AOR CODE: AOR04219

Premium

Probiotic-3

A Revolutionary Probiotic Formula

- Three highly effective probiotic strains, with clinical evidence supporting their use
- The only probiotic in Canada that includes a strain from the Clostridium family
- Reduces the growth of pathogenic bacteria while promoting the growth of beneficial bacteria
- Normalizes the inflammatory response, promotes detoxification and supports immunity

Gluten Free  Non-GMO  Vegetarian  Gastrointestinal Health Immunity

AOR Code  Variant
AOR04219  90 VEGI-CAPS

Details
Many health conscious individuals today are becoming aware of the role of beneficial bacteria in the human body. Healthy bacteria in the gut act as a barrier against harmful bacteria by preventing their attachment to the intestinal lining. Disturbances in this delicate gastrointestinal microflora increase the susceptibility to pathogens and raise the risk of infection and disease. Probiotics help to re-establish and support a normal bacterial microflora in the intestines, particularly after antibiotic use.

Probiotic-3 is a unique probiotic formula that contains three bacterial strains with specific health-promoting attributes: Enterococcus faecium T-110, Clostridium butyricum TO-A, and Bacillus subtilis TO-A. While these three strains are almost unheard of in the North American market, they have been widely used in hospitals and pharmacies throughout Asia for over 50 years. Each has been shown to survive the stomach’s acidic environment, bile acids and digestive enzymes, meaning they survive transit through the body, reaching the intestines alive and intact.

Over 30 clinical studies on Probiotic-3 in Japanese and English have highlighted such health benefits as reducing allergies, improving immunity, fighting colds and flu, promoting detoxification, reducing intestinal symptoms such as bloating and constipation and reducing travelers and antibiotic-induced diarrhea.
Discussion
Probiotic-3 contains a synergistic blend of probiotic strains that has been well studied and used in Japan for over 60 years. Probiotic-3 helps support gastrointestinal health and promotes the growth of healthy gut flora while inhibiting harmful gut bacteria.

Product Variation
**Product Code**  Size
AOR04219  90 VEGI-CAPS

Supplements Facts
**Serving Size:** 1 Capsule

<table>
<thead>
<tr>
<th>Strain</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterococcus faecium T-110</td>
<td>18 million CFU†</td>
</tr>
<tr>
<td>Clostridium butyricum TO-A</td>
<td>0.6 million CFU†</td>
</tr>
<tr>
<td>Bacillus subtilis TO-A</td>
<td>0.6 million CFU†</td>
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</tbody>
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†Colony-forming units.

Non-medical ingredients:
lactose, potato starch, polyvinyl alcohol, providone, sodium stearyl fumarate. Capsule: hypromellose.

Guarantees
AOR™ guarantees that all ingredients have been declared on the label. Contains no wheat, gluten, corn, nuts, peanuts, sesame seeds, sulphites, mustard, soy, eggs, fish or shellfish.

Adult Dosage
Take 2-3 capsules daily with/without food, or as directed by a qualified health care practitioner. Take at least 2-3 hours before or after taking antibiotics.

Cautions
Consult a health care practitioner prior to use if you have fever, vomiting, bloody diarrhea, severe abdominal pain, or if you are pregnant or breastfeeding. Do not use if you have an immune compromised condition (e.g. AIDS, lymphoma, patients undergoing long-term corticosteroid treatment). If symptoms of digestive upset (e.g. diarrhea) occur, worsen or persist beyond 3 days, discontinue use and consult a health care practitioner.

Source
Enterococcus faecium: Human strain
Clostridium butyricum: Human strain
Bacillus mesentericus: Potato skin
Main Application
Digestive health
Immunity
Allergies
Inflammation

Disclaimer
The information and product descriptions appearing on this website are for information purposes only, and are not intended to provide or replace medical advice to individuals from a qualified health care professional. Consult with your physician if you have any health concerns, and before initiating any new diet, exercise, supplement, or other lifestyle changes.

