

Beta Plus™ & Beta-TCP™

Nutritional Support for Bile Production & Biliary Status

In the 16th century, Paracelsus introduced the concept of the tartaric diseases to explain how stones are formed in the human body by the precipitation of substances from body fluids, analogous to the deposition of tartar in wine casks. Today we know that in industrialized countries more than 80% of gallstones consist mainly of cholesterol, the prevalence of gallstones is about 10%, and in people between 40 and 50 years of age the 5-year incidence is about 3%.

Bile, Defined

Bile functions as the body's "detergent" emulsification and absorption of lipids, critical for fat digestion and assimilation. Bile is produced by the liver, and is temporarily stored in the gall bladder. Bile is released into the small intestine in response to hormones, such as cholecystokinin, when fat enters the intestine. Bile consists of a mixture of bile salts, bile acids, cholesterol, bilirubin and phospholipids chiefly phosphatidylcholine. The ratio of individual lipids are critical to maintain a stable micellar concentration. The molar ratios are typically 5:15:80 for cholesterol/phosphatidylcholine/bile salts. If the bile concentration becomes too high, cholesterol will precipitate and gallstones will form in the gall bladder, a condition known as cholelithiasis.⁽¹⁾

Bile Formation

Bile salts and acids represent oxidized derivatives of cholesterol. About 80% of the cholesterol in the body will eventually be disposed of as cholic acid. The primary bile acids, cholic acid and chenodeoxycholic acid, possess a carboxylic acid side chain which confers hydrophilic properties to the lipophilic sterol ring and creates detergent-like molecules. The liver attaches taurine and glycine to bile acids to create bile salts (taurocholate or taurochenodeoxycholate and glycocholate or glycodeoxycholate, respectively). Bacterial enzymes in the colon can convert these to secondary bile acids, deoxycholate and lithocholate.

Bile and Digestion

Bile is needed for efficient uptake of oily nutrients (fats). When bile acids and bile salts first encounter ingested fats, they act as emulsifiers to create suspensions which can be broken down enzymatically. The process involves several important steps; sequentially indicated as:

1. The combined action of bile salts and pancreatic lipase initiates hydrolysis of triglycerides to free fatty acids and diglycerides, resulting in the formation of emulsions containing other lipid-soluble nutrients, including vitamins and carotenoids. The particle size of these emulsions ranges from 200 to 5,000 nm in diameter.

2. Lipase is then able to hydrolyze both di- and triglycerides to monoglycerides and free fatty acids. Lipase requires a smaller protein called colipase, another pancreatic product, to bind to triglycerides and activate the lipase.

3. Upon further release of bile salts, the lipid aggregates become smaller, from 3 to 10 nm in diameter. The normal endpoint of triglyceride digestion is a product containing 70% free fatty acid anions, 25% beta monoglycerides and 5% cholesterol. The micelles are then taken up by the epithelial cells of the brush border membrane via passive diffusion. After absorption, the fate of fatty acids depends upon their sizes. Medium chain fatty acids, with less than 10–12 carbons, pass directly from the mucosal cells into the portal blood and bind to serum albumin. Longer chain fatty acid anions are re-esterified with beta monoglycerides in the smooth endoplasmic reticulum to reform triglycerides. The newly synthesized triglycerides are complexed with apoproteins, cholesterol and phospholipids, to produce particles called chylomicrons. Chylomicrons are released from mucosal cells by exocytosis and enter the lymph, rather than entering the bloodstream directly.

Enterohepatic Circulation

Bile salts do not cross the mucosal barrier into the lymphatic system but rather they are reabsorbed as micelles in the lower region of the small intestine. Most of the bile salts released into the intestine are reabsorbed in the lower ileum where bacteria can reduce free bile acids to lithocholate and deoxycholate. The absorbed bile acids and salts are transported via the portal vein to the liver as complexes with serum albumin. The liver efficiently extracts them, conjugates them with amino acids and again secretes them as bile, which is returned to the gall bladder to continue to aid digestion. Bile salts are recirculated 2–3 times through the liver with each meal.

Betaine

Beets are a concentrated source of Betaine, which functions in the methylation of homocysteine, converting it into methionine and dimethylglycine. An elevated level of homocysteine, termed



(800) 231-5777

6801 Biotics Research Drive • Rosenberg, TX 77471
biotics@bioticsresearch.com
www.bioticscan.com

These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.

homocysteinemia, is a risk factor for cardiovascular complications. Dimethylglycine, in turn, functions as a methyl donor, thus aiding in both the detoxification and immune pathways. Betaine is often referred to as a "lipotropic factor" as it assists the liver in the processing of fats. Studies with betaine have correlated its use with liver protection. For example in one study, subjects exposed to carbon tetrachloride (CCl₄), were followed with an oral treatment of betaine. They were observed to have a significant reduction in liver necrosis, which was attributed to betaine use. In another study, following CCl₄ injection in test animals, supplemental betaine was observed to reduce liver triglycerides as well as centrilobular hepatic lipidosis.⁽³⁾

Fiber and the Binding of Bile Components

Certain kinds of dietary fiber bind bile salts. Examples include pectin (found in fruits and berries), hemicelluloses (found in cereal grains), and certain types of fiber that occur in legumes. When the diet is rich in partially soluble fiber, more bile is excreted (not reabsorbed). As a consequence, blood cholesterol levels may be reduced to account for more bile salt formation, consequently slowing the development of atherosclerosis.

