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Dr. Mahamane Mamadou holds a B.Sc. (University of Wisconsin-Madison), M.Sc. (University of Kentucky, Lexington), and Ph.D. (University of Cincinnati). Dr. Mamadou's post-doctoral fellowship was in the Department of Pharmacology and Cell Biophysics (University of Cincinnati) working on developmental gene expression.

Dr. Mamadou's teaching and research activities have been in the areas of protein chemistry, enzymology, food sciences and technology, cell and molecular biology, environmental health, biomedical engineering, and biotechnology. He has taught and conducted research at several universities and has provided consulting and research services for various industries in product development, environmental toxicology, and functional foods as dietary supplements. Dr. Mamadou continues to be actively involved in health prevention research dealing with various nutritional disorders, degenerative diseases, **and the identification of health risk biomarkers.**

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FOOD PROTEINS

A. The Importance of Dietary Proteins

Every biological system is composed mostly of protein molecules. Muscle, bone, and connective tissue as well as enzymes, receptors, antibodies, cytokines, carrier molecules, and many other molecules and hormones in humans are mostly made of proteins. Additionally, key molecules such as neurotransmitters or porphyrin rings of hemoglobin are made up or derived from amino acids. Nucleotides that are basic building blocks of DNA and RNA are also derived from amino acids. In short, life ceases when proteins and amino acids are lacking in the body.

Most of the proteins in the body (muscles, bones, connective tissue, enzymes, receptors, etc.) are constantly being degraded and regenerated according to the body's physiological needs, age, health status, stress, and various other factors. In order to replenish that constant depletion of proteins, amino acids have to be brought into the body via daily dietary intake. One of the main goals in nutrient acquisition is to provide the body with these necessary amino acids so that vital proteins and other molecules containing or derived from amino acids can be synthesized.

It is important to emphasize the importance of proteins in the diet. Although the source of proteins may be subject to variation according to religious, cultural, philosophical, or other considerations, the intake of a complete protein food source is by no means optional. In fact, the body needs nine to ten amino acids that it cannot synthesize on its own and those necessarily must be brought in via the diet. These nine essential amino acids in humans are:

- methionine (and cysteine)
- histidine
- isoleucine
- lysine
- phenylalanine (and tyrosine)
- threonine
- tryptophan
- valine

It is generally recommended that the protein intake should range between 0.6 - 0.8 g / kg of body weight per day. In some cases, up to 1 g / kg body weight per day may be suggested. Athletes and those working out daily can increase their protein intake 1.2 g / kg body weight per day to 1.7 g / kg body

weight per day. In either case, the composition in amino acids of the proteins should be taken into consideration. Any compromise in the intake of these essential amino acids constitutes an "infringement" on vital cellular needs.

What are proteins? Proteins are molecules made up of a linear chain of amino acids linked via specific chemical bonds called peptide bonds. Biochemically, a peptide bond is an amide linkage between the functional alpha carboxyl of one amino acid to the functional alpha amino group of another amino acid. The sequence of the amino acids in this linkage is determined by the information encoded in the genes (DNA sequences).

The chain of the amino acids resulting from the formation of the peptide bonds is called either a peptide or a polypeptide, depending on the number of peptide bonds. Usually, if there are fewer than ten peptide bonds in the chain, it is called a peptide. Above ten peptide bonds, it is called a polypeptide. However, a protein as a finished functional structure can be either a single polypeptide or several polypeptide chains intertwined together in a very specific structure.

B. The Importance of Protein Digestion

In order for amino acids to be bio-available and replenish the body's needs, the dietary proteins need to be hydrolyzed and the resulting amino acids must be absorbed into the enterocytes. Protein hydrolysis consists of breaking the peptide bond, thus freeing the amino acids.

The first step in human digestive protein hydrolysis is protein denaturation. Hydrochloric acid in the stomach will unwind the protein chain and expose the peptide bonds so that the various proteolytic enzymes might access them and break those bonds to release the amino acids. This process of breaking the protein bonds starts in the stomach with

pepsin and continues in the small intestine with trypsin, chymotrypsin, elastase, carboxy peptidases, amino peptidases, and other proteolytic enzymes. The desired end products should be single amino acids, dipeptides (two linked amino acids), or tripeptides (three linked amino acid). Any chain larger than four peptides could not be normally absorbed into the enterocytes and may lead to major health challenges.

What are the health challenges that could be caused by undigested or partially hydrolyzed proteins? The polypeptide chains in the diet will be progressively hydrolyzed (broken down) by the various enzymes as they move down the gastrointestinal (GI) tract. Depending on the status of the digestive system, the hydrolysis process will be more or less effective, potentially resulting in various fragments of the polypeptide chain left within the lumen of the intestine. Considering that proteins are necessary in the diet and that several proteins are normally needed and found in any protein source food, the types of fragments found will be very diverse. There will be single amino acids, dipeptides, tripeptides, and some fragments that may be four, five, six, or more amino acids in length.

