BIOCHEMISTRY III

ABSTRACT: The composition, absorption, transport, and storage of carbohydrates, lipids and proteins are discussed with particular reference to their significance in the human diet. The importance of carbohydrates, lipids and proteins are described and their relative importance in energy transformations is considered.

PREREQUISITE UNITS: Biochemistry II

READINGS: Tortora and Derrickson (12th ed): 43-54; 980; 989-1001
Tortora and Derrickson (11th ed): 43-53; 953-954; 963-976

OBJECTIVES: To be able to:

38628.Describe the general composition of nutritional carbohydrates and their absorption, transport, storage and metabolic importance.

38629.Describe the general composition of nutritional lipids and their absorption, transport, storage and metabolic importance.

38630.Describe the general composition of proteins and their absorption, transport, storage and metabolic importance.

38631.Describe the relative significance of carbohydrates, lipids and proteins in terms of:

a) importance in energy storage and energy availability
b) use during starvation conditions

38632.Describe the relative efficiencies of carbohydrates, lipids and proteins in energy storage.

38633.Describe the general composition of nutritional carbohydrates and their absorption, transport, storage and metabolic importance.

Nutritional carbohydrates include monosaccharides, disaccharides and polysaccharides. Polymers of monosaccharides are described as disaccharides if they contain two monosaccharide subunits. Short chain polysaccharides with 3 to 20 monosaccharide subunits are called oligosaccharides, and carbohydrates are called polysaccharides if they contain more than 20 monosaccharide subunits.

Monosaccharide composition

A monosaccharide is the smallest unit of carbohydrate structure. Carbohydrates have the general formula $(CH_2O)_n$. The number of carbons in a monosaccharide is usually 5 or 6, but may vary from 3 to 9. The general formulae for several types of monosaccharides are shown in Table 1. Dietary monosaccharides are primarily the hexose (6 carbon) sugars: glucose, fructose, galactose and mannose. The structural formulas of these are illustrated in Figure 1.

Table 1. General formulae for common monosaccharides

monosaccharide type	# of carbons	general formula
Trioses:	3	$C_3H_6O_3$
Tetroses:	4	$C_4H_8O_4$
Pentoses	5	$C_5H_{10}O_5$
Hexoses	6	$C_6H_{12}O_6$

Figure 1. Structural formulae of dietary monosaccharides

Although most nutritional monosaccharides are derived from disaccharides or polysaccharides, the monosaccharides, fructose, galactose, glucose, and mannose are present in some natural (unprocessed) foods. Fructose and glucose are found in most fruits and honey. Galactose is found in relatively small amounts in grapes and figs. Mannose is present in pineapples, olives and carrots.

Generally monosaccharides in natural foods provide a small proportion of the total carbohydrates in the diet, however many processed foods may contain relatively large amounts of monosaccharides, particularly fructose and glucose. This has been particularly true in the past 30 years with the production and widespread use of High Fructose Corn Syrup (HFCS). To produce HFCS, corn starch (a polysaccharide of glucose) is enzymatically digested to glucose and then the glucose is enzymatically converted to fructose. The high fructose syrup produced is then mixed with glucose (produced in an earlier step in the process). HFCS, contains between 55 and 90% fructose, and has become widely used in prepared foods, including, soft drinks, juice beverages, candies, baked goods, and breakfast cereals. In the United States corn syrup accounts for over 20% of the total carbohydrates consumed. Between 1970 and 1997, dietary fructose intake in the Unites States rose from about 225 gm per person per year to 28 kg per person per year, a 125 fold increase in consumption of fructose.

Research into the metabolic effects of high dietary fructose intake suggests that it may be a significant contributor to the current epidemic of obesity and insulin resistance diabetes in both children and adults.

Monosaccharide absorption

Monosaccharides, whether eaten directly as monosaccharides or resulting from the digestion of disaccharides and polysaccharides, are absorbed into the blood from the small intestine. Refer to Tortora 11th ed. Figure 24.20 (page 929) or 10th ed. Figure 24.25 (page 888) for an illustration of the absorption of nutrients in the small intestine.

Glucose and galactose are actively absorbed into intestinal epithelial cells by co-transport with sodium ions. The membrane protein transporter is the same for both glucose and galactose and two sodium ions are absorbed with each glucose or galactose molecule absorbed. These monosaccharides then move by facilitated diffusion into blood capillaries. Mannose absorption is similar to the absorption of glucose and galactose, but mannose requires different sodium dependent transporter molecules than those used for glucose and galactose.

