The Breakdown on Digestive Enzymes

Digestive enzymes are naturally present in all living organisms to aid in the digestion of food by breaking down large food carbohydrates, lipids and protein macromolecules into smaller building blocks that can be easily absorbed and utilized by the organism.

The Classification of Digestive Enzymes

Digestive enzymes are classified based on their target substrate, whether it is carbohydrate, lipid, or protein. Within each class of enzyme lie many types of enzymes, each targeting different substrates, and digesting them into different sizes.

Proteases and peptidases break down proteins into smaller peptides and amino acids. Amino acids, the smallest building blocks of protein, can be combined into different sequences to make diverse small or large protein molecules (peptides) that the body needs to perform various crucial functions, including replicating DNA, immune responses, building muscle, or as enzyme building blocks, among other functions. In fact, out of the 22 different standard amino acids, 9 are "essential amino acids" because the human body cannot synthesize them and must obtain them either by digesting consumed protein or from amino acid supplementation.

Lipases break apart fat into fatty acids and glycerol. Fatty acids are an extremely important source of fuel in the human body and store large amounts of energy. Glycerol is an important building block of fats synthesized by the body.

Carbohydrases catalyze the splitting of carbohydrates such as starch and sugars into simple sugars such as glucose. Glucose is an important source of energy for many of the body functions and is the brain's primary source of energy.

The Role of Digestive Enzymes

Digestion starts in the oral cavity. The simple physical digestion performed by chewing allows a higher surface area to be exposed to the saliva which contains an array of digestive enzymes that start the chemical digestion of food. These enzymes include carbohydrases such as amylase, as well as lipase. Unlike lipids and carbohydrates however, protein digestion is started in the stomach by the peptidase "pepsin", the major digestive enzyme produced in the stomach. The semi-digested product then moves to the duodenum, where it gets further degraded by a secretion from the pancreas known as "Pancreatic Juice" containing more amylase, protease and lipase. Digestion is completed in the small intestine by numerous "brush border" enzymes that break down the semi-digested products into minute particles. This process releases amino acids, sugars, fatty acids, vitamins, minerals and other essential nutrients that get absorbed through the walls of the small intestine and to a lesser extent, the colon.

The Importance of Digestive Enzymes

It may be argued that under optimal conditions a healthy human body does not need digestive enzyme supplementation. However, with more than 20 million Canadians and up to 70 million Americans afflicted with digestive diseases,[1,2] it is apparent that the digestive capability of many is not functioning optimally. In fact, many people diagnosed with digestive disorders do not have any serious symptoms,[1] and unless diagnosed, may never know that they have digestive disorders. Mild digestive enzyme deficiency or the consumption of an amount of food greater than the enzymatic digestive capability of the body will result in some undigested food passing through to the colon. Since the body cannot absorb nutrients from undigested food as well as it does from digested food, many nutrients can get excreted unutilized. Additionally, when food arrives at the colon undigested, it is metabolized by indigenous colonic microbial flora, leading to over production of carbon dioxide, methane, and/or hydrogen, which are absorbed and eliminated via the lungs, but can also lead to feelings of bloating, flatulence, abdominal pain, discomfort and even diarrhea or vomiting in some cases.[3,4] Inadequate enzymatic digestion of food can lead to avoidance of nutritious food for fear of unwanted gastrointestinal symptoms. Even in cases where the problematic food is consumed, improper digestion prevents full access to all of the nutrients present, resulting in nutrient malabsorption. Nutrient deficiency can cause serious decline in health, including degenerating eyesight, impaired immunity, mood swings, poor wound healing, and decline in the health of skin,

