An Investigation into Reversing Metabolic Syndrome with an Integrated Nutrition Protocol

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Metabolic syndrome is a growing concern as modern populations become more sedentary, more obese, and more reliant on processed foods that are typically lacking in valuable nutrients and often contain known toxins. The objective of this study was to determine the impact on metabolic syndrome of an integrated nutrition protocol, which was developed and has been successfully used to treat many chronic diseases at Pioneer Integrative Medical Clinic in Draper, Utah. The protocol included a diet emphasizing reduction of dietary sugar and five supplements rich in protein, antioxidants, omega-3 fatty acids, cellular detoxifiers, probiotics, and digestive enzymes. Four patients ranging in age from 47-66 years old participated in the 12-week study. All patients showed improvements in at least 4 of 5 factors used to diagnose metabolic syndrome. Results are preliminary yet encouraging, with patients showing greatly improved insulin sensitivity and reductions in triglyceride levels. Biomarker tests revealed improvements in HDL (good) cholesterol levels and reductions in blood pressure readings. Patients also reported enhanced energy, reduced joint pain, and significant weight loss (on average, waist circumference was reduced by 3.3 inches).

INTRODUCTION
ASSESSING METABOLIC SYNDROME

More than 100 million Americans suffer from metabolic syndrome. Sedentary, high-stress lifestyles coupled with poor diets of high-glycemic, low-fiber, and low-nutrient foods has contributed to a metabolic syndrome health crisis that is only worsening. Metabolic syndrome is defined as the presence of any three of the following five conditions (Grundy SM, et al., 2005):

- *Waist measurement* of 40 inches or more for men and 35 inches or more for women
- *Triglyceride levels* of 150 milligrams per deciliter (mg/dL) or above, or taking medication for elevated triglyceride levels
- *HDL ("good") cholesterol levels* below 40 mg/dL for men and below 50 mg/dL for women, or taking medication for low HDL levels
- *Blood pressure levels* of 130/85 or above, or taking medication for elevated blood pressure levels

- *Fasting blood glucose levels* of 100 mg/dL or above, or taking medication for elevated blood glucose levels

TOXINS MAY CONTRIBUTE TO METABOLIC SYNDROME & INSULIN RESISTANCE

Insulin resistance is a strong indicator of metabolic syndrome. Dietary interventions alone, while helpful, have proven to be incomplete to address insulin resistance, with studies correlating metabolic syndrome and insulin resistance with higher levels of toxins stored in the body. Most environmental toxins are fat-soluble, and therefore, can often get "stuck" in adipocytes, or fat cells. Increased adipocyte mass, as seen in metabolic syndrome, can then act as an endocrine organ, communicating with other tissues by producing large amounts of inflammatory cytokines within the body (Potenza and Mechanick 2009).

Many patients, even without consuming excess calories, may develop insulin resistance when toxins are present in the body (Hyman, 2010). This is because toxins interfere with glucose and cholesterol metabolism (Jones, Maguire & Griffin, 2008). Toxins can similarly contribute to obesity and other metabolic conditions by increasing inflammation, oxidative stress, and mitochondrial injury and also by altering thyroid metabolism and impairing central appetite regulation (Hyman, 2007).

Based on current environmental medicine research, our hypothesis was that along with dietary and nutritional changes, addressing cellular toxicity is a critical component of reversing metabolic syndrome and restoring insulin sensitivity.

While most clinical research is targeted at evaluating single variables, much the way a new pharmaceutical or surgical intervention would be tested, our approach was to create an integrated nutritional protocol that would simplify the treatment of metabolic syndrome and increase patient compliance.

ADDRESSING CELLULAR DYSFUNCTION SYSTEMATICALLY

Because people with metabolic syndrome suffer a wide variety of health issues and because many physicians find metabolic syndrome difficult to treat, metabolic syndrome is often managed palliatively by relieving the most distressing symptoms patients have.

