

Original Synbiotic Formula

Monograph

The Philosophy

Purpose Specific by Design and Multi-Dimensional in Applications

BioImmersion Line of Therapeutic Foods Synbiotic Formulas are designed with the specific purpose of healing and protecting the integrity and functionality of the gastrointestinal system. The diversity of Therapeutic Foods chosen for the formulas bring to life a magnitude of scientifically researched medicinal applications. Historically, fermented foods of all kinds were part of the typical dietary habit of many civilizations. Throughout history from Roman texts espousing the medicinal properties of lacto-fermented sauerkraut, to the cultures of Japan, China and Korea where pickled preparations of cabbage, turnip, eggplant, cucumber, onion, squash and carrot have been for centuries their mainstay. In fact, many of the longest living societies attribute their longevity to their regular dietary intake of lacto-fermented foods, a practice most modern industrial societies have gone away from.

Recognizing this forgotten dietary custom, BioImmersion utilizes 21st Century microbiological research, food chemistry and food technology science to develop and manufacture the Therapeutic Foods Line of synbiotic formulas; with highly researched lactic acid bacterial strains and the powerful medicinal applications of Therapeutic Foods.

Pandemic Concern: Food Borne Pathogens and Xenobiotics

In the last fifty years, a large body of experimental and clinical evidence has accumulated, which indicates that various chemicals can affect different functions of the body, including immunological and neurological systems. Immune reaction to xenobiotics (drugs, metals, and industrial chemicals) can give rise to allergy, autoimmunity and immuno-deficiency. We live in a sea of growing numbers of pollutants that weaken our immune systems, and increasingly virulent and hostile microbes waiting for opportunity to invade our bodies. **The most vulnerable areas in the body are the mucous membrane surfaces of the respiratory system**

and the gastrointestinal tract. Epidemiologist Dr. Michael Osterholm, one of the world's leading authorities on food borne disease stated that, **"Stomach cramps, abdominal pain, and diarrhea have become the number one cause for visits to hospital emergency rooms in the US surpassing chest pain."** This data is of great consequence considering that the gastrointestinal tract is the front line of our immune defense system.

The Protective Shield: The One Cell-Layer of Mucous Membrane

Our gastrointestinal tract encompasses a surface area as large as one full tennis court. It is the second largest surface area next to our respiratory system that separates the outside world from our insides. Within our gut 100,000 billion foreign microbes reside which is ten times more than our total eukaryotic cell mass of 10,000 billion cells. **In the GI tract the only barrier that separates and protects us from pathogenic organisms and dietary toxins (xenobiotics) is a one cell-layer of mucous membrane called the GI tract epithelial membrane.** Seventy percent of our immune system is localized within and behind this GI mucous membrane, making it the largest immune organ of our body. Furthermore, there is more nervous tissue in our enteric nervous system than our spinal cord, hence the added designation for our GI tract as the second brain. **Our body focuses its defense, communication and intelligence abilities at this one celled layer of mucous membrane.**

The GI Tract: Port of Infectious Diseases

Xenobiotics and Infectious Organisms assault our Gastrointestinal Tract. Food is essential for our well-being, and yet it also constitutes an enormous threat to the integrity of the digestive tract and the whole body. **During a normal life time 60 tons of food pass through the gastrointestinal canal.** In a healthy state, the absorption of small sugars, fats and proteins proceed through the intestinal wall and circulate throughout the body. Simultaneously, damaging substances from unhealthful bacteria, incompletely digested food, toxins, or chemicals are largely prevented from being absorbed and transported throughout the body. **The harsh reality of globalization and the modern life is the increase and accumulation**

of the toxic and pathogenic load on the body. As the bio-accumulation of xenobiotics (toxins) reaches a critical level in our cells, certain chemical entities, such as heavy metals, inhibit the phagocytic ability of our front line defenders, the macrophages and monocytes, from capturing and eliminating pathogens. For example, their ability to take up *Candida* and destroy them is affected by exposure to mercury. **Hence, these single cell defenders of the mucous membrane are rendered functionally deficient.**