Table 1: Enzyme sources and units accepted by Health Canada, and available conversions					
Enzyme Class	Enzyme	Source type	Sources	Units	Available conversions
Proteases	Fungal protease	Fungal	*Aspergillus flavus* var. *oryzae* *Aspergillus niger*	HUT, SAP	None
	Bacterial protease/ neutral protease	Bacterial	*Bacillus subtilis*	PC	None
	Papain, Bromelain	Plant	*Carica papaya* (Papaya) *Ananas comosus* var. *comosus* (Pineapple)	PU, GDU	1 GDU ~ 15,000 PU
	Protease	Animal	*Bos taurus* (cow) pancreas *Sus scrofa* (pig) pancreas	USP units	1 Ph.Eur. Unit = 1 BP Unit = 1 FIP Unit ~ 62.5 USP Units
Lipases	Fungal lipase	Fungal	*Aspergillus flavus* var. *oryzae* *Aspergillus niger* *Rhizopus oryzae*	LU	None
	Lipase	Animal	*Bos taurus* (cow) pancreas *Sus scrofa* (pig) pancreas	USP units	1 Ph.Eur. Unit = 1 BP Unit = 1 FIP Unit ~ 1 USP Unit
Carbohydrases	Alpha-Galactosidase	Fungal	*Aspergillus niger*	GalU	None
	Lactase, beta-galactosidase	Fungal	*Aspergillus flavus* var. *oryzae*	ALU	None
	Alpha-Amylase	Fungal	*Aspergillus flavus* var. *oryzae* *Aspergillus niger* *Rhizopus oryzae*	DU	None
	Alpha-Amylase	Plant	*Hordeum vulgare* (Barley)	DU	None
	Alpha-Amylase	Animal	*Bos taurus* (cow) pancreas *Sus scrofa* (pig) pancreas	USP units	1 Ph.Eur. Unit = 1 BP Unit = 1 FIP Unit ~ 4.15 USP Units
	Glucoamylase/ amyloglucosidase/ acid maltase	Fungal	*Aspergillus niger* *Aspergillus oryzae* *Rhizopus niveus* *Rhizopus oryzae*	AGU	None
	Cellulase	Fungal	*Aspergillus niger* *Trichoderma longibrachiatum* *Trichoderma reesei*	CU	None
	Hemicellulase	Fungal	*Aspergillus niger* *Aspergillus oryzae* *Trichoderma longibrachiatum* *Trichoderma reesei*	HCU	None
	Invertase/sucrase	Fungal	*Aspergillus niger* *Saccharomyces cerevisiae*	INVU, SU	None

bones and various other organs in the body. Enzyme supplementation can help improve the digestibility of many foods, which can improve nutrient absorption, and decrease or even eliminate many of the gastrointestinal complaints resulting from improperly digested food.

Take Lactase for Example

Lactose intolerance is a symptom of a very common enzymatic deficiency, more accurately described as lactase deficiency. Lactase is a carbohydrase that breaks down lactose (a sugar naturally abundant in milk and other dairy products) into the simpler sugars glucose and galactose, both of which can then be absorbed by the body and utilized for various crucial functions. Lactase quickly digests lactose in the small intestine so that little or no lactose reaches the colon. However, lactase levels naturally drop by varying degrees in most individuals after weaning; in fact most lactose intolerant individuals can handle one glass of milk (about 12 grams of lactose) with minor or no symptoms, while 15-18 grams of lactose are tolerated when offered with other nutrients, and intolerance becomes progressively more frequent at quantities larger than 18 grams.[4]

When lactase levels are deficient, undigested lactose reaches the colon where it is fermented by the microbial flora. This leads to an over production of gases causing bloating and flatulence,

Table 2: Enzyme targets, digestion products and foods rich in enzyme targets				
Enzyme Class	Enzyme type	Target substrate	Digestion product	Foods rich in target substrate
Proteases	Proteases	Large and mid-sized protein molecules	Mid-sized peptides and individual amino acids	Protein present in soy, spirulina, whey protein, dairy, tofu, seafood, among others
Lipases	Lipase	Lipids (fat)	Fatty acids and glycerol	White and red meat, dairy products, egg yolk, oils (such as olive oil and coconut oil), nuts (almonds, pistachios, walnuts, hazelnuts), coconut, among others
Carbohydrases	Amylase, Glucoamylase	Complex, long chain carbohydrate molecules (starch)	Mid and small chain carbohydrates (such as maltose) and simple sugars (such as glucose)	Starch, such as that present in rice, potatoes, wheat, corn, bananas, chestnuts, beans such as fava beans, lentils and peas and others
	Alpha-Galactosidase	Complex and branching sugars	Simple sugars (such as glucose)	Legumes (beans, peanuts), cruciferous vegetables (cauliflower, broccoli, cabbage, Brussels sprouts, among others)
	Invertase	Sucrose	Simple sugars (fructose and glucose)	Sweet fruit such as pineapple and apricot
	Cellulase, Hemicellulase	Cellulose (fibre)	Simple sugar (glucose)	Fibrous vegetables and fruit such as persimmons, potato skins, corn, celery
	Lactase	Lactose	Simple sugars (glucose and galactose)	Dairy products (such as milk, and to a lesser extent cheese and yogurt)

in addition to acidifying the colon and increasing the osmotic load, causing loose stools and diarrhea.[5] It has been reported that the clinical representation of lactose intolerance may also extend to systemic complaints such as headache, vertigo, memory impairment, lethargy, muscle and joint pains, allergy, cardiac arrhythmia, mouth ulcers, and sore throat.[6,7] It has been hypothesized that lactose fermentation by the colonic flora could generate toxic metabolites such as acetaldehyde and protein toxins which can alter cell signaling mechanisms and can therefore be responsible for these systemic symptoms.[6,8]

Avoidance of lactose can lead to a decrease in the intake of many important nutrients, most notably calcium and other nutrients crucial for bone health. Supplementating with the enzyme lactase helps improve the digestion of lactose before it wreaks havoc in the colon, thus it can be seen how lactase supplementation can help alleviate symptoms of lactose intolerance and improve nutrient intake and absorption.