The integrated nutritional protocol tested in this study was designed to address the following factors in cellular dysfunction:

1. *Toxicity* – toxins interfere with cellular communication and toxins can also damage cellular DNA
2. *Oxidation* – oxidative stress damages all parts of a cell and turns valuable nutrients into harmful waste within cells
3. *Inflammation* – inflammation leads to damaged cell membranes and interferes with cells' ability to coordinate body functions
4. *Less than optimal mitochondrial function* – weakened mitochondria cannot fuel proper function within or between cells

MATERIALS AND METHODS

NUTRITIONAL PROTOCOL

Our Health Co-op sponsored the clinical study to evaluate the health benefits of five of its nutritional supplements (in use at Pioneer Integrative Medical Clinic for 2 years before the study commenced): Constant Health, Soothing Greens, Probiotics 16, Fish Oil, and Pancreatic Enzymes products.

Patients were also asked to follow a special dietary protocol. The first two weeks allowed only lean meats, vegetables, and nuts. Patients were then allowed to introduce fruits during weeks three and four; legumes during weeks five and six; and grains during week seven. Patients were asked to refrain from sugar and dairy throughout those seven weeks and to reintroduce them sparingly.

THE STUDY PROCESS

Participants were selected at Pioneer Integrative Medicine Clinic. The study included four patients, both male and female, with ages ranging from 47-66 years old. This was a voluntary pilot study, and all participants signed a consent form prior to beginning the study. Study participants included pre-diabetic patients with a variety of health problems including high blood pressure, hyperinsulinemia, low HDL levels, high triglycerides, obesity, hypothyroidism, colitis, irritable bowel syndrome, and depression. All participants met the criteria for "metabolic syndrome," as defined above. Participants received complete blood chemistry panels at the beginning and end of the 12-week study. They also received complementary nutritional supplements used in the study.

All clinical evaluations were performed at Pioneer Integrative Medicine Clinic. All patients were evaluated by Pioneer Integrative Medicine personnel prior to initiation of the study to determine if the study protocol would have any possible negative interactions with current medicinal treatments. Participants continued the use of all medications deemed necessary by their doctor during the study period.

The study included an initial clinical exam including a subjective and objective evaluation of health. Lab tests were performed as part of the initial and final exam to evaluate the biomarkers of health listed in Table 1 below.

Table 1 - Biomarkers of Health		
Blood Sugar	Lipid Panel	
Insulin	Serum cholesterol	C-reactive protein
Plasma glucose	HDL	Hemoglobin A1C
Fasting glucose	LDL	
2-Hour glucose tolerance	Serum triglycerides	

The study consisted of a 12-week period where patients were instructed to use Constant Health, Soothing Greens, Probiotics 16, Pancreatic Enzymes 4X, and Fish Oil daily. Study participants were encouraged to use each supplement as directed on product labels.

In addition to pre- and post-study evaluations, there was an additional clinical exam at 6 weeks to monitor the patient's progress and assess any possible side effects or concerns the patients may have experienced as a result of the treatment program. All study patients had their blood pressure monitored in each of the 3 clinical visits.

Weekly phone calls were conducted to follow the progress of patients, monitor compliance of the study protocol and answer any questions. During these phone conversations, general perceptions of health and well-being were monitored in the study patients.

RESULTS

Patients showed decreased levels of serum triglycerides, insulin, blood sugar fluctuations, and waist circumference. Patients also showed increased HDL cholesterol levels. All markers indicate increased insulin sensitivity, improved blood sugar metabolism, and better overall health. In the early weeks of the study, some patients reported intestinal discomfort due to the protocol's increase in their fiber intake. This discomfort was present for only the first few weeks and resolved completely in all four patients. At the end of the study, patients reported more energy, weight loss, less joint pain, better intestinal function, and overall better health.

All patients experienced improvement in at least 4/5 factors used to diagnose metabolic syndrome.

On average, triglycerides decreased by over 100 points in each patient, bringing all but one patient significantly under the 150 mg/dL mark. Hemoglobin A1C, used to determine blood sugar control, decreased by a median of 0.2, bringing all but one patient under the 6.0 diabetic indicator mark. This patient did however have the most significant drop of 2.1.