Nutritional Support of Bile Formation

Bile. Bile salts, along with other components, including cholesterol, electrolytes and water are stored in the gallbladder. Bile salts act as an enzyme aide, and serve to enhance the absorption of fatty acids and some fat-soluble vitamins. Bile also serves as a fat emulsifier, thus increasing the surface area of the fat, and allowing it to become water-soluble. Thus bile aids aide in the absorption of fatty acids and cholesterol via the formation of micelles. The micelles, soluble in chime, are then easily absorbed by epithelial cells. Bile also serves in a protective mechanism, functioning to maintain the intestinal barrier against invading microorganisms.^(4,5)

Pancrelipase. (*Pancreatic lipase*) Pancrelipase functions in the hydrolysis of triacylglycerol in the presence of bile salts, and therefore functions in the absorption of dietary fats and lipids. Accordingly, in the presence of gastric lipase, triacylglycerol is hydrolyzed to monoglycerides and free fatty acids. Pancrelipase preparations have been shown to reduce fecal fat, indicating an improvement in the fat digestive process with the use of Pancrelipase.^(6,7)

Taurine. Taurine is a highly charged cysteine derivative, synthesized *in vivo* from the essential amino acid methionine. When conjugated to bile acids, an increased polarity of the bile acid results, thus increasing its amphipathic (detergent-like) properties. In one study dietary taurine was demonstrated to enhance the degradation of cholesterol and subsequent excretion via bile acids.⁽⁸⁾ In animal studies supplementary taurine was demonstrated to both increase serum HDL, and significantly decrease total cholesterol.⁽⁹⁾ Additionally, a significant increase in the concentration of fecal total bile acids has been observed with taurine supplementation.⁽¹⁰⁾ The action of taurine on serum cholesterol was attributed to the facilitation of hepatic cholesterol 7- alpha-hydroxylase activity.⁽¹¹⁾

Vitamin C. The enzyme noted above, cholesterol 7-alpha-hydroxylase, is the enzyme responsible for the initial step in the catabolism of cholesterol to conjugated bile acids. This enzyme is a vitamin C dependent enzyme. In studies supplemental vitamin C was shown to reduce total

plasma cholesterol and triglycerides, which was correlated to a marked modification in apolipoprotein patterns.^(12,13) In patients with gallstones, vitamin C was shown to influence the environment of the gallbladder, resulting in a higher concentration of phospholipids, along with a changed ratio of bile acids, indicating an influence of vitamin C on the formation of gallstones.⁽¹⁴⁾ Additionally, in women, an inverse correlation between serum ascorbic acid and the prevalence of both clinical and asymptomatic gallbladder symptomology was observed.⁽¹⁵⁾

References

1. Welch GN, Loscalzo J. Homocysteine and atherothrombosis. *N Engl J Med.* 1998;338:1042-1050.
2. Murakami T, Magamura Y, Hirano K. The recovering effect of betain on carbon tetrachloride-induced liver injury. *J Nutr Sci Vitaminol (Atokyo)* 1998 Apr;44(2):249-55.
3. Junnila M, Barak *et al.* Betain reduces hepatic lipidosis induced by carbon tetrachloride in Sprague-Dawley rats. *Vet Hum Toxicol* 1998. Oct;40(5):263-6.
4. Ogata Y, Nishi M, Nakayama H, Ohnishi Y, Tashiro S. Role of bile in intestinal barrier function and its inhibitory effect on bacterial translocation in obstructive jaundice in rats. *J Surg Res.* 2003 Nov;115(1):18-23.
5. Walls CL, Jechorek RP, Erlandsen SL. Inhibitory effect of bile on bacterial invasion of enterocytes: possible mechanism for increased translocation associated with obstructive jaundice. *Crit Care Med.* 1995 Feb;23(2):301-7.
6. Delhave M, Meuris S, Gohimont AC, Buedts K, Cremer M. Comparative evaluation of a high lipase pancreatic enzyme preparation and a standard pancreatic supplement for treating exocrine pancreatic insufficiency in chronic pancreatitis. *Eur J Gastroenterol Hepatol.* 1996 Jul;8(7):699-703.
7. Valerio D, Whyte EH, Schlamm HT, Ruggiero JA, Blackburn GL. Clinical effectiveness of a pancreatic enzyme supplement. *JPEN J Parenter Enteral Nutr.* 1981 Mar-Apr;5(2):110-4.
8. Yokogoshi H, Oda H. Dietary taurine enhances cholesterol degradation and reduces serum and liver cholesterol concentrations in rats fed a high-cholesterol diet. *Amino Acids.* 2002;23(4):433-9.
9. Yokogoshi H, Nanami K, Hida Y, Miyachi, Oda H. Dietary taurine enhances cholesterol degradation and reduces serum and liver cholesterol concentrations in rats fed a high-cholesterol diet. *J Nutr.* 1999 Sep;129(9):1705-12.
10. Kishida T, Ishikawa H, Tsukaoka M, Ohga H, Ogawa H, Ebihara K. Increase of bile acids synthesis and excretion caused by taurine administration prevents the ovariectomy-induced increase in cholesterol concentrations in the serum low-density lipoprotein fraction of Wistar rats. *J Nutr Biochem.* 2003 Jan;14(1):7-16.
11. Nishimura N, Umeda C, Oda H, Yokogoshi H. The effect of taurine on the cholesterol metabolism in rats fed diets supplemented with cholestyramine or high amounts of bile acid. *J Nutr Sci Vitaminol (Tokyo).* 2003 Feb;49(1):21-6.
12. Santillo M, Santangelo F, Belfiore A, Masturi M, Mondola P. Effect of ascorbic acid administration on B and E apoproteins in rats fed a cholesterol enriched diet. *Horm Metab Res.* 1993 Mar;25(3):156-9.
13. Santillo M, Mondola P, Santangelo F, Gioielli A, Iossa S, Basilisco A, De Mercato R. Changes in apoprotein distribution between lipoprotein classes of hypercholesterolemic rats treated with ascorbate. *Int J Biochem Cell Biol.* 1995 Mar;27(3):257-62.
14. Gustafsson U, Wang FH, Axelsson M, Kallner A, Sahlin S, Einarsson K. The effect of vitamin C in high doses on plasma and biliary lipid composition in patients with cholesterol gallstones: prolongation of the nucleation time. *Eur J Clin Invest.* 1997 May;27(5):387-91.
15. Simon JA, Hudes ES. Serum ascorbic acid and gallbladder disease prevalence among US adults: the Third National Health and Nutrition Examination Survey (NHANES III). *Arch Intern Med.* 2000 Apr 10;160(7):931-6.