Some Clinical Studies on Enzyme Supplementation

Alpha-galactosidase is an enzyme that breaks down complex and branching carbohydrates, such as those found in legumes, and cruciferous vegetables (see table 2). What is interesting about this enzyme is that it is not produced by the human body, therefore the complex and branching carbohydrates pass through the stomach and upper intestine undigested. They are then fermented by the indigenous colonic microbial flora, producing excess gas which can lead to feelings of bloating, abdominal distension and flatulence;[3] this is commonly associated with eating beans and other cruciferous vegetables. Alpha-galactosidase supplementation was clinically shown to reduce gas production following a meal rich in fermentable carbohydrates, since supplementation decreases the amount of fermentable carbohydrates by breaking them down before they can be metabolized by the colonic flora.[3]

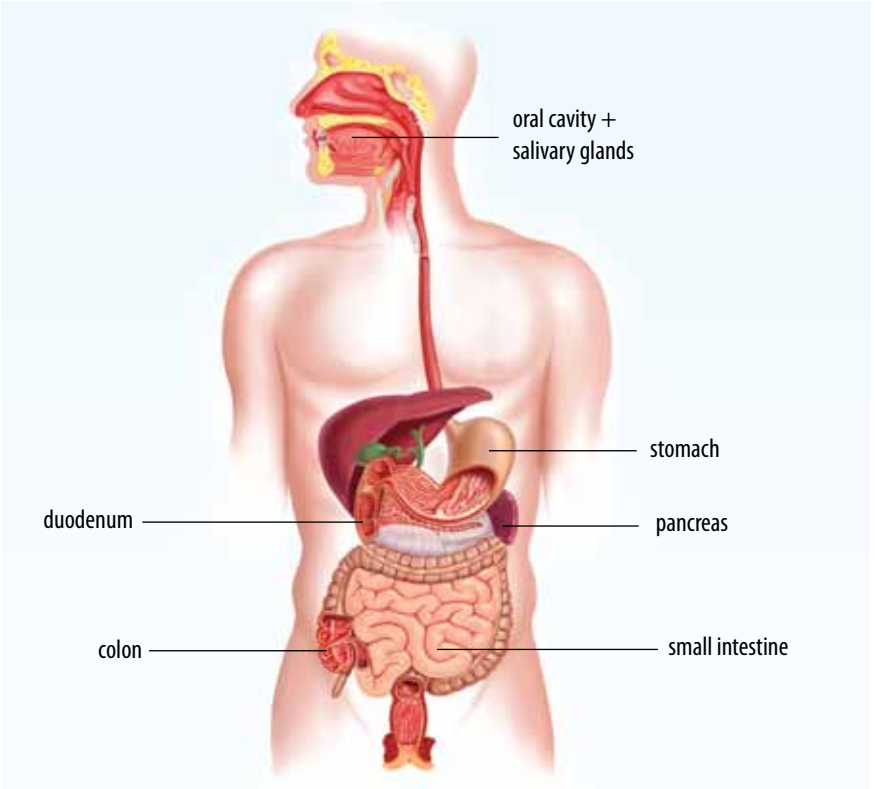
It is well known that a healthy diet should contain an abundance of fibrous vegetables and fruits. However, an overabundance of fibrous vegetable and fruit intake, especially in cases of delayed gastric emptying or hypochlorhydria (low stomach acidity), can cause polymerization of the semi-broken down food in the stomach. This can create a sticky complex acting as glue, which can bind to other foodstuffs resulting in a dark, hard, sticky foreign body that can keep growing, known as phytobezoar.[9] Phytobezoars can cause symptoms of epigastric pain, nausea, or vomiting[10] and can progress to gastric ulcers.[9] Phytobezoars can also migrate into the intestine causing intestinal blockages.[9] Since phytobezoars are bound by cellulose, enzymatic therapy by cellulase has proven to be effective in many cases.[11] Cellulose is a complex carbohydrate, also known as fiber; it is the structural component of the cell wall of green plants and many forms of algae. Cellulose is digested by the enzyme cellulase, however because the human body does not contain or produce cellulase, cellulose is mostly undigestible by the human body. Low dose cellulase

supplementation along with a healthy diet abundant in fibrous raw vegetables and fruits is therefore useful to help reduce the risk of phytobezoar formation since the cellulase can break down cellulose before it becomes problematic.