Likewise, fasting glucose levels all dropped below 100 mg/dL, bringing all patients within the normal fasting glucose range. Waist circumference dropped by an average of 3.3 inches, with one patient reporting a 40 lb. weight loss. HDL levels increased on average by 6.6 points.

Some patients experienced slightly elevated overall cholesterol health markers given the increased focus on protein and allowance of high animal protein intake during the 12-week study. The philosophy underlying this part of the protocol was an emphasis on lowering sugar intake in ways that were most manageable for patients and would yield the earliest positive results and experience of improved health. At the end of the protocol, patients were encouraged to begin reducing animal protein consumption at a time when they would not have to manage intense sugar cravings at the same time.

DISCUSSION

Dietary interventions can be more efficacious than medications for reducing the incidence of metabolic syndrome (Potenza and Mechanick 2009). With this knowledge, a clinical nutritional protocol was instituted in this study to target some of the major associated areas of dysfunction occurring in cases of metabolic syndrome.

Chronic inflammation within the body has been associated with the development or progression of almost all chronic diseases, including metabolic syndrome and associated cardiovascular disorders. Furthermore, obesity has been shown to elevate C-reactive protein (CRP) levels, a protein that rises in response to systemic inflammation (Basu et al 2006). Anti-inflammatory foods and dietary supplements have been shown to reduce inflammation in the body, and therefore, play a role in preventing many disease processes. The nutritional protocol implemented in this study is rich in nutrients and cofactors that may help reduce the overall inflammatory burden. EPA and DHA, omega-3 fatty acids found in fish oil, are well known anti-inflammatory agents. These fatty acids compete with the more pro-inflammatory omega-6 fatty acids for incorporation into cell membranes. When humans ingest fish or fish oil, the EPA and DHA can lead to a significant decrease in inflammatory markers such as

interleukin-1 (IL-1), interleukin-2 (IL-2), tumor necrosis factor-alpha (TNF-α) and cyclooxygenase-2 (COX-2) (Simopoulos 2002; Giugliano et al 2006).

Metabolic syndrome has also been found to be a "predictor" of coronary heart disease and cardiovascular risk (Carpentier et al 2006). Omega-3 fatty acids decrease platelet aggregation and vasoconstriction, indicating their potential cardioprotective role. Finally, the omega-3 fatty acids in fish oil have been investigated for their role in preventing and/or diminishing insulin resistance (Carpentier et al 2006).

The recommended nutritional protocol also contains potent anti-inflammatory herbs, including turmeric and boswellia. Turmeric, as well as boswellia, have been used traditionally for centuries and are both known to reduce the expression of several markers of inflammation (Aggarwal et al 2007; Ammon 2006).

Low fiber diets are known to increase the risk of metabolic syndrome, and it is thought that fiber can improve insulin sensitivity by blunting postprandial glycemic and insulin responses (Otsuka et al 2010). Epidemiological evidence strongly suggests that a higher amount of fiber in the diet is associated with lower body weight and body mass index (BMI) (Howarth et al 2001). Furthermore, diets high in protein can increase satiety, decrease food intake, and may promote body weight maintenance after weight loss (Westerterp-Plantenga et al 2009). The effect of protein on these metabolic targets could promote weight loss and, therefore, benefit patients with metabolic syndrome.

Additional nutrients contained in the nutritional protocol, such as chromium, biotin and vanadium, have also been found to counteract important underlying problems associated with metabolic syndrome. Recent trials have indicated that a combination of chromium and biotin in individuals with blood sugar dysregulation can significantly decrease fasting blood sugar levels, improve glucose management and enhance lipid metabolism (Albarracin et al 2008; Singer and Geohas 2006). Similarly, the trace element vanadium appears to enhance the insulin-signaling pathway in liver and muscle tissue in humans (Srivastava and Mehdi 2005).