To place your order for **Beta Plus™ & Beta-TCP™** or for additional information please contact us below.



(800) 231-5777

6801 Biotics Research Drive • Rosenberg, TX 77471
biotics@bioticsresearch.com
www.bioticscan.com

These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.

BioDoph-7 Plus®

A unique blend of probiotics and prebiotics, along with additional support for a healthy GI tract

Classically defined, probiotics are “a preparation of, or a product containing viable, defined microorganisms in sufficient numbers, which alter the microbiota (typically by colonization) in a compartment of the host, and by that, exert beneficial health effects in this host.”⁽¹⁾ Traditionally, probiotics have consisted of species from the genera *Lactobacillus* and *Bifidobacterium*, however other strains have demonstrated beneficial effects.

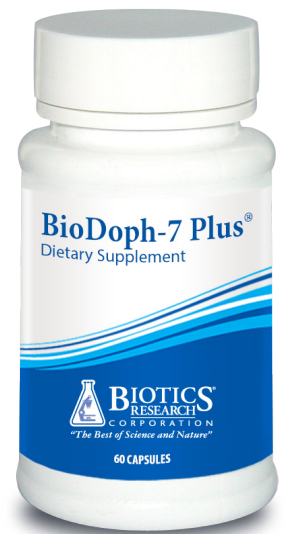
Documented research has indicated important benefits associated with the use of probiotic bacteria, including improved digestion, enzymatic activity and overall health. For example, *L. plantarum* is recognized as a major colonizer⁽²⁾ and was shown to “decrease translocation, improve mucosal status, improve liver status, improve the immunologic status of the mucosa, and to reduce mucosal inflammation.” Subsequently, *L. plantarum* is considered to be an integral part of the host’s immunologic defense.⁽³⁾ Probiotics have also shown to have a modulating effect on the immune system. A probiotic combination of *Lactobacilli* species, *Bifidobacteria* species and a *Streptococcal* strain was shown to be immunomodulating by virtue of both the upregulation of IL-10 production by dendritic cells, and the decreased production

of interferon-gamma by T-cells. Also noted was a “diminished proinflammatory effect via a decrease in the lipopolysaccharide production of IL-12.”⁽⁴⁾

BioDoph-7 Plus® supplies ingredients that:

- Improves digestive function
- Improves immunologic status
- Increases beneficial anaerobes
- Decreases “unfriendly” organisms
- Stimulates phagocytosis
- Soothes gastric mucosa

Like probiotics, prebiotics also play a beneficial role in GI health, via their alteration of the gut flora composition in favor of beneficial bacterial.⁽⁵⁾ Prebiotics are categorized as a “nondigestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon.”⁽⁶⁾ The prebiotic inulin demonstrated beneficial results with administration, by virtue of its ability to stimulate the enumeration of the colonic *Bifidobacteria* population, thus improving the composition of the gut flora.⁽⁷⁾ Arabinogalactan from



(800) 231-5777

6801 Biotics Research Drive • Rosenberg, TX 77471
biotics@bioticsresearch.com
www.bioticscan.com

These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.

larch is also an effective prebiotic fiber. In the large intestine it is actively fermented by friendly intestinal microflora, resulting in an increased number of beneficial anaerobes, while simultaneously decreasing unfriendly organisms such as *Clostridia*.⁽⁸⁾ Marshmallow root extract, also considered a prebiotic, supplies polysaccharides, including arabinogalactans and glucan. It stimulates phagocytosis, and has been shown to alleviate local irritation of the gastric mucosa.⁽⁹⁾

Thus, when considering overall health benefits, the combination of prebiotics and probiotics supplied by **BioDoph-7 Plus**[®] are a judicious choice, having documented success in improving gastrointestinal health. Additionally, by utilizing a prophylactic approach, gastrointestinal complaints may be addressed in a means that will promote optimal wellness.