An exciting preliminary clinical study was published in which elite cyclists were supplemented with an enzyme combination containing the fungal carbohydrases amylase, cellulase and hemicellulase, in addition to a meal replacement prior to exercise. The results of this study show an increase in endurance (or time to exhaustion) during exercise by 43%, which was attributed to the more rapid digestion of carbohydrates provided in the meal replacement, thereby improving the availability of simple sugars to be absorbed and utilized by the cells for energy.[12]

In another clinical study published by Glade and colleagues in 2001,[13] an enzyme combination containing the fungal carbohydrases amylase, cellulase and lactase as well as lipase and bromelain (a protease found in pineapple) was given to bedridden nursing-home patients. Total digested protein concentration increased significantly, which means faster and higher availability of protein for absorption and use in crucial pathways required by the body. Albumin concentration also increased slightly, which is crucial for hormone transport, especially thyroid hormones.[14] Albumin is also a marker of inflammation (since it is down-regulated in inflammatory states), helps prevent the photo-degradation of folic acid,[15] and is a very abundant and important antioxidant.[16] Finally, the study showed an increase in lymphocyte counts, and it is well known that a higher lymphocyte count is a (beneficial) marker of a more active immune system.

Short bowel syndrome is a malabsorption disorder that is caused by either the surgical removal of the small intestine, or due to the complete dysfunction of a large segment of the bowel. With a large section of the small intestine out of commission, large amounts of nutrients do not get absorbed,



leading to abdominal pain, diarrhea or steatorrhea, malnutrition and fatigue. Many small bowel syndrome patients suffer from deficiencies in vitamins A, D, E, K and B12, folic acid and minerals calcium, magnesium, iron, zinc, which can manifest as anemia, easy bruising, muscle spasms, poor blood clotting and bone pain, all of which are due to the decreased colonic absorption of nutrients present in food. It was shown in a clinical study that providing short bowel syndrome patients with an enzyme powder consisting of fungal lipase, the carbohydrases amylase, cellulase, lactase, as well as bromelain (protease) resulted in considerable improvement of symptoms and improved digestion, since enzyme supplementation provided the body with easier access to the nutrients available in food.[17]

Enzyme Units and Conversions

Unlike many other substances, enzymes are not measured by weight, but rather by 'activity'. The activity of an enzyme is defined as "The amount of enzyme that catalyzes the conversion of 1 micromole of substrate per minute", or in the case of digestive enzymes, the amount of enzyme required to digest 1 micromole of the appropriate substrate (i.e. protein, fat or carbohydrates) in 1 minute under the conditions optimal for said specific enzyme which can include certain temperature, pH, substrate used, etc. The optimal conditions required for each enzyme to display its most efficient digestive capabilities differ. Enzyme activity is a more appropriate measure of how much actual enzyme you're getting than weight, because 10 mg of one enzyme can digest substrates much more efficiently than the exact same weight of another enzyme due to differences in enzyme activity strengths. In this case, the higher the activity, not the weight, the more beneficial the enzyme can be.

A common issue faced by many aiming to increase their enzyme intake is that many enzyme manufacturers use different enzyme units to represent their enzyme activity. Unfortunately, the different enzyme units imply different assay methods, which can include different testing conditions. Enzymes work differently under different conditions, and each enzyme has its own optimal conditions where

it displays its most efficient digestive capability. Therefore mathematical conversion between the units may not be possible or accurate and has to be obtained experimentally by carrying out all the relevant assays on each enzyme using all the different conditions. In the case of pancreatic enzymes, the relevant enzymatic assays for many different units have been carried out and the results well studied, therefore the conversion between the studied different units in the case of pancreatic enzymes is possible (See table 1). However, while it is possible to convert between pancreatic lipase FIP, USP and LU units, it is not possible to use the same conversion for lipase from another source such as fungal lipase, since both lipases behave differently under different pH's.

The good news is, in order to allow the consumer to properly compare different brands and products, Health Canada has mandated that all manufacturers use the same internationally recognized units for all their enzyme products[18] (see table 1). This will make choosing the product easier in the near future.

Enzyme Supplementation and You

The human body is adaptable and can handle much of what we throw into it; therefore digestive enzymes should only be taken when needed. The appropriate digestive enzymes may be useful for you if you consistently suffer from gastrointestinal discomfort from a certain type of food, or if you know you may be having a meal that could cause a larger than normal burden on your digestive system. In both cases, your body is not producing enough enzymes to break down the food eaten, and the left over undigested food is excreted without optimal nutrient extraction, in addition to being fermented in the colon causing gastrointestinal problems and damage. Therefore, the occasional extra help from digestive enzyme supplementation can help the digestibility of food, improve nutrient intake and alleviate most if not all of the gastrointestinal symptoms associated with improper digestion due to overwhelming the body's natural enzymes with more than they can handle. You can refer to table 2 to determine which enzyme can best digest the food known to be problematic for you. As with most supplements, it is always best to consult your qualified health care practitioner for questions and to know if enzyme supplementation is right for you. ■

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