Research
Background

A Clinically Tested Probiotic Formula

Although associated with spoiled food and infections, not all bacteria are harmful. As humans, we carry more bacterial cells in our bodies than human cells. Most of these bacteria are found in our gastrointestinal tract where billions of bacteria reside in a delicate equilibrium that is essential to our health. This mutually beneficial relationship between enterobacteria and the human body is important for the maturation of the immune system, for a normal inflammatory response, for a healthy gastrointestinal tract, and for many other aspects of health. The intestinal flora is essential for digestion and produces several important nutrients from otherwise indigestible foodstuffs.

While antibiotic use is sometimes necessary in order to fight infection, it can cause disturbances in the delicate gastrointestinal microflora, resulting in increased susceptibility to pathogens and elevated risk of infection and disease. Probiotics help to re-establish and support a normal bacterial microflora in the intestines, which act as a barrier against harmful bacteria by preventing their attachment to the intestinal lining.

Probiotic-3 is a probiotic formula that has been used clinically for more than 50 years in Japan and across Asia. Extensive clinical research has highlighted the following beneficial effects of the three strains used in Probiotic-3:

*Enterococcus faecium* T-110

*E. faecium* T-110 is a natural resident of the human gastrointestinal tract that produces lactic acid as a byproduct of carbohydrate fermentation. Lactic acid reduces the gastrointestinal pH thus preventing the growth of harmful bacteria.

*Clostridium butyricum* TO-A

*C. butyricum* TO-A is also a natural resident of the human gastrointestinal tract and breaks down
dietary fiber into several beneficial nutrients, one of which is butyric acid. Butyric acid is an important source of nourishment for the colonocytes (the cells of the lower gastrointestinal tract) and reduces inflammation and intestinal permeability. This strain has also been shown to have antagonistic effects against several pathogenic bacterial strains such as *C. difficile*, *H. pylori* and *E. coli*.

**Bacillus subtilis** TO-A

*Bacillus subtilis* TO-A supports the growth of *E. faecium* and *C. butyricum* as well as the growth of several strains of the beneficial *Bifidobacterium* species.

**Microflora in the Gastrointestinal Tract**

The gastrointestinal tract (GIT) of an adult person is an approximately 6.5m convoluted tube that is divided into the upper portion consisting of the oral cavity, esophagus and the stomach and the lower portion which consists of the small and large intestines. Because of the multiple folds and finger-like projections – called microvilli – the surface area is approximately 200 times that of the skin! The GIT houses a diverse and complex microbial population, only a fraction of which have been identified and studied.

The lower portion of the human gastrointestinal tract (GIT) is a more densely populated ecosystem than the planet, with billions of bacteria, yeasts and fungi calling it home. Many of these microorganisms have beneficial effects on human health, making the GIT a key organ in the body.

Each organism is classified into a different genus, species and strain, producing thousands of similar yet separate organisms performing distinct functions. These organisms are grouped into three broad categories:

- **Commensals** - which are neither good nor bad
- **Symbionts** - which are beneficial to health
- **Pathobionts** - which cause toxicity and disease

However, all the symbionts can be classified as one of the following:

1. *Lactobacillus*
2. *Bifidobacterium*
3. Others which include yeast, E. coli, propinobacterium, etc.

The term ‘probiotics’ was first used in 1953 to indicate beneficial strains which can be taken in order to promote bacterial life, in contrast to harmful antibiotics which kill microorganisms. The WHO definition of probiotic is “live organisms which, when administered in adequate amounts, confer health benefits to the host.” Some of the health benefits are:
· Creates a barrier against pathogens that cause disease
· Generates various nutrients like vitamins B2, B12, K, etc.
· Helps absorption of important minerals like calcium
· Helps produce important digestive enzymes
· Promotes healthy cholesterol levels
· Stimulates the immune system
· Enhances bowel motility and relieves constipation
· Maintains integrity of the gut lining, preventing "leaky gut"
· Reduces inflammation and allergic reactions
· Helps promote detoxification
· Prevents colonization of pathogenic bacteria by competing for space

Probiotics have been used for centuries, but only over the past 100 years have they been studied in depth. Japan is the world leader in the use of probiotics in various types of foods like yogurt, candy, milk, desserts, etc.