Fructose is absorbed into intestinal epithelial cells and then into blood capillaries by facilitated diffusion. The transporter proteins for fructose are different from the ones used for other monosaccharides and fructose is not co-transported with sodium. Fructose absorption appears to be dependent on glucose absorption; in the absence of glucose, fructose absorption is very slow.

Monosaccharide transport

Monosaccharides are water soluble and, once absorbed into the blood, are transported dissolved in the plasma of the blood. Monosaccharides have a variety of metabolic functions and various tissues and cells have the ability to use monosaccharides directly, however, the liver modifies or stores most monosaccharides before they are distributed widely in the blood stream.

Monosaccharide storage

The veins draining the digestive organs are directed through the hepatic portal vein to the liver and the liver modifies or stores many of the monosaccharides that arrive there. Under the influence of the hormone insulin, the liver converts excess glucose to glycogen. Glucose is also stored as glycogen in muscle cells. There is no significant storage of monosaccharides other than glucose, however, all absorbed monosaccharides can be converted to glucose. If the glycogen storage capacity of the liver and muscles is exceeded, excess carbohydrate is converted to lipids (fats).

Metabolic importance of monosaccharides

Carbohydrates are the most abundant organic molecules on earth and they have several important functions in living organisms. Most carbohydrate is produced by plants by a process called photosynthesis. The main product of photosynthesis is glucose. Other carbohydrates (other monosaccharides as well as disaccharides and polysaccharides) are synthesized from glucose.

In humans, glucose is the principal molecule oxidized in cellular respiration to produce the ATP required for all cellular activities that require energy.

In addition to being used for energy, carbohydrates, mainly in the form of monosaccharides, are components of biologically important molecules such as RNA, DNA, ATP and NAD. These particular molecules contain ribose or deoxyribose; 5 carbon sugars, which are synthesized from glucose.

Carbohydrates (usually oligosaccharides or polysaccharides), joined with other molecules such as proteins and lipids, also have important functions. Carbohydrates joined to proteins (glycoproteins) are abundant in the extracellular matrix, particularly in connective tissues. For example, hyaluronic acid is a complex of carbohydrates that forms the core of several glycoproteins. In synovial joints, hyaluronic acid forms a viscous fluid that is an excellent lubricant. Similarly, glycoproteins contribute to the elastic and other important properties of cartilage and other connective tissues.

Glycoproteins are also important components of cell membranes, with the protein portion on or in the phospholipid bilayer, and the carbohydrate portion (oligosaccharides chains) projecting from the outer surface of cells. These glycoproteins, along with glycolipids (carbohydrates complexed with lipids) form a glycocalyx which serves a number of functions relating to cell surface identity. For example, cell to cell recognition, the ability of cells to recognize each other, is important during embryonic development so that cells can sort themselves out into various tissues. Carbohydrates on the surface of cells are also essential for the immune system to be able to distinguish between the body's own cells and those of an invading pathogen. The cell surface antigens responsible for ABO blood types are oligosaccharide chains of glycoproteins and glycolipids.

Most cells also contain a variety of enzymes, hormones, structural proteins and transport proteins that are glycoproteins.

In addition to forming part of the glycocalyx, glycolipids, particularly ones containing the monosaccharides galactose and mannose, are abundant in nerve tissue. For example, a particular type of phospholipid called a ganglioside accounts for about 15% of the lipids found in membranes of the myelin sheath surrounding parts of nerve cells.

Disaccharide composition

The major dietary disaccharides are sucrose (consisting of glucose and fructose), lactose (containing galactose and glucose) and maltose (containing two glucose units).   The structures of these disaccharides are illustrated in Figure 2.

Figure 2. Structural formulae of the dietary disaccharides sucrose, lactose and maltose

Most dietary sucrose is extracted from sugar cane and sugar beets. Lactose is present in milk. Relatively small amounts of the disaccharide maltose are present in apricots, cherries, raspberries and honey.

Disaccharide absorption

Disaccharides are not absorbed directly from the digestive tract. Before being absorbed, they are digested to monosaccharides by enzymes produced in the small intestine. Sucrose is digested to glucose and fructose by the enzyme sucrase. Lactose is digested to galactose and glucose by lactase, and maltose is digested to glucose by maltase. The absorption of these monosaccharides was described earlier.