Probiotics are dietary supplements that contain viable microorganisms to reintroduce beneficial bacteria to the gastrointestinal tract. The principal effect of probiotics is to enrich the gut microflora. However, probiotics are also known to enhance gut barrier function, have antimicrobial effects, and provide metabolic activities that result in the salvage of energy and absorbable nutrients (Guarner and Malagelada 2003). It is due to this last mechanism that recent research has focused on the role of gut flora in obesity. There is now evidence that gut

dysbiosis (or microbial imbalances) can affect host metabolism and energy storage. Furthermore, development of obesity and type 2 diabetes (glucose dysregulation) is characterized by specific changes in the gastrointestinal tract's bacterial populations, specifically markedly reduced *Bifidobacterium* species (Cani and Delzenne 2009). It has further been suggested that metabolic disorders such as metabolic syndrome may be linked to microbiota-associated changes and low-grade chronic inflammation (Cani and Delzenne 2009; Tilg 2010).

Additional nutrients within the current studied nutritional protocol include digestive enzymes and the amino acid glutamine. Dietary enzymes are used to promote good digestion and enhance nutrient absorption. Improperly digested foods may contribute to gastrointestinal inflammation and promote the growth of dysbiotic intestinal flora. Glutamine provides fuel for the healthy function of enterocytes and may contribute to an enhancement of overall digestive function. Antioxidant nutrients and phytochemicals provided within the nutritional protocol also target the overall inflammatory process by counteracting the effects of free radicals and oxidative stress on the gastrointestinal tract and systemically.

Given the overall evidence suggesting a multitude of benefits of the various nutrients and cofactors contained within the nutritional protocol, it was not surprising that benefits were evident in patients with metabolic syndrome in the present study. While there are certain limitations of the study, including its small patient population, the benefits seen from an integrated nutritional approach to metabolic syndrome are exciting. Interestingly, recent clinical studies are concluding that metabolic syndrome, a clinical state defined by three or more clinical "syndromes", is best treated by a more comprehensive protocol including dietary changes and therapeutic interventions (Carpentier et al 2006). This study proposes such a protocol that may prove to be effective when investigated in a larger patient population.

CONCLUSION

While further research is recommended, these initial findings are promising. The nutritional supplement protocol including Constant Health does appear to support the ability to restore insulin sensitivity and metabolic function, reduce weight, and promote overall improved health and well-being.

APPENDIX A - PRODUCTS USED IN INTEGRATIVE NUTRITION PROTOCOL

Constant Health -- Constant Health, a nutritional drink mix with rice protein, served as the base formula for the study. Constant Health was designed to promote cellular detoxification and improve intestinal and immune system function. With more than 40 ingredients, the formula makes it easier for patients to: (1) boost protein intake, which is valuable for stabilizing blood sugar, and (2) ingest therapeutically-significant amounts of health-promoting detoxifiers, antioxidants, anti-inflammatory compounds, vitamins, minerals, and fiber.

Amino acids and phytonutrients in Constant Health are known to support the body's production of the body's most critical endogenous detoxifying protein, glutathione (Valério et al., 2009; Griffith, 1999) and help the liver and the colon eliminate toxins.

Curcumin, which has been used in Indian Ayurvedic medical therapies for thousands of years (Aggarwal, Suhr, & Shishoda, 2007), has been studied for its anti-inflammatory properties, reducing high blood pressure, and even limiting symptoms of depression (Kim et al., 2009; Epstien, 2008; Morimoto et al., 2008).

There are multiple sources of soluble and insoluble fiber in Constant Health which have been shown to have a variety of positive metabolic effects on weight, insulin sensitivity, and inflammatory response (Weickert & Pfeiffer, 2008). Fiber can lower cholesterol and improve insulin resistance, providing beneficial effects on metabolic syndrome. Soluble fiber, like that found in Constant Health is fermented into short-chain fatty acids (SCFAs) in the colon by gut bacteria. SCFAs are able to suppress both liver glucose and lipid production (Potenza and Mechanick 2009).

Soothing Greens -- Soothing Greens, a powdered formula, was added to boost intake of slippery elm, in particular, which has been studied for its value in helping rebuild the integrity of intestinal mucosa. The Soothing Greens formula also provides valuable phytonutrients, additional protein and fiber, and a source of spore-forming probiotics (Ganeden's BC30 strain was designed to survive gastric acids and support population of friendly bacteria in the intestines).