For any probiotic, the following are important requirements:

1. Clinically studied. The more studies, the better (as there is a strong placebo effect to contend with). Products not subject to clinical study need to be viewed with caution.

2. The right strains that are naturally found in humans.

3. Resistant to mutation, i.e. not subject to genetic change so that these beneficial organisms don’t become toxic themselves or help spread antibiotic resistance.

4. Must be stable and resistant to stomach acid, bile salts and digestive enzymes. It also helps if the organisms are room temperature stable for convenience, i.e. when travelling.

5. Must have a documented ability to deliver health benefits, for example stimulating the immune system, having anti-allergic effects, supporting detoxification, etc.

6. Strains must be compatible with each other and not only that but be synergistic. Most products contain a random combination of strains thrown together with no idea if they are compatible except a hope that they will work together and not kill each other.
Research

The Role of *Clostridium butyricum* In Relieving Inflammation and Supporting the Immune System

Humans carry more bacterial cells than human cells. Most of these bacteria are found in our gastrointestinal tract where billions of bacteria reside in a delicate equilibrium that is essential to our health. This mutually beneficial relationship between enterobacteria and the human body is important for the maturation of the immune system, for a normal inflammatory response and for a healthy gastrointestinal tract. The intestinal flora is also essential for digestion and produces several important nutrients from otherwise indigestible foodstuffs.

Healthy gut bacteria act as a barrier by preventing the attachment of harmful bacteria to the intestinal mucosa. Disturbances in this delicate gastrointestinal microflora increase the susceptibility to pathogens and raise the risk of infection and disease. Probiotics help to re-establish and support a normal bacterial microflora in the intestines.

Probiotic-3 is a probiotic formula that has been used clinically for more than 50 years in Japan. Probiotic-3 contains three unique bacterial species with specific health promoting attributes:

*Enterococcus faecalis*

*E. faecalis* is a natural resident of the human gastrointestinal tract that produces lactic acid as a by-product of carbohydrate fermentation. Lactic acid reduces the gastrointestinal pH thus preventing the growth of harmful bacteria.

*Clostridium butyricum*

*C. butyricum* is also a natural resident of the human gastrointestinal tract and breaks down dietary fibre into several beneficial nutrients one of which is butyric acid. Butyric acid is an important source of nourishment for the colonocytes (the cells of the lower gastrointestinal tract) and reduces inflammation and intestinal permeability. It also acts on the intestinal tract to improve bowel activity. Butyrate exerts potent effects on a variety of colonic mucosal functions such as inhibition of inflammation and carcinogenesis, reinforcing various components of the colonic defence barrier and decreasing oxidative stress. In addition, butyrate may promote satiety. Two important mechanisms include the inhibition of nuclear factor kappa B activation (anti-inflammatory effect) and histone deacetylation (anti-proliferative/anti-carcinogenic effect).

*Bacillus mesentericus*

*B. mesentericus* supports the growth of *S. faecalis* and *C. butyricum* as well as the growth of several strains of the beneficial Bifidobacterium species.
The bacterial strains in Probiotic-3 work in symbiosis to support the proliferation of bifidobacteria and prevent the growth of harmful bacteria which improves the gastrointestinal ecosystem. Probiotic-3 is the only probiotic in Canada which contains *Clostridium butyricum*.