References

1. Havenaar R and Huis In't Veld, MJR. 1992 Probiotics: a general view. *Lactic acid Bacteria in Health and Disease*, Vol.1 (ed. B.J.B. Wood), pp. 151-170, Elsevier Applied Science Publishers, Amsterdam.
2. Ahrne S, Nobaek S, Jeppsson B, Adlerverth I, Wold AE, Molin G. The normal bactericillus flora of healthy human rectal and oral mucosa. *J Appl Microbiol.* 1998 Jul;85(1):88-94.
3. Molin G. *Probiotics in foods not containing milk or milk constituents, with special reference.*
4. Hart AL, Lammers K, Brigidi P, Bitali B, Rizzello F, Ginonchetti P, Campieri M, Kamm MA, Knight SC, Stagg AJ. *Modulation of human dendritic cell phenotype and function by probiotic bacteria.* *Gut.* 2004 Nov;53(11):1602-9.
5. Gibson GR. *Dietary modulation of the human gut microflora using the prebiotics oligofructose and inulin.* *J Nutr.* 1999 Jul;129 (7 Suppl):1428S-41S.
6. Gibson GR and Roberfroid MB. *Dietary modulation of the human colonic microbiota – introducing the concept of prebiotics.* *J of Nutrition.* 1995. 125, 1401-1412.
7. Manning TS, Gibson GR. *Microbial-gut interactions in health and disease.* *Prebiotics. Best Pract Res Clin Gastroenterol.* 2004 Apr;18 (2):287-98.
8. Fitzpatrick A, Roberts A, Witherly S; *Agrofood Industry Hi-Tech.* 2004 Jan/Feb.
9. *The Complete German Commission E Monographs* (ed. Blumenthal M)

Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving
Proprietary Blend	400 mg
Inulin (from Chicory root)*, Arabinogalactans (from Larch)*, Marshmallow (Althea officinalis) (extract) (root)*, Bifidobacterium bifidum*, Bifidobacterium lactis*, Bifidobacterium breve*, Lactobacillus paracasei*, Lactobacillus plantarum*, Lactobacillus salivarius*, Streptococcus thermophilus*	

* Daily Value not established

Other ingredients: Vegetarian capsule shell (modified cellulose) and magnesium stearate (vegetable source).

Each capsule of **BioDoph-7 Plus**[®] contains more than 20 billion organisms at time of manufacture.

Contains an ultra-trace amount (0.3 ppm) of milk constituents which are used in the fermentation of probiotic ingredients.

This product is gluten free.

RECOMMENDATION: One (1) capsule one (1) to two (2) times each day as a dietary supplement or as otherwise directed by a healthcare professional.

KEEP OUT OF REACH OF CHILDREN

Store in a cool, dry area and refrigerate after opening.
Sealed with an imprinted safety seal for your protection.

Product # 1285 Rev. 01/15

To place your order for **BioDoph-7 Plus**[®] or for additional information please contact us below.



(800) 231-5777

6801 Biotics Research Drive • Rosenberg, TX 77471
biotics@bioticsresearch.com
www.bioticscan.com

These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.

Gastrazyme™

Nutritional Support for the Gastrointestinal Tract

Although digestion begins in the mouth, the gastrointestinal tract is an important component of digestion. From a nutritional viewpoint the gastrointestinal tract is considered one of the most important organs in the body. Maintaining a health digestive tract is considered premier in optimal health, as poor digestion can cause a multitude of seemingly unrelated problems. Nutritional health and gastrointestinal health are thus closely correlated. **Gastrazyme™** combines a number of nutritional components intended to sustain a healthy digestive tract, including:

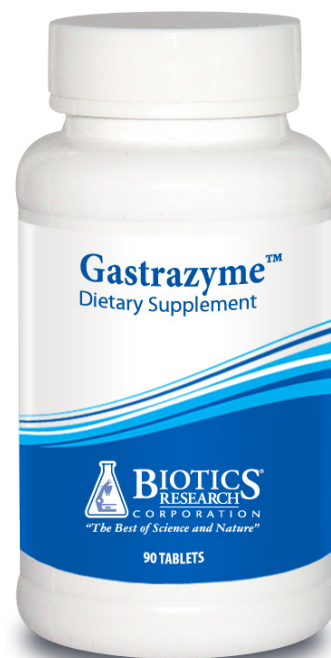
Methionine S-Methyl Sulfonium

Early studies have recognized the effectiveness of raw cabbage juice in normalizing gastric and intestinal function. Glutamine and methionine derivatives present in this juice are believed to be the active principles. Specific attention has focused on methionine S-methyl sulfonium (MMS) in the chlorinated form. MMS occurs in a variety of fruits and vegetables, such as cabbage. Traditionally, this compound has been designated "Vitamin U", although it does not meet the classic definition of a vitamin. MMS is readily absorbed and accumulates in the body, especially in the kidney and liver.⁽¹⁾ A variety of sulfur-containing agents, including MMS have documented benefits, including stimulation of the formation of gastrointestinal mucus, and the binding of free radicals. They may also serve as antioxidants, and act as methyl donors for a variety of acceptors. One study indicated that little damage to rats pretreated with MMS by gavage occurred following exposure to reserpine.^(2,3) Similar results were obtained using MMS up to forty hours after ethanol exposure in lab animals.⁽⁴⁾ Other research has shown that oral administration of MMS or cysteine aided in normalizing gut function in certain patients.⁽⁵⁾ An additional study concluded that MMS supported the normal healing process of the stomach following exposure to nonsteroidal anti-inflammatory agents (NSAIDs).⁽⁶⁾ It is not surprising then, that such versatile compounds can benefit gastrointestinal health.