Repairing conditions of hyper-permeability in the intestines and bowels, which is commonly referred to as a "leaky gut." The gut is routinely exposed to a multitude of microorganisms, food allergens, and toxins; and the gut must be able to distinguish between nutritional and harmful elements (Vaarala, Atkinson, & Neu, 2008). Slippery elm in the formula has been studied for its ability to

promote a healthy gut barrier for better nutrient absorption and toxin elimination (Langmead, 2001).

Probiotics 16 – Probiotics 16, with 5 bifidobacterium strains and 11 lactobacillus strains, was designed to support intestinal and immune system health. It is a relatively new discovery that gut microflora may impact metabolic alterations and potentially obesity (Cani and Delzenne 2009). The amounts and ratios of certain microbial species are reduced in obese individuals, including several beneficial intestinal microbes such as *Bifidobacterium* species. It has also been reported that intestinal *Lactobacilli* species play a role in glucose regulation (Mikelsaar et al 2010).

Pancreatic Enzymes 4X – Pancreatic Enzymes 4X; with amylase, lipase, and protease; was designed to improve digestion of carbohydrates, fats, and proteins.

Fish Oil – Fish Oil offers omega 3 fatty acids, EPA and DHA. Fish oil is a well-known anti-inflammatory and has been studied for its role in lowering triglyceride levels as well as blood pressure. High dose fish oil can reduce inflammation and decrease triglycerides, both common in metabolic syndrome (Potenza and Mechanick 2009).

Table 2.1 below shows the directions given to patients for the study.

Table A.1 – Dietary Supplements & Directions for Use

Supplements	**Prescribed Amounts and Usage**
Constant Health (drink mix)	1 scoop – Once daily for first 4 weeks 1 scoop – Twice daily for final 8 weeks
Soothing Greens (drink mix)	1 scoop – Once daily for first 4 weeks
Probiotics 16	1 capsule – Twice daily for 12 weeks
Pancreatic Enzymes 4x	1 capsule – Three times daily with meals for 12 weeks
Fish Oil 1000mg	1 softgel – Three times daily for 12 weeks

APPENDIX B – SUPPLEMENT FACTS PANELS FOR PRODUCTS USED

Table B.1 - Constant Health Supplement Facts Panel

Supplement Facts

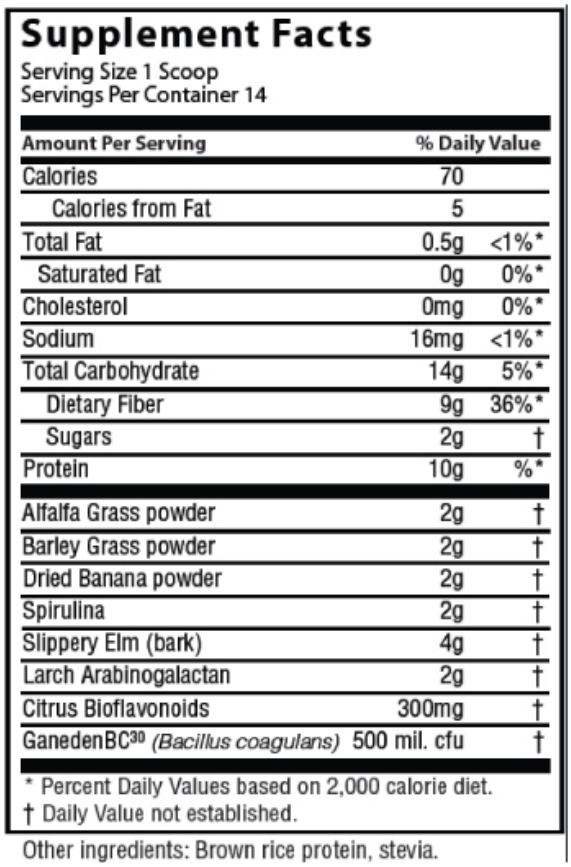
Serving Size 1 Scoop
Servings Per Container 28