**Gut Flora to Tregs to Suppression of Autoimmunity**

It is important to understand at the outset that autoimmunity and allergies are caused by a damaged immune system, and repairing the damage cures the diseases. Damage to the immune system typically represents a break in the continual development of immune cells in the lining of the intestines. Immune cell development in the gut is dependent on bacteria, the gut flora. Damage to the gut flora, e.g. by antibiotics, processed foods that lack flora feeding fiber or extreme diets, disrupts development of immune cells. Typically, loss of the immune cells that keep the aggressiveness of the immune system in check, regulatory T cells or Tregs, results in autoimmunity. Fix the gut flora and autoimmunity recedes.

**Health Requires Suppression of the Aggressive Immune System**

For simplicity, I am focusing on the T cells of the immune system that develop in the intestines and either kill other human cells that are dangerous, e.g. virus-infected or cancer cells, or provide protection by regulating the aggression, Tregs. Normal functioning of the immune cells permits elimination of damaged or dangerous human cells, while at the same time avoiding rampages of lethally armed T killers. Examples of untamed T killers in action are degenerative autoimmune diseases, such as arthritis, asthma, prostatitis, celiac, Hashimoto’s thyroiditis, type I diabetes, inflammatory bowel diseases and atherosclerosis.

**Milk Births Baby Immune System**

It should not be surprising that the focus of immune system development is the gut. We start as babies with explicit links between nourishment and immunological protection. Milk connects the immune systems of mother to baby. Immune cells from the mother in milk are transferred and colonize the respiratory and digestive system of the baby — the mother’s immune system coats and buffers the baby’s exposure to the world. Milk hormones close the baby’s gut and milk bacteria are the first probiotics that exploit the milk prebiotics (bifidus factor, human milk oligosaccharides) to produce a gut flora. [Also note that most commercial probiotics are adapted to grow on cow’s milk and hence these dairy probiotics do not survive in adults.] The lymphatic system of the breast terminates at the nipple and samples antigens/pathogens from the baby’s mouth, resulting in baby-specific secretory antibodies that return in the milk. Milk supports a starter set of gut flora, essentially dairy probiotics that stimulates development of the baby immune system, but inhibits adult gut flora that would digest the protective components of milk. Formula, on the other hand, is inflammatory to the baby gut, because it supports adult gut flora before the immune system is ready. Inflammation and stimulation of innate immunity is sufficient, if supported with high levels of sanitation, to permit survival of babies fed formula. Milk of any type is incompatible with adult gut flora, so breast milk will attack adult gut flora and adult gut flora will digest and inactivate the otherwise beneficial components of the milk.
Aggressive and Suppressive Cells of Immune System Develop in Intestines

Gut bacteria are required for the development of immune T cells in the lining of the intestines. Mice grown without gut flora do not have functional immune systems. In humans, extensive antibiotic treatment produces defective immune systems that are either overly aggressive, i.e. autoimmune, or susceptible to infection and cancer. They can't be both. Aggressive T killers are stimulated to develop by filamentous bacteria and Tregs develop in response to members of the Clostridium family. In a healthy body, there is a balance between aggression and suppression; there are functional defenses against infection and cancer, while also avoiding autoimmune disease and allergies.

Suppressive Tregs are Deficient in Autoimmunity

Immune cells result from replicative divisions of stem cells. Antibody producing B cells are produced through a million random rearrangements of antibody genes and those B cells producing antibodies against common self-proteins are killed (clonal deletion). Similarly, T cells are produced by rearrangements of receptors and those that would recognize self are eliminated. The T cells then migrate to the intestines where they can develop into killer T cells or Tregs, in response to gut flora. The Tregs act to suppress killer T cells that mistakenly recognize healthy self-cells. Thus, the initial elimination of self-attacking T cells or for B cells that produce antibodies that bind to normal cells, is not perfect and the Tregs are needed to avoid the mistakes. Tregs are necessary to avoid the immune attack on healthy cells that is the basis of autoimmunity.