In his article, "*A Single Blood Test for Detection of Food Allergy, Candidiasis, Microflora Imbalance, Intestinal Barrier Dysfunction, and Humoral Immunodeficiencies*", immunologist Aristo Vojdani PhD, the owner of Immunosciences Lab, emphasizes that ***the gastrointestinal tract is the port of infectious diseases.*** Infectious organisms (such as pathogenic bacteria) assault our GI tract through a variety of evolutionary developed mechanism. Some pathogenic bacteria release exotoxins that bind to digestive enzymes, such as the proteolytic enzymes trypsin and pepsin, rendering them dysfunctional. This results in the incomplete digestion of dietary proteins and becomes a problem when other pathogens release endotoxins that destroy protective SIgA molecules on the GI membrane surface, causing the tight junctions to open, allowing these undigested peptides and infectious organisms to pass into circulation thereby causing inflammation, food allergies, autoimmune and infectious diseases. **In summary, protecting the GI tract mucous membrane and maintaining its integrity is of the utmost importance.**

Intestinal Integrity: Structure and Composition of the Protective Barrier

A Healthy Microfloral Community is dominated by the *Lactobacillus* and *Bifido* Genera. The healthy intestinal wall is coated with hundreds of different species of micro-organisms both healthful and unhealthy bacteria numbering in the billions. **This protective coating of microorganisms acts in concert with the physical barrier provided by the cells lining of the intestinal tract and other factors such as SIgA to provide the body with important filter-like protection.** Damaging substances like toxins, chemicals, metabolic byproducts (wastes), unhealthy bacteria and bacterial-generated materials are filtered out and eliminated.

Simultaneously, the critical factors needed for life, such as nutrients and water, are absorbed into circulation and made available to billions of cells. **The structure and composition of the protective coating barrier is pivotal.** Consider as an analogy the atmosphere surrounding the earth and its role in protecting our environment. The atmosphere acts as a selective barrier making sunlight available for life-sustaining photo-synthesis, while simultaneously preventing the sun's disease-causing ultraviolet light from penetrating. **Comparably, the selective barrier in the intestine is composed of bacteria, soluble fiber and proteoglycan molecules forming a three dimensional matrix for the bacteria to exist and grow on.** Providing the good bacteria (Lactobacillus and Bifido organisms) with a proper spacing and structure is important for the maximal performance and function of their populations.

ATCC - American Type Culture Collection is a non-profit bio resource center in Washington DC. It is one of the largest depositories and research centers for bacterial cultures in the world. ATCC authenticates and preserves the mother cultures. They are the gold standard - the 100% warranty for bacterial identification (DNA map and fingerprint of the strain) and are the prototype of BioImmersion Original Bacterial Strains.

Therapeutic Foods Original Bacterial Strains

Therapeutic Foods Original Synbiotic Formulas are based on ATCC prototypical bacterial strains with confirmed molecular identity. Molecular identity is based on 16sRNA sequence and is confirmed routinely to provide the highest quality and functionality of the organisms. Collected DNA sequence data are compared with DNA sequences of the strains provided by ATCC. The specific ATCC Original strains are chosen by our scientists for their strength, compatibility, safety and their 40 years of proven ability to perform: ***Lactobacillus acidophilus (ATCC 4356), Bifidobacteria longum (ATCC 15707), Streptococcus thermophilus (ATCC 19258), Lactobacillus rhamnosus (ATCC 7469) and Lactobacillus plantarum (ATCC 8014).***