Polysaccharides structure

The main nutritional polysaccharide in human diets is starch (a polymer of glucose). Starch is found in relatively large quantities in cereal grains such as rice, wheat and corn (including processed foods derived from cereal grains, such as bread, breakfast cereals and baked goods that are made from flour), potatoes, yams and other root crops. The structure of starch is illustrated in Figure 3.

Figure 3. Structure of Starch Starch is a mixture of amylose and amylopectin. Amylose, the type of starch illustrated here, consists of 100-1000 glucose subunits joined together in an unbranched chain. Amylopectin is a form of starch consisting of branched chains of 300-6000 glucose subunits.

Polysaccharide absorption

Like disaccharides, polysaccharides cannot be absorbed directly from the digestive tract. Starch is digested to maltose by enzymes (amylases) from the salivary glands and the pancreas. Maltose (see Figure 2) is then digested by maltase to glucose, which is absorbed as described previously.

The polysaccharide cellulose is present in many plant foods, including beans, peas, cereal grains, fruits and nuts. Cellulose is not digestible by humans and is therefore, not considered to be a nutrient. Nevertheless, cellulose is important as fibre in the diet. It may aid digestion and help protect against certain digestive tract diseases such as cancer. A high fiber diet increases stool size and helps prevent constipation. Populations that have high fiber diets have a lower incidence of diverticular disease (outcroppings that develop on weak areas of the large intestine), cardiovascular disease, and colonic cancer, than populations with low fiber intakes.

2. *Describe the general composition of nutritional lipids and their absorption, transport, storage and metabolic importance.*

Lipid composition

Lipids represent a diverse group of molecules. Probably the most universal feature which characterizes lipids is their insolubility in water. Although lipids have a variety of structures and a variety of important functions, most lipids ingested by humans are in the form of triglycerides. Only the structure of triglycerides and their components will be described here. Triglycerides consist of three fatty acid molecules attached to a glycerol. The most common fatty acids in nature are stearic acid and palmitic acid. Both are saturated fatty acids in which the hydrocarbon chain has only single bonds between the carbon atoms. Stearic acid has 18 carbons in the hydrocarbon chain and palmitic acid has 16. Figure 4 illustrates the structure of a triglyceride.

Figure 4. Structural formula of a triglyceride
In this triglyceride the upper two fatty acids are stearic acid and the lower fatty acid is palmitic acid. Both are saturated fatty acids.

Two fatty acids which are required in the diet (essential fatty acids) are linoleic acid and linolenic acid. These are both unsaturated fatty acids. Unsaturated fatty acids have double or triple bonds between one or more carbon atoms in the hydrocarbon chain of the fatty acid. The structure of linoleic acid and linolenic acid are shown in Figure 5.

Figure 5. Structural formulae of the essential fatty acids
Linoleic acid and linolenic acid are both unsaturated fatty acids.

Lipid absorption

Before being absorbed, triglycerides must first be digested by lipase enzymes produced by: (i) glands in the tongue, (ii) the stomach, and (iii) the pancreas. During digestion, two of the fatty acids are removed from each triglyceride. The main products resulting from triglyceride digestion are therefore monoglycerides (glycerols with one fatty acid attached) and fatty acids.

Monoglycerides and long chain fatty acids are not absorbed into blood capillaries. Bile salts and lecithin from the liver are involved in the absorption of monoglycerides and long chain fatty acids. Bile salts have both polar (hydrophilic) non-polar (hydrophobic) components and form tiny spheres called micelles. Micelles have an external polar surface that can dissolve in water.

The non-polar core of micelles is able to dissolve monoglycerides and fatty acids. Thus micelles provide a transport mechanism within the watery contents of the small intestine.

When micelles reach the inner surface of intestinal villi, the fatty acids and monoglycerides diffuse through the epithelial cell membranes, leaving the micelles behind. Micelles can continue to transport more fatty acids and monoglycerides to the intestinal villi.

Within the epithelial cells of the intestine, new triglycerides are synthesized from available fatty acids and monoglycerides. The triglycerides form complex aggregates with phospholipids and cholesterol, and become coated with proteins. These large aggregates are called chylomicrons. The chylomicrons leave the epithelial cells by exocytosis.

Lipid transport

Because the chylomicrons are large, they cannot enter capillaries, but instead enter the lacteals of the lymphatic system. From there they travel through the thoracic duct which empties into the left subclavian vein. Chylomicrons quickly get removed from the blood in the liver and adipose tissue. When the chylomicrons pass through the capillaries of the liver and adipose tissue, enzymes digest the triglycerides in the chylomicrons to fatty acids and glycerol. The fatty acids and glycerol then diffuse into liver cells (hepatocytes) and adipose cells and are once again resynthesized into triglycerides. Hepatocytes synthesize lipoproteins which complex with triglycerides for transport to other body cells.