Autoimmunity Starts with Inflammation, but Requires Deficient Tregs

Bacterial or viral infections, or physical damage causing inflammation is the first step in autoimmunity. It is the inflammation that initiates the interactions between proteins, autoantigens, of normal cells and cells of the immune system that bind, internalize, fragment and present the antigen fragments/peptides to activate B or T cells with corresponding receptors. The activated B cells make antibodies specific for the antigen and the T cells will kill cells displaying the antigen. It is interesting that most proteins are not autoantigens and are never involved immune reactions. Only proteins with an unusual triplet of basic amino acids, similar to the quartet of basic amino acids used to transport proteins into the cell nucleus, are candidates to be autoantigens or allergens. In fact, since nuclear proteins already have a quartet, i.e. the nuclear localization signal, they are common autoantigens. The last requirement for autoimmunity is a deficiency in Tregs, because if the Tregs are functioning, they will block attack on healthy cells. Treg deficiency usually results from loss of the type of gut bacteria that stimulate Treg production in the lining of the intestines, i.e. species of Clostridium.

Hospitals are Notorious for Clostridium difficile Infections

Fecal transplants are now recommended as a safe and efficacious treatment for C. difficile hospital infections. That makes sense, because hospitals are where antibiotics are routinely used and C. difficile can only infect people missing their healthy species of Clostridium. Thus, the hospitals wipe out the gut flora with antibiotics and then recolonize them with their own antibiotic resistant C. difficile
Autoimmune Diseases are Treated/Exacerbated with Antibiotics

Both the aggressive and the suppressive immune cells require gut flora, so after initial antibiotic treatment wipes out bacteria required for suppression and results in autoimmunity, the remaining aggressive half of the immune system can be eliminated by blasting the remaining gut flora with more antibiotics. Of course this will leave a highly compromised, incompetent immune system that will ultimately yield more extreme symptoms. This is the typical medical progression for Crohn’s disease, for example. The alternative is just fixing the gut flora to begin with and curing autoimmunity.

Cure Autoimmunity by Feeding Clostridium Resistant Starch

Autoimmune diseases, by their symptoms, show that sufficient gut flora to stimulate the aggressive half of the immune system is still present. What is missing are the Clostridium species that convert soluble fibre, such as resistant starch, into short chain fatty acids, e.g. butyrate. Patients treated with antibiotics usually walk away from the hospital with a suggestion to eat some yogurt to repopulate their missing gut flora. Unfortunately, dairy probiotics don’t survive in the gut and cannot repair the gut flora and immune system. The result, after the gut fails to repair and the immune system crashes, is autoimmunity. There is a more appropriate possibility to avoid or fix autoimmunity. Some people suffering from autoimmunity (and with remnants of their gut flora intact) have simply fed their gut flora on resistant starch and achieved complete recoveries. Others fail to respond because their gut flora is too severely damaged and necessary bacterial species are gone. Those individuals need to eat the missing species of bacteria and some probiotics (more common in Asia) contain Clostridium species. Consistent with this use of soluble fiber to feed gut bacteria that produce butyrate and stimulate the suppressive immune system are reports of healing by combining potato starch and probiotics with Clostridium butyricum. Repair of the suppressive immune system by repair of gut flora (including fecal transplants) and feeding gut flora with appropriate soluble fiber, may be a general approach to the cure of most autoimmune diseases and allergies.

References


Article adapted from “Cooling Inflammation” written by reputed researcher Dr. Art Ayers

Market Trends

There are many different types of probiotic supplements available on the market today. Most contain multiple bacterial strains which are typically researched separately as single strains, and are usually not studied in combination with one another. Some of these combinations have very little or no history of use and may be antagonistic to each other and, worse still, may alter the gut flora in an undesirable way.
Many probiotic products tout health benefits that are theoretical in nature, but have not been proven in clinical research. These products often contain large numbers of different strains in high doses, however the concept of ‘more is better’ does not apply in the case of probiotics. Rather, the important points to focus on are whether the strains included are synergistic with each other, and whether they have been shown in clinical studies to be safe and effective.