Amount Per Serving		% Daily Value
Calories	140	
Calories from Fat	20	
Total Fat	2.5g	4%*
Saturated Fat	0.5g	1%*
Cholesterol	10mg	3%*
Sodium	30mg	1%*
Total Carbohydrate	11g	4%*
Dietary Fiber	5g	20%*
Sugars	4g	†
Protein	20g	40%
Vitamin A	2500IU	50%
Vitamin C	500mg	833%
Vitamin D3	500IU	125%
Vitamin E	50IU	167%
Vitamin K	20mcg	25%
Thiamine	5mg	333%
Riboflavin	5mg	294%
Niacin	10mg	50%
Vitamin B6	5mg	250%
Folate	200mcg	50%
Vitamin B12	500mcg	833%
Biotin	150mcg	50%
Pantothenic acid	5mg	50%
Calcium	150mg	15%
Phosphorus	100mg	10%
Iodine	75mcg	50%
Magnesium	150mg	38%
Zinc	7.5mg	50%
Selenium	35mcg	50%
Copper	1mg	50%
Manganese	1mg	50%
Chromium	200mcg	167%
Molybdenum	37.5mcg	50%
Potassium	200mg	6%
Apple Fiber	1000mg	†
Apple Pectin	250mg	†
Bioperine	10mg	†
Boron	0.75mg	†
Boswellia Serrata	250mg	†
Calcium d-Glucarate	150mg	†
Cellulose	500mg	†
Ginger Root Powder	50mg	†
Grapeseed Extract	100mg	†
Guar Gum	500mg	†
L-Glutamine	1000mg	†
L-Glycine	1000mg	†
Milk Thistle	150mg	†
N-Acetyl-Cysteine	150mg	†
Quercetin	250mg	†
Red Raspberry Seeds	500mg	†
Slippery Elm	250mg	†
Stevia	50mg	†
Turmeric	250mg	†
Vanadium	1.5mg	†

* Percent Daily Values are based on a 2,000 calorie diet.
† Daily Value not established.

Ingredients: Brown rice protein, natural vanilla flavoring, apple fiber, glycine, glutamine, guar gum, cellulose, xylitol, red raspberry seeds, calcium ascorbate, apple pectin, slippery elm bark, quercetin, curcumin, boswellia serrata, potassium phosphate, n-acetyl-cysteine, milk thistle seed, ascorbic acid, calcium carbonate, calcium d-glucarate, magnesium aspartate, grape seed extract, ginger root, stevia extract, mixed tocopherols (d-alpha tocopherols, plus d-beta, d-gamma, d-delta tocopherols), bioperine, niacin, zinc methionate, thiamine, riboflavin, pyridoxine, pantothenic acid, vanadyl sulfate, copper gluconate, manganese gluconate, vanadium sulfate, natural beta-carotene, boron, methylcobalamin, folate, chromiun polynicotinate, biotin, natural kelp, amino acid chelate, selenomethionine, vitamin K, cholecalciferol, silicon dioxide.

Table B.2 - Soothing Greens Supplement Facts Panel



Supplement Facts

Serving Size 1 Scoop
Servings Per Container 14

Amount Per Serving		% Daily Value
Calories	70	
Calories from Fat	5	
Total Fat	0.5g	<1%*
Saturated Fat	0g	0%*
Cholesterol	0mg	0%*
Sodium	16mg	<1%*
Total Carbohydrate	14g	5%*
Dietary Fiber	9g	36%*
Sugars	2g	†
Protein	10g	%*
Alfalfa Grass powder	2g	†
Barley Grass powder	2g	†
Dried Banana powder	2g	†
Spirulina	2g	†
Slippery Elm (bark)	4g	†
Larch Arabinogalactan	2g	†
Citrus Bioflavonoids	300mg	†
GanedenBC30 *(Bacillus coagulans)*	500 mil. cfu	†

* Percent Daily Values based on 2,000 calorie diet.
† Daily Value not established.

Other ingredients: Brown rice protein, stevia.