Our pedigreed strains of lactic acid bacteria are human strain that have four decades of scientifically proven research backing their performance in

protecting the integrity of the GI tract mucus membrane. They are proven performers in neutralizing food borne pathogens and xenobiotics. The pedigreed lactic acid bacterial organisms successfully pass through stomach acid and bile, and effectively colonize and protect the mucous membrane. The formulas combine compatible bacterial strains that allow and enhance their mutual functionality and purpose. **They not only coat the mucous membrane but, per their strain specific attributes, are able to neutralize dietary toxins, mutagens, carcinogens and infectious organisms.**

Microbiome Technology

Our Original cultures are produced by a proprietary system that begins with the careful selection of strain-specific media in order to stimulate accelerated cell division. The optimal nutritional profile of these media guarantees cells that are compact and have significantly stronger and thicker cellular walls. These physical characteristics result in greatly increased viability over an extended shelf life. Incubated cells are then subjected to a unique “dry-preservation” technology that maintains ultra-low moisture content resulting in higher recovery of the bacteria. These ultra-low moisture levels enable a longer shelf life than would be typically expected in freeze-dried, preserved cultures. **Original Cultures have consistently proven to out-perform all other competitors in Food-industry applications.**

Purpose Specific by Design: Protect, Counteract and Neutralize

Therapeutic Foods Synbiotic Formulas with the Original Bacterial Strains are specifically designed to protect, counteract and neutralize dietary toxins, mutagens, carcinogens and pathogens.

Toxins

Many agricultural commodities are vulnerable to attack by a group of fungi that are able to produce toxic metabolites called **mycotoxins**. Among various mycotoxins, **aflatoxins** have assumed significance due to their deleterious effects on humans. **They are potent toxic, carcinogenic, mutagenic and immuno-suppressive agents.** Mold mycotoxins can compromise the blood-brain barrier and induce a neurodegenerative process of protein and antigen liberation, provoking IgG, IgM, or

IgA against different neuronal antigens which may result in chronic sensory neuropathy, demyelinating sensorimotor neuropathies or MS. **The contamination of food with aflatoxins is a worldwide problem.** There is a need for strategies to reduce or inactivate these toxins. **The Therapeutic Foods strain of lactic acid bacteria successfully bind mycotoxins in general:** *L. rhamnosus* binds AFB1 in vivo and reduces bio-absorption of the toxin from the gut. *L. acidophilus* and *B. longum* neutralize AFB1 and AFM1 by binding mechanisms. *S. thermophilus* reduces content of **ochratoxin A**.

Mutagens

A mutagen is a natural or human made agent (physical or chemical) which can alter the structure or sequence of DNA. **Mutagens may cause impaired cell function, cell death or cell transformation into cancer cells.** It is supposed that mutagenesis is a necessary step in carcinogenesis and tumor formation. For example, the question of diet and breast cancer has attracted public attention because evidence is growing that diet may be contributing to the incidence of breast cancer in our country. In fact, it has been estimated that more than half of all breast cancers in the United States might be related to diet. One source of dietary carcinogens that might influence the incidence of human breast cancer is called cooked meat mutagens because they are formed through heating protein-rich foods such as meats and fish. These cooked meat mutagens are called **heterocyclic amines**. Although other chemicals can induce breast cancer in experimental animals, heterocyclic amines are the only mammary carcinogen known to be present in everyday human diets. **Dietary mutagens and carcinogens include nitrosamines.** Nitrosamines occur commonly because their chemical precursors, amines and nitrosating agents, occur commonly and the chemical reaction for nitrosamine formation is quite facile. Cured meats can contain nitrosamines because meats contain amines, and sodium nitrite, a nitrosating agent, is added to cured meats as a preservative. Nitrosamines are found in significant amounts in pork and its derivatives, cheese and beer. They are potent DNA methylating agents, particularly on guanine residues. Approximately 300 of these compounds have been tested, and 90% of them have been found to be carcinogenic, in a wide variety of experimental animals. Since nitrosamines are metabolized the same in human and

animal tissues, it seems highly likely that humans are susceptible to the carcinogenic properties of nitrosamines.