**AOR Advantage**

AOR’s Probiotic-3 provides three human probiotic strains that were carefully chosen to ensure synergy and safety with the others. As a result, these strains truly act in a synergistic manner as probiotic and prebiotic, meaning that each strain supports the proliferation of the others; therefore, there is no need for additional prebiotics such as inulin, FOS, or GOS to ensure their survival. This probiotic formula is also shelf-stable, making it easy to travel with, and is safe for use in infants and seniors.

Amongst the plethora of probiotic supplements on the market, Probiotic-3 stands out. It has a long history of use, having been clinically studied for over 50 years, and is used regularly in hospitals and pharmacies throughout Asia. Clinical studies have shown wide-ranging health benefits including allergy reduction, improved immunity, reduced bloating, constipation and diarrhea, and even enhanced detoxification. Additionally, Probiotic-3 is the only probiotic product in Canada that contains a strain of bacteria from the *Clostridium* family, which has been shown to have antagonistic effects against several pathogenic bacteria such as *C. difficile*, *H. pylori*, and *E. coli*.

**References**


Abstract

Effectiveness of probiotic therapy for the prevention of relapse in patients with inactive ulcerative colitis.


AIM: To evaluate the effectiveness of probiotic therapy for suppressing relapse in patients with inactive ulcerative colitis (UC).

METHODS: Bio-Three tablets, each containing 2 mg of lactomin (Streptococcus faecalis T-110), 10 mg of Clostridium butyricum TO-A, and 10 mg of Bacillus mesentericus TO-A, were used as probiotic therapy. Sixty outpatients with UC in remission were randomly assigned to receive 9 Bio-Three tablets/day (Bio-Three group) or 9 placebo tablets/day (placebo group) for 12 mo in addition to their ongoing medications. Clinical symptoms were evaluated monthly or on the exacerbation of symptoms or need for additional medication. Fecal samples were collected to analyze bacterial DNA at baseline and 3-mo intervals. Terminal restriction fragment length polymorphism and cluster analyses were done to examine bacterial components of the fecal microflora.

RESULTS: Forty-six patients, 23 in each group, completed the study, and 14 were excluded. The relapse rates in the Bio-Three and placebo groups were respectively 0.0% vs 17.4% at 3 mo (P = 0.036), 8.7% vs 26.1% at 6 mo (P = 0.119), and 21.7% vs 34.8% (P = 0.326) at 9 mo. At 12 mo, the remission rate was 69.5% in the Bio-Three group and 56.6% in the placebo group (P = 0.248).
cluster analysis of fecal flora, 7 patients belonged to cluster I, 32 to cluster II, and 7 to cluster III.

CONCLUSION: Probiotics may be effective for maintaining clinical remission in patients with quiescent UC, especially those who belong to cluster I on fecal bacterial analysis.

Three-Combination Probiotics Therapy in Children With Salmonella and Rotavirus Gastroenteritis.


Huang YF, Liu PY, Chen YY, Nong BR, Huang IF, Hsieh KS, Chen KT.

GOALS: Quantitative Vesikari scales and qualitative severe diarrhea (Vesikari scale ≥11) assessments were used to grade the Salmonella-induced and rotavirus-induced gastroenteritis severity. A significant reduction in severe diarrhea (Vesikari score ≥11) was used to evaluate the efficacy of three-combination probiotics (BIO-THREE).

BACKGROUND: Several studies have shown that rotavirus and Salmonella infections are the leading causes of infectious gastroenteritis. Although probiotics have been effective in some studies, the use of 3-combination formulation probiotics is rare.

STUDY: This single-center, open-label, randomized, controlled trial included 159 patients (age range, 3 mo to 14 y) hospitalized with infectious gastroenteritis between February 2009 and October 2010.