Table B.3 - Fish Oil 1000mg Supplement Facts Panel

Supplement Facts

Serving Size 1 Softgel
Servings Per Container 180

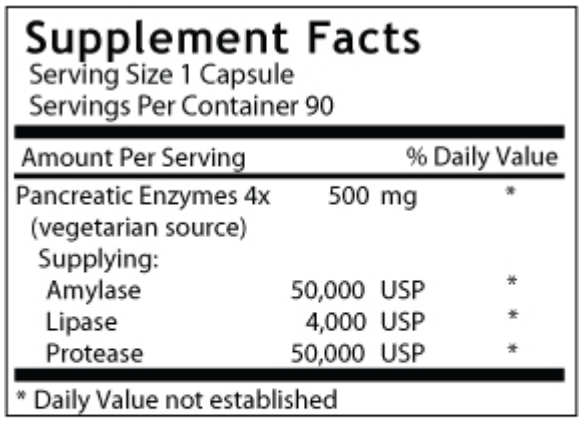
Amount Per Serving		% Daily Value
Calories	10	
Calories from Fat	10	
Total Fat	1g	2%*
Saturated Fat	0g	0%*
Polyunsaturated Fat	0g	0%*
Monounsaturated Fat	0g	0%*
Cholesterol	5mg	0%*
Fish Oil	1,000mg	**
EPA (Eicosapentaenoic Acid)		**
DHA (Docosahexaenoic Acid)		**
Omega-3	300mg	**

*Percent Daily Values based on a 2,000 calorie diet
** Daily Value not established

Other Ingredients: Gelatin, vegetable glycerin, mixed tocopherols.

This product contains fish (anchovy, mackerel, sardine) ingredients.

Table B.4 - Pancreatic Enzymes 4x Supplement Facts Panel



Supplement Facts

Serving Size 1 Capsule
Servings Per Container 90

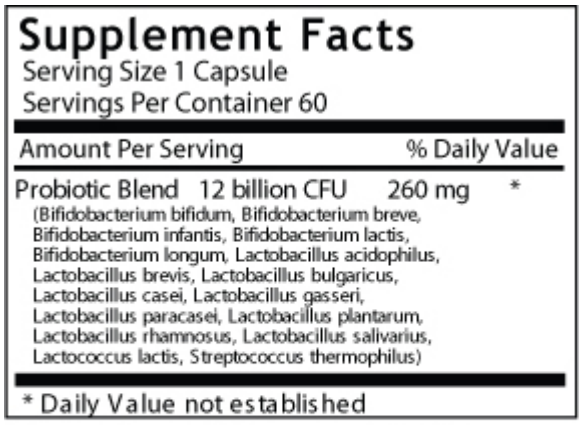
Amount Per Serving		% Daily Value
Pancreatic Enzymes 4x (vegetarian source)	500 mg	*
Supplying:		
Amylase	50,000 USP	*
Lipase	4,000 USP	*
Protease	50,000 USP	*

* Daily Value not established

Vegetarian source enzymes are equivalent in activity to 2000mg pancreatin USP.

Other ingredients: Hydroxypropyl methyl cellulose, microcrystalline cellolose, silica, magnesium stearate

Table B.5 - Probiotics 16 Supplement Facts Panel



Supplement Facts

Serving Size 1 Capsule
Servings Per Container 60

Amount Per Serving		% Daily Value
Probiotic Blend	12 billion CFU 260 mg	*
(Bifidobacterium bifidum, Bifidobacterium breve, Bifidobacterium infantis, Bifidobacterium lactis, Bifidobacterium longum, Lactobacillus acidophilus, Lactobacillus brevis, Lactobacillus bulgaricus, Lactobacillus casei, Lactobacillus gasseri, Lactobacillus paracasei, Lactobacillus plantarum, Lactobacillus rhamnosus, Lactobacillus salivarius, Lactococcus lactis, Streptococcus thermophilus)		

* Daily Value not established

The numbers of viable bacterial cells CFUs (Colony Forming Units) per capsule listed above are at the time of manufacture.

Other ingredients: Corn Maltodextrin, hydroxy-propyl methylcellulose, purified water.

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The contents of Constant Health target health beginning at the cellular level and cascading up to tissues, organs and ultimately overall metabolic function. Table 1 shows the ingredients for Constant Health.