Therapeutic Foods selected strains of bacteria are effective in reducing or neutralizing nitrosamines, heterocyclic amines and other dietary mutagens:

Lactobacillus acidophilus neutralizes pyrolysates, dietary mutagens that are carcinogenic. ***Bifidobacteria longum*** reduces incidence of liver, colon and mammary cancers in rats caused by 2-Amino-3-methylimidazo[4,5-f]quinoline (IQ), a heterocyclic amine mutagen/carcinogen formed from the cooking of meat. ***Lactobacillus rhamnosus*** binds and removes pyrolysates, aflatoxin B1 and Trp-P. ***Streptococcus thermophilus*** reduces mutagenic and carcinogenic effect of the substance N-methyl-N-nitro-N-nitrosoguanidine. Studies have shown that ***Lactobacillus plantarum*** can eliminate toxic components from food. The significant removal of selected mutagens, but not other substrates, by Therapeutic Foods lactic acid organisms suggests that these strains may be useful for dietary detoxification.

Carcinogens

In the industrialized nations of the West such as the United States and Europe, the predominant types of cancer include breast, colon and prostate cancer. In the U.S. population of about 300 million, about 1.2 million new cases of cancer are detected every year. Many scientists agree that the Western diet contributes to about 40% of human cancer. More than 50% of all cancer cases occur in cells that are in direct contact with the outside environment, including the skin, lungs, genitals and the digestive tract. It has been estimated that 75% of cancers are caused by exposure to toxic chemicals. All types of diets, including those that are defined as balanced diets, contain both toxic and protective substances. The risk of developing cancer may depend upon the relative consumption of protective versus toxic substances.

Amongst the protective substances, a healthy microbiotic flora is most important. Therapeutic Foods line of synbiotic formulas are designed to protect against the development of cancer: ***Lactobacillus acidophilus*** inhibits the formation of precancerous colon lesions in animal trials where the carcinogen azoxymethane was used to induce the development of colon cancer. In trials where

1,2 di-methylhydrazine was used to induce colon cancer development, ***Lactobacillus acidophilus*** reduces colon lesions formation. ***L. acidophilus*** reduced the number of colon cancers caused by the toxin and by increased meat intake. ***Bifidobacteria longum*** reduces development of precancerous lesions in rat colons in trials using azoxymethane. ***B. longum*** showed significant inhibitory effect on colon, mammary and liver carcinogenesis induced by 2-amino-3-methylimidazo [4,5-f]quinoline, a heterocyclic amine (100% inhibition for the colon, and 80% inhibition for the liver). ***Lactobacillus rhamnosus*** also decreases the development of colon cancer in rats caused by this carcinogen. Lactic acid bacteria are proposed to have several beneficial effects, including the inactivation of carcinogens. Studies have shown the potential of ***Lactobacillus acidophilus***, ***Streptococcus thermophilus*** and ***Bifidobacterium longum*** to prevent the induction of DNA damage. Many studies show that most lactic acid bacteria tested could strongly inhibit genotoxicity in the GI tract of the rat and that viable lactic acid bacteria are required for the protective effect in vivo.

The Approaching Crisis: Infectious Disease

Food and waterborne diseases are a worldwide present-day concern. Gastrointestinal diseases in the US are on the increase. **The result of globalization is that harmful microbes travel with the world commerce.** Mexico, Central America and South America have become major exporters of food to the USA. The risk and vulnerability is exemplified in the 1996 outbreak of Cyclosporiasis that affected large numbers of people in the United States and Canada. This epidemic gave rise to a fair amount of panic until it was established that *Cyclospora* is a food borne agent of diarrheal disease and was being spread by Guatemalan raspberries. New outbreaks of *Cyclospora* have occurred: one was spread by mesclun lettuce and another by fresh basil in pesto sauce. The fact that much of the foods that we obtain from the developing world are vegetables and fruits magnifies the risk. Surveillance is questionable because medical laboratories do not routinely test for some of the microbes that are known to cause food or waterborne disease, and because medical research science has not yet identified all of the responsible organisms. Food borne diseases have escalated as the frequency of people eating out in restaurants or buying "take-out" has increased. The challenge of providing public health education

for the over nine million people employed as food handlers many of whom do not speak English compounds the exposure to diverse and toxic pathogens.