RESULTS: Patients were grouped according to the pathogen identified (48, Salmonella; 42, rotavirus; and 69, unknown origin). The total diarrhea duration was significantly shorter for children who received BIO-THREE.

CONCLUSIONS: Seven-day BIO-THREE administration demonstrated high efficacy and safety in infants and children with severe gastroenteritis. The incidence of severe gastroenteritis was significantly reduced in the rotavirus origin and BIO-THREE intervention groups.

Effects of dietary supplementation with clostridium butyricum on the growth performance and humoral immune response in Miichthys miuy.


Song ZF, Wu TX, Cai LS, Zhang LJ, Zheng XD. J Zhejiang
The effects of dietary supplementation with Clostridium butyricum on growth performance and humoral immune response in Miichthys miuuy were evaluated. One hundred and fifty Miichthys miuuy weighing approximately 200-260 g were divided into five groups and reared in 15 tanks with closed circuiting culture system. The animals were fed 5 diets: basal diet only (control) or supplemented of the basal diet with C. butyricum at doses of 10^3 (CB1), 10^5 (CB2), 10^7 (CB3) or 10^9 (CB4) CFU/g. Compared with the control, the serum phenoloxidase activity was significantly increased by the supplementation.

**Effect of Clostridium butyricum on fecal flora in Helicobacter pylori eradication therapy.**


Shimbo I, Yamaguchi T, Odaka T, Nakajima K, Koide A, Koyama H, Saisho H.

AIM: To investigate the effect of probiotic bacterium, Clostridium butyricum MIYAIRI 588 strain (CBM) on the changes of the fecal flora in Helicobacter pylori (H. pylori) treatment.

METHODS: Thirty-five patients with gastric or duodenal ulcers positive for H. pylori were randomized either to 1 wk amoxicillin, clarithromycin, lansoprazole (Group 1) or to the same regimen supplemented with CBM 7 d ahead of the triple therapy (Group 2). Stool samples were collected before and 2, 4, 7, 15, and 22 d after the starting eradication therapy, and were examined intestinal flora. Patients were required to keep a diary record of their condition.

RESULTS: Obligate anaerobes decreased significantly on d 2, 4, 8 and 15 in Group 1. On the other hand, they did not decrease significantly in Group 2. The Escherichia coli was dominant bacterium in Enterobacteriaceae, but that was replaced by other species such as Klebsiella and Enterobacter after eradication in Group 1. The change was suppressed in Group 2. Abdominal symptoms were less frequent in Group 2 than in Group 1.

CONCLUSION: The combined use of CBM reduced the changes in the intestinal flora and decreased the incidence of gastrointestinal side effects.

**Probiotic mixture decreases DNA adduct formation in colonic epithelium induced by the food mutagen 2-amino-9H-pyrido[2,3-b]indole in a human-flora associated mouse model.**


Horie H, Zeisig M, Hirayama K, Midtvedt T, Moller L, Rafter J.

Consumption of probiotic bacteria such as bifidobacteria has been shown to reduce the risk of colon cancer in animal models. However, the composition and metabolic activities of the intestinal flora of experimental animals are significantly different from those of humans. The aim of the study was to examine whether the probiotic mixture, which consisted of Streptococcus faecalis, Clostridium butyricum and Bacillus mesentericus, could decrease DNA adduct formation induced by 2-amino-9H-pyrido[2,3-b]indole (2-amino-alpha-carboline; AAC) in the colonic epithelium of a human-flora-
associated (HFA) mouse model. Ten HFA mice were divided into a control group (n=4) and a probiotic group (n=6). The control group was administered AAC for 3 days and sacrificed 24 h after the last dose. The probiotic group was administered the probiotic mixture for 2 weeks prior to the administration of AAC. Analysis of DNA adducts with the 32P-high-performance liquid chromatography method was performed on stomach, jejunum and colonic epithelium, representing direct exposure sites of AAC, and colon wall, liver and kidney, representing indirect exposure sites. The mean level of the DNA adducts in the colonic epithelium of the probiotic group was significantly lower than that of control group, while the mean levels at the other sites did not differ significantly between the groups. The results indicated that the probiotic mixture could decrease the DNA adduct formation in the colonic epithelium induced by AAC.