A small amount of dietary fats contain short-chain fatty acids (having fewer than 12 carbon atoms). These short chain fatty acids can be absorbed by simple diffusion into blood capillaries similar to the route taken by monosaccharides.

Lipid storage

If required, triglycerides (both the glycerol and the fatty acids) can be degraded for energy production. If sufficient energy is available from glucose or stored carbohydrates, triglycerides are stored in adipose cells as a large single droplet of triglycerides. Hepatocytes also store some triglycerides. When excess carbohydrates are ingested, hepatocytes also synthesize new fatty acids and glycerol from glucose. These can be sent as triglycerides complexed with proteins for storage in adipose tissue.

Metabolic importance of lipids

In addition to being a storage form and source of energy, lipids have a large number of important biological functions. Phospholipids form the major structural component of cellular membranes. Specialized lipids also play important roles as vitamins, enzyme cofactors, and electron carriers in energy metabolism. Many hormones and intracellular messengers are also lipids. The lipid cholesterol is a component of membranes, a component of bile, and also serves as a precursor for the synthesis of other biologically important lipids such as the steroid hormones estrogen and testosterone, and vitamins A, D, E, and K

3. ***Describe the general composition of proteins and their absorption, transport, storage and metabolic importance.***

Protein Composition

Proteins are abundant and diverse, with thousands of different proteins carrying out a multitude of functions in all cells. They have a great range in size from being fairly small to being very large and complex. In spite of their diversity in structure and function, all proteins are constructed from building blocks of the same 20 amino acids. The different arrangement and number of these amino acids in the protein form the basis for the various structures and functions of proteins.

All amino acids have a common core structure consisting of a central carbon atom attached to an amino group and a carboxyl group. Different amino acids have different side groups on the central carbon. The simplest side group is a single hydrogen atom as in the amino acid glycine. The amino acid alanine has a methyl (CH_3) group attached to the central carbon and others such as arginine have more complex side groups. The generalized formula of an amino acid is illustrated in figure 6 and the structural formulae of several of the 20 amino acids are illustrated in Figure 7.

Figure 6. Generalized structure of an amino acid

Glycine **Alanine**

Arginine

Figure 7. **Structural formulae of the amino acids glycine, alanine and arginine**. The side groups attached to the central carbon are circled. The other 17 amino acids have a variety of other side groups.

Protein Absorption

Proteins must be enzymatically digested to their component amino acids before absorption can occur. The mechanism of absorption of amino acids is similar to the mechanism of the absorption of glucose. Specialized transport proteins are necessary to transport amino acids into the intestinal epithelial cells, and this transport is coupled with the transport of sodium. Additional transporters are necessary to transport amino acids from the intestinal cells into the blood by facilitated diffusion. This stage of the transport is not coupled to sodium transport.

Protein transport

The absorbed amino acids are transported as solutes dissolved in the plasma of the blood. Amino acids can be taken up directly by most cells of the body and are primarily used to build proteins. Usually only a relatively small portion of the dietary protein ends up being used to provide energy through the oxidative breakdown of amino acids.

Protein storage

Neither amino acids nor proteins are stored in humans. Proteins are synthesized by cells as they are required. Amino acids are either absorbed from the diet, or synthesized by cells, to supply the appropriate amino acids necessary for protein synthesis. About half of the 20 amino acids cannot be synthesized by humans, or are not synthesized in sufficient quantities, and must be obtained from food. Amino acids that cannot be synthesized in the body are called essential amino acids, and must be available in foods for normal health.

Metabolic importance of proteins

The primary function of dietary proteins is to provide amino acids for the synthesis of new proteins required by the body. Proteins have enormous diversity and complexity and they participate in essentially all aspects of cellular metabolism. They also form essential components of virtually all of the structural components of cells, tissues and organs. Regulatory proteins, such as the hormone insulin, help regulate metabolism. Enzymes such as sucrase and ATPase, are proteins which catalyze specific biochemical reactions; contractile proteins such as actin and myosin enable muscle contraction; immunological proteins such as antibodies and interleukins protect against invading organisms; transport proteins such as hemoglobin, carry vital substances through the body; and structural proteins such as keratin in the skin provide a framework for cells, tissues and organs.