Infections

One of the basic physiological functions of the resident microbiota (flora) is that it functions as a microbial barrier against microbial pathogens. In European studies, published through FEMS Microbiology Letters, *Salmonella typhimurium* and enteropathogenic *Escherichia coli* were found to adhere to the brush border of differentiated human intestinal Caco-2 cells in culture, where as *Yersinia pseudotuberculosis* and *Listeria monocytogenes* adhered to the periphery of undifferentiated Caco-2 cells. These aggressive enterovirulent strains invaded the Caco-2 cells. ***Lactobacillus acidophilus*** inhibited both cell association and invasion of Caco-2 cells by enterovirulent bacteria in a concentration-dependent manner. The mechanism of inhibition of both adhesion and invasion appear to be due to both steric hindrance of human enterocytic pathogen receptors by whole-cell ***Lactobacillus acidophilus*** rather than to a specific blockade of receptors and by the production of a bactericidal substance by the ***Lactobacillus***. The ability of enteroinvasive pathogens to disseminate into the deep tissues by cellular apoptosis induction is well documented. ***Streptococcus thermophilus*** were able to inhibit the apoptosis of macrophages induced by *Salmonella*. The result suggests that ***S. thermophilus*** can play a role in apoptotic mechanisms, as the inhibition of apoptosis would avoid pathogen dissemination. **Verocytotoxin** producing *Escherichia coli*, such as *E. coli* s0157 are emerging food borne pathogens worldwide. They are responsible for a range of illnesses in humans from mild diarrhea to hemorrhagic colitis and hemolytic uremic syndrome in humans. ***Bifido longum*** was found to neutralize *E. coli*. Oral administration of ***B. longum*** exerts marked inhibitory effects on ulcerative colitis in mice. Administration of methotrexate to rats on an elemental diet results in severe enterocolitis and death. ***Lactobacillus plantarum***, an integral part of the healthy gastrointestinal micro ecology, provided therapeutic benefits to help in the recovery from enterocolitis. ***L. plantarum*** reduces the number of infections in patients after liver transplantation. ***L. plantarum*** fermented oat given to healthy volunteers significantly reduces the gut content of potentially pathogenic microorganisms such as *Enterobacteriaceae*, *S. aureus* and *enterococci*. **The microbiota mix in the synbiotic formulas was**

chosen for the specific purpose of preventing pathogenic bacteria from growing, invading and causing disease.

Therapeutic Foods: Multi-Dimensional in Application

BioImmersion Inc. honors many centuries of fermented foods traditions from all over the world with a line of powerful Therapeutic Foods Synbiotic Formulas. The Therapeutic Foods chosen for the synbiotic formulas function as the carrier for the bacterial organisms and work synergistically with the Original microbiotic mix for the specific purpose of repairing, healing and protecting the mono-cellular GI tract membrane. The diversity and power of the Therapeutic Foods provides a magnitude of important scientifically researched medical applications.

The Original Synbiotic Formula is a synbiotic composed of ATTC prototypical bacterial strains with confirmed molecular identity and inulin as prebiotic and carrier for the bugs. A synbiotic formula is the combination of probiotic and prebiotic. Prebiotics are non-digestible dietary fiber such as inulin, fructo-oligosaccharides and resistant starches, and are used for the purpose of stimulating the growth and activity of specific bacterial strains in the GI tract. By pairing a specific probiotic with specific prebiotic scientists are creating synbiotic compounds able to target specific disease states.