Vitamin A is required for the normal differentiation and development of epithelial cells, as well as for epithelial cell integrity. Because the

gastrointestinal mucosa is rapidly overturning, its nutrient requirement is relatively high. Vitamin A deficiency has been shown to result in a reduction of cell division and differentiation of the intestinal cells, and consequentially a decline in the number of goblet cells⁽⁷⁾ in the crypt and villus.⁽⁸⁾ Inadequate vitamin A status has also been correlated with impaired barrier function of the GI tract,⁽⁹⁾ as well as immune system impairment⁽¹⁰⁾ Other studies have determined that the prevalence and severity of diarrhea diseases are particularly reduced with vitamin A supplementation⁽¹¹⁾, and that supplementation with vitamin A significantly reduced the prevalence of gastrointestinal distress, including diarrhea and loose stools.⁽¹²⁾

Natural Carotenoids, including betacarotenes, gamma carotenes, zeaxanthin, lutein and cryptoxanthin, are common dietary constituents, notably concentrated in orange and dark green, leafy vegetables. They complement vitamin E as lipid-soluble antioxidants, and indisputably are more effective scavenger of singlet oxygen than alpha tocopherol. In addition to serving as antioxidants, carotenoids are known to support healthy immune function.⁽¹³⁾ Beta-carotene also supports intercellular communication, and accordingly tissue integrity.⁽¹⁴⁾ Natural mixed carotenoids have been reported to be better assimilated and have demonstrated a greater effective lipophilic antioxidant activity *in vivo* than synthetic beta-carotene.⁽¹⁵⁾ Mixed carotenoids have also been shown to exhibit better biological activity than beta-carotene alone.⁽¹⁶⁾ Additionally, long-term supplementation (12 weeks) with mixed carotenoids was shown to ameliorate UV damage, resulting in erythema in humans.⁽¹⁷⁾



(800) 231-5777

6801 Biotics Research Drive • Rosenberg, TX 77471
biotics@bioticsresearch.com
www.bioticscan.com

These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.

Gamma Oryzanol, a phytosterol ferulate mixture extracted from rice bran oil, contains ferulic acid, which has documented evidence as a strong antioxidant. Ferulic acid has shown marked antioxidant properties when utilized in *in vitro* assays, as evidenced by autooxidation of methyl linoleate (MeLo) and ascorbate/Fe(2+)-mediated lipid peroxidation in rat microsomes.⁽¹⁸⁾ In the evaluation of gamma oryzanol via an oxidation accelerate test, gamma-oryzanol was found to be an organic radical scavenger, with the ability to prevent AMVN-triggered lipoperoxidation, resulting in improved oxidative stability of oils very prone to lipoperoxidation.⁽¹⁹⁾ Gamma oryzanol has also been shown to normalize intestinal function in rats subjected to reserpine or physical stress⁽²⁰⁾ as well as in mice subjected to sleep deprivation.⁽²¹⁾

Chlorophyllin, a derivative of chlorophyll, has the ability to bind divalent metal ions. Research studies in humans have indicated that DNA damage by aflatoxin can be decreased by as much as 55% through chlorophyllin supplementation.⁽²²⁾ A separate study indicated that chlorophyll was able to protect DNA against damage from heterocyclic amines *in vitro*.⁽²³⁾ Chlorophyllins have also demonstrated antioxidant properties.⁽²⁴⁾

References

- Gessler NN; Bezzubov AA. S-methyl methionine (vit U) pharma cokinetics in rats and man. *Farmakol Toksikol* 1987; 50: 49-51.
- Salim AS. Role of oxygen-derived free radicals in mechanism of acute and chronic duodenal ulceration in the rat. *Dig Dis Sci* 1990; 35: 73-79.
- Salim AS. Administration of sulfhydryls to stimulate the healing of ischemia- induced acute gastric mucosal injury in the rat. *J Pharm Sci* 1991; 80: 539-541.
- Salim AS. Role of sulfhydryl-containing agents in the healing of erosive gastritis and chronic gastric ulceration in the rat. *J Pharm Sci* 1992; 81: 70-73.
- Salim AS. Sulfhydryl-containing agents stimulate the healing of duodenal ulceration in man. *Pharmacology* 1992; 45: 170-180.
- Salim AS. Sulfhydryl-containing agents in the treatment of gastric bleeding induced by nonsteroidal anti-inflammatory drugs. *Can J Surg* 1993; 36 (1): 53-58.
- Rojanapo W, Lamb AJ, Olson JA. The prevalence, metabolism and migration of goblet cells in rat intestine following the induction of rapid, synchronous vitamin A deficiency. *J Nutr* 1980; 110:178-88.[Medline]
- Warden RA, Strazzari MH, Dunkley PR, O'Loughlin EV. Vitamin A-deficient rats have only mild changes in jejunal structure and function. *J Nutr* 1996; 126:1817-26.[Medline]
- Thurnham DI, Northrop-Clewes CA, McCullough FS, Das BS, Lunn PG. Innate immunity, gut integrity, and vitamin A in Gambian and Indian infants. *J Infect Dis* 2000; 182(suppl):523-8.[Medline]
- Ross AC, Stephensen CB. Vitamin A and retinoids in antiviral responses. *FASEB J* 1996; 10:979-985.
- Duggan, C, Gannon, J and Walker, WA. Protective nutrients and functional foods for the gastrointestinal tract. *Am J Clin Nutr.* 2002 May; 75(5):789-808
- Barreto M, Santos L, Assis A, et al. Effect of vitamin A supplementation on diarrhea and acute lower respiratory tract infections in young children in Brazil. *Lancet* 1994; 344:228-31 [Medline]
- Jyonouvi H et al. Immuno-stimulating actions of carotenoids: enhancement of *in vitro* and *in vivo*. antibody production to T-dependent antigens. *Nutr Cancer* 1994; 21:47-58.

