyhydroxy alcohol with potentially active carbonyl group which may be aldehyde or keto group. Carbohydrates can be classified on the basis of carbon atom present in the carbohydrates. Carbohydrates are classified into four types monosaccharides, disaccharides, oligosaccharides, polysaccharides. Monosaccharides cannot be hydrolyzed further into simpler form. Disaccharides give two monosaccharides on hydrolysis. Polysaccharides may be homopolysaccharides and heteropolysaccharides.

Monosaccharides

Monosaccharides cannot be hydrolyzed further into simpler form of carbohydrates. Monosaccharides are easily absorbed in intestines. All other types of carbohydrates like disaccharides and polysaccharides are not absorbed directly. All disaccharides and polysaccharides are ultimately converted to monosaccharides. Monosaccharides are important in the body especially glucose, fructose and galactose. Glucose is the most important carbohydrate in human body(Paulsen H et al, 1968).Glucose is formed from the hydrolysis of complex carbohydrates including starch, dextrin. Glucose is found in the blood and provides energy to the body. Glucose is also formed from breakdown of glycogen in the body. Fructose is a reducing sugar and forms osazone crystals. Fructose is found in fruit and is also found in honey. Fructose can be obtained in the body by action of sucrase on sucrose. Galactose is also a reducing sugar and forms rod shaped crystals (Campbell et al., 2010).

Hemiacetal

Aldehyde can react with an alcohol to form a hemiacetal.

Hemiketal

A ketone can react with an alcohol to form a hemiketal.

Disaccharides

Disaccharides consist of two sugars that are linked by a glycosidic linkage. This glycosidic linkage is formed by a condensation reaction that takes place between the two sugars units, resulting in the loss of a hydrogen atom

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from one monosaccharide and a hydroxyl group from the other. Disaccharides are broken down into two monosaccharide, in the small intestine during the process of digestion (Fox et al., 2002).

Sucrose

Sucrose contains glucose and fructose. Sucrose is found in sugarcane. Sucrose is non reducing sugar. Sucrose formula is $C_{12}H_{22}O_{11.}$ Sucrose is hydrolyzed by sucrase into fructose and glucose. Plants form sucrose and other animals can not make sucrose. It is naturally found in plants. Pine apple and apricot are major sources of sucrose. Sucrose is hydrolyzed into glucose and fructose. Over ingestion of sucrose have adverse health effects like dental caries. In dental caries, oral bacteria change sugars into acids that attack tooth enamel. Over consumption of sucrose is also associated with metabolic syndrome like diabetes mellitus (Alexander et al., 2004). A study was done on rats in which rats were fed a diet containing two third of sucrose, in the beginning triglyceride level was increased and later on insulin resistance was developed (Fukuchi et al., 2004). In another study rats were fed sucrose-rich diets that developed hypertriglyceridemia, hyperglycemia and insulin resistance (Lombardo et al., 1996).

Maltose

Maltose is also called malt sugar. It contains two molecules of glucose that are joined with an α (1→4) linkage. Maltose is hydrolyzed by maltase in intestine. Maltose is a reducing sugar and it forms osazone crystals. Maltose occurs in the body as an intermediate product of starch digestion. (Starch is a polysaccharide.) When maltose is hydrolyzed, it yields two molecules of glucose (Amy et al., 1996).

Lactose

This is also called milk sugar. Lactose is a disaccharide that is found in milk. Lactose is a large sugar molecule that is made up of two smaller sugar molecules, glucose and galactose. Lactose is hydrolyzed by lactase in intestines. Lactose intolerance is when a person has difficulty or is unable to digest milk due to lack of lactase (Harrington et al., 2008, Venema, 2008). Children with suspected lactose intolerance can be assessed clinically by dietary lactose elimination or by tests including noninvasive hydrogen breath testing or invasive intestinal biopsy determination of lactase (and other disaccharidase) concentrations. Management includes use of lactase-treated dairy products or oral lactase supplementation, limitation of lactose-containing foods, or dairy elimination (Heyman, 2006)

Polysaccharides

Polysaccharides cannot be directly utilized by the body. They must first be broken down into monosaccharide, the only sugar form the body can use. Polysaccharides contain up to 60,000 simple carbohydrate molecules. Polysaccharides are polymeric carbohydrate structures, formed of repeating units (either mono- or disaccharides) joined together by glycosidic bonds. Unlike other saccharides, polysaccharides tend to not have a sweet taste. Some examples of polysaccharides include starch, cellulose and glycogen (Heidelberger et al., 1942).

Starch

Starch is a storage form of glucose in the body. Starch is made up of amylose and amylopectin. Starch contains amylase (10-20%) and amylopectin (80-90%). Starch gives blue colour with iodine solution. In starch linkage between glucose residues is 1-4 and at branch point linkage is of 1-6 (Lentfer et al., 2002).