Inulin in the Therapeutic Foods Original Formulas is derived from chicory. Inulin is a carbohydrate belonging to a class of compounds known as fructans and is a soluble non-digestible dietary fiber. The viscous nature of inulin protects and improves the survival of the bacterial organisms crossing the upper part of the gastrointestinal tract, thereby enhancing their effects in the large bowel. Since inulin is resistant to digestion in the upper gastrointestinal tract it reaches the large intestine essentially intact, where it becomes the colon food for the important Bifido genera of indigenous lactic acid organisms. It is recommended that a minimum of 10% of ingested calories and about 20% of the food volume should be colonic food (food for the good colonic bacteria).

Inulin Confers Many Important Medical Applications

Inulin shifts gut ecology in favor of friendly bacteria: the best known nutritional effect of inulin is its ability to stimulate bifidobacterial growth in the intestine. In a healthy gut, *B. infantis* and *B. breve* are thought to be predominant in infants whereas *B. adolescentis* and *B. longum* are prevalent in adults. Consistently nourishing Bifidobacteria with inulin allows them to “out compete” potential pathogenic organisms thereby reducing their negative effect. As the *Bifido-bacteria* grow, they secrete lactic acid, lowering GI tract pH which helps suppress the growth of such harmful bacteria as *C. difficile*, *E. Coli*, *Salmonella* and *Campylobacter*.

Inulin and gut permeability: Butyric acid is produced in the gut as a byproduct from the fermentation of inulin by *Bifidobacteria*. Butyric Acid is used by the colonocytes (epithelial cells lining the colon) as their preferred energy source which facilitates healthy cell metabolism, cell turnover and the establishment of tight junctions, thereby reducing inflammation, absorption of macromolecules and translocation of pathogenic organism.

Inulin reduces the risk of colon cancer: it is well published that butyric acid also stimulates stem cell differentiation within the colon thereby reducing the risk of colon cancer.

Inulin helps protect against viral infections: in a study conducted at Johns Hopkins, 123 infants who were fed inulin with their cereal showed reduced incidence of fever, less antibiotic use, fewer doctor visits, less vomiting and fewer daycare absences.

Inulin is proven to have positive effect on cardiovascular health: a double blind, placebo controlled randomized clinical trial was carried out in 12 obese, hypertriglyceridemic and hypercholesterolemic subjects between 19 and 32 years old. The oral inulin administration reduced total cholesterol, LDL, DLDL and tryglyceride levels.

In another study, plasma triacylglycerol concentrations and hepatic lipogenesis were lower after inulin than after placebo ingestion. These findings support the use inulin for reducing risk factors for atherosclerosis.

Inulin can be beneficial in the management of diabetes: although inulin has a pleasant sweet taste, as an undigested fiber with zero Glycemic Index, it has no effect on blood glucose levels, nor does it effect insulin levels and therefore can be used safely.

Inulin fructans enhance calcium and magnesium absorption and is clinically proven to increase bone density: a study published in the American Journal of Clinical Nutrition showed that inulin increased calcium retention in adolescents by 15%. This increase in calcium absorption and bone density resulted after supplementing the

diet with 8 grams of inulin per day. **Inulin improves bowel habit:** Inulin is a highly viscous non-digestible soluble dietary fiber and therefore increases faecal biomass and water content of the stools (stool weight is increased as much as 2 grams per gram of inulin ingested), the result is improved regularity and reduced constipation.

Therapeutic Foods Synbiotic Formula are 100% Pure

BioImmersion Inc. Manufactures and encapsulates the Therapeutic Foods Synbiotic Formulas without any added excipients: fillers, binders and flowing agents (such as magnesium stearate). Each vegetarian capsule or loose powder contains only 100% pure probiotic bacterial blend and the special Therapeutic Foods extracts and whole foods blends.

Therapeutic Foods range of products responds to the reality of today's negligible dietary patterns and answers the required nutritional needs to achieve and preserve good health. Our products are extensively and properly analyzed and documented to ensure consistent delivery of the highest levels of active ingredients.

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