- Zhang LX, et al Carotenoids up-regulate connexin 43 gene expression dependent of their provitamin A or antioxidant properties. *Cancer Res* 1992; 52:5707-5712.
- Ben-Amotz A, Levy Y. Bioavailability of a natural isomer mixture compared with synthetic all-trans beta-carotene in human serum. *Am J Clin Nutr.* 1996 May; 63(5):729-34.
- Murthy, KN, Rajesha, J, Swamy, MM, Ravishankar, GA. Comparative evaluation of hepatoprotective activity of carotenoids of microalgae. *J Med Food.* 2005 Winter; 8(4):523-8.
- Heinrich, U, Gartner, C, Wiebush, M, Wichler, O, Sies, H, Tronnier, H, Stahl, W. Supplementation with beta-carotene or a similar amount of mixed carotenoids protects humans from UV-induced erythema. *J Nutr.* 2003 Jan; 133(1):98-101.
- Germano MP, D'Angelo V, Biasini T, Sanogo R, De Pasquale R, Catania S. *J Ethnopharmacol.* 2006 Jan 18; [Epub ahead of print] Evaluation of the antioxidant properties and bioavailability of free and bound phenolic acids from *Trichilia emetica* Vahl.
- Juliano C, Cossu M, Alamanni MC, Piu L. Antioxidant activity of gamma oryzanol: mechanism of action and its effect on oxidative stability of pharmaceutical oils. *Int J Pharm.* 2005 Aug 11; 299(1-2):146-54.
- Itaya K, et al. Studies on gamma oryzanol (2) the anti-ulcerogenic action. *Nippon Yuakurigaku Zasshu* 1976; 72:1001-1011.
- Ichimaru Y, Moriyama M, Ichimaru M, Gomita Y. Effects of gamma-oryzanol on gastric lesions and small intestinal propulsive activity in mice. *Nippon Yakurigaku Zasshi.* 1984 Dec; 84(6):537-42. Japanese.
- Barrett JR. Cancer. Plants provide prevention. *Environ Health Perspect.* 2002 Apr; 110(4):A180.
- Dashwood R, Guo D. Protective properties of chlorophylls against the covalent binding of heterocyclic amines to DNA *in vitro* and *in vivo*. *Princess Takamatsu Symp.* 1995; 23:181-9.
- Ong TM, Whong WZ, Stewart J, Brockman HE. Chlorophyllin: a potent antimutagen against environmental and dietary complex mixtures. *Mutat Res.* 1986 Feb; 173(2):111-5.

Supplement Facts

Serving Size: 1 Tablet

	Amount Per Serving	% Daily Value
Vitamin A (as natural mixed carotenoids and palmitate) (IU ratio 2.5:1)	3,500 IU	70%
Gamma Oryzanol (from rice)	100 mg	*
Chlorophyllins (from Mulberry leaf)	20 mg	*
Vitamin U Complex (DL-methylmethionine sulfonium chloride)	10 mg	*
Superoxide Dismutase (from vegetable culture †)	15 mcg	*
Catalase (from vegetable culture †)	15 mcg	*

* Daily Value not established

Other ingredients: Cellulose, modified cellulose gum, modified cellulose, silica and magnesium stearate (vegetable source).

† Specially grown, biologically active vegetable culture containing naturally associated phytochemicals including polyphenolic compounds with SOD and catalase, dehydrated at low temperature to preserve associated enzyme factors.

This product is gluten and dairy free.

RECOMMENDATION: One (1) tablet three (3) times each day as a dietary supplement or as otherwise directed by a healthcare professional.

KEEP OUT OF REACH OF CHILDREN

Store in a cool, dry area.
Sealed with an imprinted safety seal for your protection.

Product # 1140 Rev. 05/16

To place your order for **Gastrazyme™** or for additional information please contact us below.



(800) 231-5777

6801 Biotics Research Drive • Rosenberg, TX 77471
 biotics@bioticsresearch.com
 www.bioticscan.com

These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.

Hydro-Zyme™ & HCl-Plus™

Nutritional Support for Digestion

The stomach produces a variety of substances that promote digestion and assimilation. Gastric juice contains hydrochloric acid and pepsinogens, precursors of the family of proteolytic enzymes called pepsins. Parietal cells produce both stomach acid and intrinsic factor, a protein required to bind vitamin B₁₂, prior to its absorption by the small intestine. The secretion of H⁺ by parietal cells requires an ATPase (H⁺, K⁺) to pump H⁺ out of the cell. Chloride ion is exported separately, so that the resulting product is HCl. The pump is activated by histamine stimulation of a cell surface receptor involving cyclic AMP. Drugs such as Omeprazole act by inhibiting this enzyme.