4. ***Describe the significance of carbohydrates, lipids and proteins in terms of:***
   a) ***importance in energy storage and energy availability***
   b) ***use during starvation conditions***

a) Importance in energy storage and energy availability

Efficiency and importance of carbohydrates in energy storage

The storage form of carbohydrates in humans is glycogen. Glycogen is synthesized from glucose and is stored in muscles and the liver. Glycogen is readily catabolized back to glucose to help regulate glucose levels in the blood, and thus to provide energy as required. Glucose concentration in the blood is maintained at about 75 mg glucose per 100 ml of blood and is normally kept between 60 and 90 mg per 100 ml to provide a constant and uniform supply of glucose to cells. Although most tissues can use fatty acids for energy, glucose is normally the source of energy that is utilized by the brain and erythrocytes. Except under conditions of prolonged starvation, glucose is the only fuel that the brain can use for energy.

Over the short term, glycogen reserves are the first source of glucose whenever blood glucose drops, such as between meals, and glycogen stores are replenished whenever glucose levels are high, such as after meals.

Glycogen stores are limited to about 1% of the total energy available from body chemicals and can provide only enough glucose for about a day's energy requirements. When glycogen stores are depleted, lipids are used for energy.

Efficiency and importance of lipids in energy storage

Lipids, in the form or triglycerides, represent the major energy reservoir of the body, accounting for about 77% of the total body energy available. Triglycerides are stored in adipose tissue and, in the absence of food intake, degradation of triglycerides in most individuals can provide about two month's worth of energy.

Efficiency and importance of proteins in energy storage

Proteins represent a potential source of about 22% of the total energy available in the body. However, because proteins play such vital roles in structure and metabolism, the extensive utilization of proteins for energy would result in death long before that amount of energy could be made available.

b) Use of carbohydrates, lipids and proteins during starvation conditions

Under starvation conditions, glycogen reserves are the first to be used to maintain blood glucose levels. Because glycogen reserves are not large, within a day of starvation the glycogen reserves will be exhausted.

When glycogen stores are exhausted, triglycerides are catabolized for energy. Fatty acids produced by triglyceride degradation are transported to cells to be oxidized and used for ATP production. Tissues such as the heart and skeletal muscles can use fatty acids for energy rather than glucose, thus leaving more glucose to be available for use by the brain.

During starvation, after all the glycogen is used up, some protein is catabolized even though there may be sufficient lipid available to satisfy the energy needs. Under starvation conditions, some protein catabolism is required because a product of protein catabolism (oxaloacetate) is required for glucose synthesis. More details about the synthesis of glucose will be discussed in a later study unit called Energy Metabolism I. Protein catabolism is minimized in two ways. Because of the use of fatty acids by skeletal muscles and the heart, more glucose is available for brain function. When glucose levels are low, such as between meals or under starvation conditions, the liver produces substances called ketone bodies that are utilized by the heart, kidneys and brain, further reducing the need for glucose.

In summary, under starvation conditions, once glycogen stores are exhausted, lipids are used for energy. Only when lipid stores are exhausted is there significant utilization of proteins for energy.

5. *Describe the relative efficiencies of carbohydrates, lipids and proteins in energy storage.*

The energy content of food is usually expressed in calories per gram. As summarized in Table 2, lipids are approximately twice as efficient at energy storage and production as either carbohydrates or proteins. Lipids can store and produce about 9.5 calories per gram, while carbohydrates and proteins will yield about 4.2 and 4.3 calories per gram respectively.

Table 2. Energy potentially available from carbohydrates, lipids and proteins.

molecule	available energy per gram	proportion of total body energy stored
carbohydrate	4.2 Calories per gram	1 %
lipid	9.5 Calories per gram	77%
protein	4.3 Calories per gram	22%

A Calorie (with a capital C) is equivalent to 1000 calories (with a lower case c). A calorie is the amount of heat required to increase the temperature of 1 ml of water 1 degree Celsius. Therefore 1 Calorie (kilocalorie) is the amount of heat that is required to increase the temperature of 1 litre of water 1 degree Celsius.

Because triglycerides are hydrophobic, they are stored as fat droplets free of water. Glycogen, on the other hand, is hydrophilic and is stored in a hydrated form, containing about twice as much water (by weight) as lipids. The net effect of this is that stored lipid is about six times as efficient, on a gram for gram basis, than stored glycogen. Although proteins can be used for energy, they are not primarily energy storage molecules.