These single amino acids, dipeptides, and tripeptides will be absorbed within the enterocytes. However, the larger fragments that could not be absorbed normally within the enterocytes will have several fates, including:

- They could be used as foods by the microflora and potentially lead to the formation of excess hydrogen sulfide and toxic amines
- They could ultimately be hydrolyzed after a long transit time in the GI tract, but only after they have affected the system in a positive or negative manner, depending on their biological function
- They could follow a paracellular passage and get into blood circulation, thereby leading to allergic reactions and/or other inflammatory conditions

One of the major consequences resulting from these fragments is that some of them could have very potent biological activity. In fact, many biologically active neurotransmitters are only four to six amino acids in length. For instance, if not completely hydrolyzed, casein in milk could generate short fragments ranging from four to eight amino acids in length, where each may have very effective opioid types of activities. Similar observations have been made with the gluten found in wheat. Although those two proteins were cited here, really any protein could generate fragments with various biological activity. It should be noted that it is not the kind of protein that is the problem, but it is rather the lack of complete hydrolysis (i.e., the inefficiency of the digestive enzymes to fully digest the proteins into its simpler components) that can bring health challenges.

One of the clinical effects of this maldigestion of proteins could be behavioral changes, including the types of neurological disorders seen with people on drugs and alcohol. In recent years, research has indicated that one of the causative factors associated with autism and ADD may be an inability to fully digest certain proteins. Most notably, these researchers cite the kinds of proteins found in milk and wheat that the patients tend to crave. Besides these known clinical disease conditions, there are also episodic cases when people get "drunk" or experience a "high" feeling from eating certain foods. Some of these cases may be attributed to partially hydrolyzed polypeptides, resulting in peptides that could affect the nervous system.

It does appear that when the patients are removed from wheat or casein, their symptoms are improved. This was especially noted in relation to autism, for instance. It has been noted in clinics that some patients taking supplemental proteolytic enzymes improve their condition. The focus on secretin as a form of treatment for autism in recent years may also point to this condition's basis in a digestive disorder. That is because secretin is

a GI hormone that is secreted within the duodenum when stimulated by some of the contents of the stomach chyme. Upon secretion, secretin travels via the blood circulation and stimulates the pancreas to secrete bicarbonates. The function of the bicarbonate is to neutralize the acidic chyme and thus to prevent it from denaturing pancreatic enzymes in the duodenum. Under conditions where secretin is deficient, the bicarbonate secretion from the pancreas may be impaired, thereby resulting in the stomach acid deactivating and denaturing the pancreatic enzymes. Thus, the proteins that were only partially digested by pepsin in the stomach will not be further hydrolyzed, thereby resulting in various fragments with potent and diverse biological activity on the whole organism. This may explain the benefits of secretin as observed with some autistic patients.

Put more specifically, the secretin has helped prevent the denaturation of digestive enzymes. Because of the difficulties associated with the sources and availability of secretin, there has been some reservations regarding its application. In one particular study that refuted the secretin benefit, porcine secretin was used in only one injection, which may not be enough to elicit any remedy. Additionally, some questions were raised about the effectiveness of the source or nature of the secretin in that study. However, irrespective of the form or the source of secretin as a viable therapy for autism, the focus should be on the digestibility of proteins, as many patients may have fragments with potent opioid-like activities that could result in mental and behavior challenges.

In conclusion, the following points should be repeated.

- Proteins are necessary in the diet. This is especially true regarding complete proteins (i.e., the ones containing the essential amino acids). Any decline in daily protein intake could compromise metabolic homeostasis, immune function, mental alertness, and all biosynthetic functions that replenish

vital molecules. Lack of proteins will further accelerate the aging process, enhance catabolism (muscle, bone, and connective tissue breakdown), and promote both infections and degenerative disorders.

- Protein digestion and amino acid absorption should be optimized in order to ensure vitality and prevent any deleterious impact by partially hydrolyzed peptides with neurological or other effects. Additionally, the hydrolysis of proteins and the absorption of amino acids will minimize the generation of toxic amines by the microflora as well as the ultimate mutagenic effects of these toxic metabolites.
- Casein and gluten should not be considered as the only culprits of sources of opioid peptides. In fact, depending on its amino acid sequence, level of hydrolysis in the GI tract, and the types of biologically active peptides that could be generated from it, any protein may pose health problems if it is not fully hydrolyzed into the single amino acids, dipeptides, or tripeptides that are ultimately absorbed into the enterocytes.
- The digestion of macromolecules as a whole is a dynamic process resulting in the temporal production of various length fragments, some of which have different biological functions acting along the GI tract.
- Digestion should be optimized and ensured through good nutrient acquisition.

Thus, considering the vital need of proteins in the diet, every effort should be taken to ensure their hydrolysis so that the remaining amino acids could be absorbed and used by the body.