Hydrochloric acid is a strong mineral acid which functions to maintain gastric pH between 1.5 to 2.5. Acidity serves three important roles; low pH kills microorganisms in food, it activates pepsinogen, and it unfolds (denatures) proteins, making them more accessible to proteolytic degradation. The gastric lining is protected from the strong acidic environment by a thick layer of mucus.

The incidence of low stomach acid (hypochlorhydria) increases with age. Atrophic gastritis occurs in 20% to 30% of healthy, elderly, individuals, and is the most common cause of reduced gastric acid production⁽¹⁾. An estimated 30-50% of people over the age of 60 are believed to produce inadequate stomach acid,⁽²⁾ although, only 16% hyposecretors in healthy elderly people has been reported⁽³⁾. In extreme cases, the stomach does not produce acid (achlorhydria) and gastric pH approaches neutrality. Other causes of low gastric acid production include malnutrition and excessive use of antacids and H₂ receptor antagonists.

Inadequate stomach acid is linked to maldigestion. This can promote inadequate mineral uptake, due to malabsorption of iron, calcium, zinc and others,⁽²⁾ and increased risk of intestinal infections due to *Candida albicans* and parasites^(1,4). In diabetics, the prevalence of achlorhydria, together with related anemia due to vitamin B₁₂ malabsorption, has been estimated to range from 12 to 41%⁽⁵⁾. Achlorhydria and hypochlorhydria have been linked to peptic ulcer disease and to *Helicobacter pylori* overgrowth⁽⁶⁾. Hypochlorhydria can also cause an increased bacterial colonization of the small intestine. (In addition to gastric acid, other factors that limit bacterial colonization include normal bile flow and peristalsis.) It has also been suggested that gastric acid acts as an antitumor defense, and that achlorhydria predisposes patients to gastric cancer⁽⁷⁾.

Nutrients that Support the Formation of Gastric Acid

Betaine HCl and Glutamic Acid HCl. Betaine is trimethylglycine, a normal metabolite and a methyl donor. In the protonated form, betaine HCl gives up a proton and chloride ion in aqueous solutions, that is, hydrochloric acid.

Therefore, betaine hydrochloride represents a dietary source of hydrochloric acid⁽²⁾. (When protonated with HCl, glutamic acid yields hydrochloric acid in aqueous solutions.) Like betaine HCl, glutamic acid HCl represents a supplemental form of gastric acid.

Ammonium Chloride. Gastric cells require chloride as the raw material for hydrochloric acid production. Excreted chloride ion is reabsorbed by the intestine after a meal, causing a temporary, postprandial rise in serum chloride levels. Chloride represents a major anion electrolyte required to maintain optimal pH, and to maintain osmotic balance in the body.

Vitamin B₆. The absorption of pyridoxal phosphate is positively influenced by gastric acid secretion⁽⁸⁾. Vitamin B₆ deficiency is linked to deficiencies of trace minerals.

Pancreatin is a commercial preparation of porcine pancreas, highly enriched in pancreatic enzymes, including trypsin, chymotrypsin, carboxypeptidase, as well as amylase (starch digestion) and lipase (fat digestion). Porcine pancreatin contains these enzymes in a ratio similar to human pancreas, and the digestive enzymes of human and porcine pancreas possess similar properties. Pancreatic enzymes can be denatured by exposure to gastric acid, therefore, the pancreatin in **Hydro-Zyme™** is coated to preserve activity during transit through the gastrointestinal tract⁽⁹⁾.

A note on pancreatin activity measurement; measurement of proteolytic activity of pancreatin has been defined by the U.S. Pharmacopoeia, based upon the digestion of a standard protein, casein. Pancreatin 4X possesses 4 times the activity of pancreatin 1X (25 USP units of proteolytic activity per milligram). Therefore, 10 mg of pancreatin 4X per tablet of **Hydro-Zyme™** provides 1,000 USP units.

Proteolytic Enzymes in Digestion

A wide assortment of proteolytic enzymes (proteases) is required to degrade proteins to amino acids and peptides. They are manufactured in cells as inactive precursors called zymogens, which must be activated after they have been released into the intestinal lumen. Ingested proteins first encounter proteolytic enzymes of the stomach. Pepsin refers to a closely related group of proteases produced by the gastric mucosa. The zymogen and pepsinogen, is activated both by HCl and by autocatalytic action. This enzyme exhibits maximal activity at low pH (high gastric acid). Upon leaving the stomach, chyme, (food particles mixed with gastric juice) is



(800) 231-5777

6801 Biotics Research Drive • Rosenberg, TX 77471
biotics@bioticsresearch.com
www.bioticscan.com

These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.

neutralized in the intestine by bicarbonate secreted by the pancreas. (The presence of acidic chyme in the duodenum triggers pancreatic secretion.) Thus, hypochlorhydria may be associated with secondary pancreatic insufficiency. After neutralization, chyme is subjected to a battery of powerful pancreatic enzymes. The exocrine pancreas produces potent proteolytic enzyme peptidases, such as trypsin and alpha chymotrypsin, as their zymogens form, trypsinogen and chymotrypsinogen, respectively. Trypsin possesses a very high degree of peptide bond specificity in cleaving bonds adjacent to arginine and lysine. Chymotrypsin has a different substrate specificity; it cleaves peptide bonds adjacent to large, non-polar amino acids, such as aromatic amino acids and methionine. Other pancreatic proteases include elastase, which break down connective tissue. Activation of pancreatic zymogens begins in the intestine to prevent their premature activation, which could damage the pancreas. Trypsin activates most of the zymogens released into the intestine. Trypsin itself is first activated from trypsinogen by the enteric enzyme, enteropeptidase.