Dextrin

Dextrins are produced by hydrolysis of glycogen or starch and are a group of low-molecular-weight carbohydrates. Dextrins are intermediary products of starch digestion, also, and are formed by the action of amylases on starches. They render the disaccharide maltose on hydrolysis. Dextrin is extracted from corn, wheat, potatoes, or rice. Dextrins can be produced from starch using enzymes like amylases **(**Susana et al., 1995).

Glycogen

Glycogen is the storage form of glucose in the body especially in skeletal muscles and liver. Glycogen is also called animal starch. Glycogen is analogous to the starch in plants. Glycogen is very similar to amylopectin, having a high molecular weight and branched-chain structures made up of thousands of glucose molecules. The main difference between glycogen and amylopectin is that glycogen has more and shorter branches, resulting in a more compact, bush like molecule with greater solubility and lower viscosity. Glycogen is the source of energy most often used for exercise (Sujatha et al., 2010*).*

Cellulose

Cellulose is a natural polymer, a long chain made by the

linking of smaller molecules. The links in the cellulose chain are a type of sugar: ß-D-glucose. It comprises over 50% of the carbon in vegetation and is the structural constituent of the cell walls of plants. Cellulose is, therefore, the most abundant naturally-occurring organic substance. It is characterized by its insolubility, its chemical inertness and its physical rigidity. This polysaccharide can be digested only by herbivores such as cows, sheep, horses, etc., as these animals have bacteria in their rumens (stomachs) whose enzyme systems break down cellulose molecules. Humans can not digest cellulose due to lack of cellulase enzyme (Brown et al., 2007).

Glycosaminoglycans

Glycosaminoglycans, or GAGs, are naturally-occurring carbohydrates found in the cartilage, connective tissue, joint fluid, and skin. Glycosaminoglycans are unbranched polysaccharides composed of repeating units of alternating uronic acids and amino sugars Glycosaminoglycans (GAGs) are present on the surfaces of all adherent animal cells and in extra cellular matrices(Solini A et al, 1994).

Sialic acid

N-acetylneuraminic acid is one of the essential glyconutrients for cell communication and functioning in the human body. It is most commonly found sialic acid in mammalian cells. It is often found as a terminal residue of oligosaccharide chains of glycoproteins. Sialic acid imparts negative charge to glycoproteins, because its carboxyl group tends to dissociate a proton at physiological pH (Lawrence, 1997)

DISCUSSION

Carbohydrates are commonly classified as mono-saccharide, disaccharides, oligosaccharides and poly-saccharides. Plants produce carbohydrates by photo-synthesis. In most animals, carbohydrates are the quickly accessible reservoir of energy. The main function of carbohydrates is to provide energy, but they also play an important role in the structure and function of the body organs and nerve cells (Benedict et al., 2010). Glucose is broken down upto pyruvate and lactate, in aerobic glycolysis end product is pyruvate but in case of anaerobic glycolysis end product is lactate. In aerobic glycolysis net gain of ATP is eight, while in case of anaerorobic glycolysis net gain of ATP is two. The reason of less ATP production in anaerobic glycolysis is that NADH2 produced in this pathway is consumed when pyruvate is converted to lactate. Disaccharides are broken down by their respective enzymes like lactase, maltase and sucrose (Stortz et al., 2009). Starch is hydrolyzed by amylase. If glucose is in excess it can be converted to glycogen, two sites are in body where glucose is stored like muscle and liver. Liver glycogen maintains blood glucose level while muscle glycogen does not maintain blood glucose. Liver lacks enzyme glucose 6 phosphatase that converts glucose 6 phosphate to glucose (McCurdy et al., 2010). The brain needs to use glucose as an energy source, since it cannot use fat for this purpose. It is for this reason that the level of glucose in the blood must be constantly maintained above the minimum level. Sources of glucose are dietary carbohydrates and glycogen. Many harmones regulate the blood glucose level.

Why do cancers have high aerobic glycolysis

If carcinogenesis occurs by somatic evolution, then common components of the cancer phenotype result from active selection and must, therefore, confer a significant growth advantage. A near-universal property of primary and metastatic cancers is upregulation of glycolysis, resulting in increased glucose consumption, which can be observed with clinical tumour imaging. It has been evaluated that persistent metabolism of glucose to lactate even in aerobic conditions is an adaptation to intermittent hypoxia in pre-malignant lesions. However, upregulation of glycolysis leads to microenvironmental acidosis requiring evolution to phenotypes resistant to acid-induced cell toxicity. Subsequent cell populations with upregulated glycolysis and acid resistance have a powerful growth advantage, which promotes unconstrained proliferation and invasion (Robert et al., 2004).

Glycolysis links p53 function with NF-κB signaling: Impact on cancer and aging process

In 1930, Otto Warburg observed that cancer cells produce an increased amount of their energy through aerobic glycolysis and subsequently, this was called the Warburg effect. During aging, the capacity for mitochondrial respiration clearly declines and aerobic glycolysis appears to compensate for the deficiency in oxidative metabolism. This shift in energy production, both in aging and cancer, could protect from the toxic effects of oxygen free radicals whereas increased glycolysis can have adverse effects. It was recently demonstrated that the glycolysis-linked protein O-glycosylation can potentiate the catalytic activity of IKKβ and subsequently trigger NF-κB signaling. It seems that tumor suppressor oncogene p53 has an important role in the regulation of protein O-glycosylation since p53 is a potent inhibitor of glycolysis, for example, via TIGAR

protein expression. Aging is known to repress the function of p53 and this could enhance glycolysis and NF-κB signaling (Antero et al., 2010).

Roles of p53, Myc and HIF-1 in Regulating Glycolysis — the Seventh Hallmark of Cancer

Despite diversity in genetic events in oncogenesis, cancer cells exhibit a common set of functional characteristics. Otto Warburg discovered that cancer cells have consistently higher rates of glycolysis than normal cells. The underlying mechanisms leading to the Warburg phenomenon include mitochondrial changes, upregulation of rate-limiting enzymes/proteins in glycolysis and intracellular pH regulation, hypoxia-induced switch to anaerobic metabolism, and metabolic reprogramming after loss of p53 function. The regulation of energy metabolism can be traced to a “triad” of transcription factors: c-MYC, HIF-1 and p53. Oncogenetic changes involve a nonrandom set of gene deletions, amplifications and mutations, and many oncogenes and tumor suppressor genes cluster along the signaling pathways that regulate c-MYC, HIF-1 and p53. Glycolysis in cancer cells has clinical implications in cancer diagnosis, treatment and interaction with diabetes mellitus. Many drugs targeting energy metabolism are in development (Yeung et al, 2008)

Evolution of the coordinate regulation of glycolytic enzyme genes by hypoxia

Two billion years of aerobic evolution have resulted in mammalian cells and tissues that are extremely oxygen-dependent. Exposure to oxygen tensions outside the relatively narrow physiological range results in cellular stress and toxicity. Consequently, hypoxia features prominently in many human diseases, particularly those associated with blood and vascular disorders, including all forms of anemia and ischemia. Bioenergetic enzymes have evolved both acute and chronic oxygen sensing mechanisms to buffer changes of oxygen tension; at normal PO oxidative phosphorylation is the principal energy supply for eukaryotic cells, but when the PO falls below a critical mark metabolic switches turn off mitochondrial electron transport and activate anaerobic glycolysis. Without this switch cells would suffer an immediate energy deficit and death at low PO. An intriguing feature of the switching is that the same conditions that regulate energy metabolism also regulate bioenergetic genes, so that enzyme activity and transcription are regulated simultaneously, albeit with different time courses and signaling pathways (Keith, 2003)

Glycolysis and Proteases as Targets for the Design of New Anti- Trypanosome Drugs

Glycolysis is considered as a promising target for new drugs against parasitic trypanosomatid protozoa, because this pathway plays an essential role in their ATP supply. Trypanosomatid glycolysis is unique in that it is compartmentalized, and many of its enzymes display specific structural and kinetic features. Structure- and catalytic mechanism-based approaches are applied to design compounds that inhibit the glycolytic enzymes of the parasites without affecting the corresponding proteins of the human host. For some trypanosomatid enzymes, potent and selective inhibitors have already been developed that affect only the growth of cultured trypanosomatids, and not mammalian cells. Examples are developed concerning all enzymes in the hexoses part with also others concerning glyceraldehyde-phosphate dehydrogenase and pyruvate-kinase for the trioses part. Concerning cysteine protease inhibitor development, a great number of irreversible alkylating agents have shown their efficacy towards the active site cysteine of parasite proteases. This includes fluoro-methylketones, epoxides, diazomethylketones, and vinyl-sulfones to mention a few. These functional groups are activated electrophiles that react with the nucleophilic cysteine of the active site and are generally quite selective for cysteine versus serine. They are thought to be also reactive to numerous other nucleophiles in the body, especially other thiols. This potentially hampering property seems not to be detrimental for two reasons: first a recent report has shown that cysteine protease inhibitors containing a vinylsulfone electrophile are uncreative towards thiols such as glutathione and can be considered to be inert in the absence of catalytic machinery. Secondly, irreversible inhibitors are shown to be less toxic than presumed in the parasite treatment, owing to some bioselectivity displayed by the parasite itself (Lakhdar et al., 2002).

Phylogenetic Analysis of Glycolytic Enzyme Expression

Although differences among species in enzyme maximal activity or concentration are often interpreted as adaptive and important for regulating metabolism, these differences may simply reflect phylogenetic divergence. Phylogenetic analysis of the expression of the glycolytic enzymes among 15 taxa of a North American fish genus (Fundulus) indicated that most variation in enzyme concentration is due to evolutionary distance and may be no adaptive. Additionally, two pairs of enzymes ovary, indicating coevolution. Thus, metabolic flux may be modulated by many different enzymes rather than by a

single rate-limiting enzyme (Pierce et al., 1997).

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