Pancreatic exopeptidases are represented by carboxypeptidases, which cleave amino acids from the carboxyl terminus of peptides. Carboxy-peptidases are derived from the zymogens, procarboxypeptidase A and B. Additional peptidases which serve to degrade peptides, are produced by the intestinal mucosa. For example, aminopeptidases cleave off amino acids from the N terminus of peptides.

Pancreatic secretions contain a variety of other digestive enzymes, in addition to proteases. Amylase cleaves the 2 (1-4) glycoside linkages of amylose to yield maltose molecules. These di- and tri-saccharides are hydrolyzed to glucose at the intestinal brush border. Lipase hydrolyzes triglycerides to free fatty acids and monoglycerides, in the presence of a helper polypeptide called colipase, and bile salts, which serve to emulsify digested fats.

Betaine HCl and glutamic acid HCl supplements should not be chewed. They should be taken with meals. Such supplements may be inappropriate when there are ulcerative gastrointestinal conditions and when aspirin or other analgesics are being used.

References

1. Saltzman, JR *et al.* Bacterial overgrowth without clinical malabsorption in elderly hypochlorhydric subjects. *Gastroenterology* 1994; 106: 615-623.
2. Wright, Jonathan V., Dr. Wright's Guide to Healing with Nutrition. *Keats* 1990; pp 30-50.
3. Hurwitz, A *et al.* Gastric acidity in older adults. *JAMA* 1997; 278: 9-662.
4. Giannella, RN *et al.* Influence of gastric acidity on bacterial and parasitic infections. *Annals Int Med* 1973; 78: 271-276.
5. Rabinowitch IM. Achlorhydria and its clinical significance in diabetes. *Am J Dig Dis* 1949; 16: 322-333.
6. Berstad K, Berstad A. *Helicobacter pylori* infection in peptic ulcer disease. *Scan J Gastroenterol* 1993; 28: 561-567.
7. Seery JP. Achlorhydria and gastric carcinogenesis. *Lancet* 1991; 338: 1508-1509.
8. Middleton HM. Intestinal hydrolysis of pyridoxal 5-phosphate *in vitro* and *in vivo* in the rat.
9. Guarner, I *et al.* Fate of oral enzymes in pancreatic insufficiency. *Gut* 1993; 34: 708-712.

To place your order for **Hydro-Zyme™** and **HCl-Plus™** or for additional information please contact us below.

Hydro-Zyme™ is available in 90-count (#1262) and 250-count (#1263) bottles.

Supplement Facts

Serving Size: 1 Tablet

	Amount Per Serving	% Daily Value
Vitamin B6 (as pyridoxine hydrochloride)	2 mg	100%
Betaine Hydrochloride	150 mg	*
Glutamic acid (as L-Glutamic acid hydrochloride)	50 mg	*
Ammonium Chloride	35 mg	*
Pancreatin 4X (porcine)	10 mg	*
Pepsin (1:10,000)	10 mg	*

* Daily Value not established

Other ingredients: Vegetable culture †, cellulose, stearic acid (vegetable source), modified cellulose gum, silica and food glaze.

† Specially grown, biologically active vegetable culture (from organic *Pisum sativum*, *Lens esculenta* and/or *Cicer arietinum*) containing naturally associated phytochemicals including polyphenolic compounds with SOD and catalase, dehydrated at low temperature to preserve associated enzyme factors.

This product is gluten and dairy free.

RECOMMENDATION: One (1) tablet with each meal as a dietary supplement or as otherwise directed by a healthcare professional.

KEEP OUT OF REACH OF CHILDREN

Store in a cool, dry area.
Sealed with an imprinted safety seal for your protection.

Product # 1262 Rev. 07/15

HCl-Plus™ is available in 90-count (#1230) bottles.

Supplement Facts

Serving Size: 1 Tablet

	Amount Per Serving	% Daily Value
Vitamin B6 (as pyridoxine hydrochloride)	2 mg	100%
Betaine (as betaine hydrochloride)	115 mg	*
Glutamic Acid (as L-Glutamic acid hydrochloride)	50 mg	*
Ammonium Chloride	35 mg	*
Pepsin (1:10,000)	10 mg	*

* Daily Value not established

Other ingredients: Vegetable culture †, cellulose, stearic acid (vegetable source), modified cellulose gum, and silica.

† Specially grown, biologically active vegetable culture containing naturally associated and/or organically bound phytochemicals including polyphenolic compounds with SOD and catalase, dehydrated at low temperature to preserve associated enzyme factors.

This product is gluten and dairy free.

RECOMMENDATION: One (1) tablet with each meal as a dietary supplement or as otherwise directed by a healthcare professional.

KEEP OUT OF REACH OF CHILDREN

Store in a cool, dry area.
Sealed with an imprinted safety seal for your protection.

Product # 1230 Rev. 09/14



(800) 231-5777

6801 Biotics Research Drive • Rosenberg, TX 77471
 biotics@bioticsresearch.com
 www.bioticscan.com

These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.