A new factor from Bacillus mesentericus which promotes the growth of Bifidobacterium. Microbios; 2000, 101(399):105-14.


It was reported previously that supernatants of cultures of Bacillus mesentericus TO-A promote the growth of Bifidobacterium species. In this study, a new growth-promoting factor, BM-1, was purified from the supernatant of such a culture and its chemical structure was determined. BM-1 was identified as 3,3-dihydroxyazetidine, and it promoted the growth of several strains of Bifidobacterium.

The role of probiotic cultures in the control of gastrointestinal health.

J Nutr; 2000, 130(2 Suppl):396S-402S.

Rolfe RD.

The use of probiotics to enhance intestinal health has been proposed for many years. Probiotics are traditionally defined as viable microorganisms that have a beneficial effect in the prevention and treatment of specific pathologic conditions when they are ingested. There is a relatively large volume of literature that supports the use of probiotics to prevent or treat intestinal disorders. However, the scientific basis of probiotic use has been firmly established only recently, and sound clinical studies have begun to be published. Currently, the best-studied probiotics are the lactic acid bacteria, particularly Lactobacillus sp. and Bifidobacterium sp. However, other organisms used as probiotics in humans include Escherichia coli, Streptococcus sp., Enterococcus sp., Bacteroides sp., Bacillus sp., Propionibacterium sp. and various fungi. Some probiotic preparations contain mixtures of more than one bacterial strain. Probiotics have been examined for their effectiveness in the prevention and treatment of a diverse spectrum of gastrointestinal disorders such as antibiotic-associated diarrhea (including Clostridium difficile-associated intestinal disease), infectious bacterial and viral diarrhea (including diarrhea caused by rotavirus, Shigella, Salmonella, enterotoxigenic E. coli, Vibrio cholerae and human immunodeficiency virus/ acquired immunodeficiency disorder, enteral feeding diarrhea, Helicobacter pylori gastroenteritis, sucrose maltase deficiency, inflammatory bowel disease, irritable bowel syndrome, small bowel bacterial overgrowth and lactose intolerance. Probiotics have been found to inhibit intestinal bacterial enzymes involved in the synthesis of colonic carcinogens. There
are many mechanisms by which probiotics enhance intestinal health, including stimulation of immunity, competition for limited nutrients, inhibition of epithelial and mucosal adherence, inhibition of epithelial invasion and production of antimicrobial substances. Probiotics represent an exciting prophylactic and therapeutic advance, although additional investigations must be undertaken before their role in intestinal health can be delineated clearly.

**Probiotic Bio-Three induces Th1 and anti-inflammatory effects in PBMC and dendritic cells.**


**Hua MC, Lin TY, Lai MW, Kong MS, Chang HJ, Chen CC.**

AIM: To investigate the immune response of peripheral blood mononuclear cells (PBMCs) and dendritic cells (DCs) that were stimulated by probiotic preparations.

METHODS: PBMCs were isolated, cultured, and stimulated with Bio-Three (a mixture of Bacillus mesentericus, Clostridium butyricum and Enterococcus faecalis; 10(5), 10(6) and 10(7) CFU/mL for 24 h). Cytokine production of (1) circulating PBMCs; (2) PBMCs stimulated by probiotic preparation; (3) monocyte-derived DCs; and (4) DC and T cell co-culture was determined by enzyme-linked immunosorbent assay. Phenotypic analysis of circulating PBMCs was also investigated by flow cytometry. Blood was obtained from individuals who consumed Bio-Three (10(9) CFU/d B. mesentericus, C. butyricum and E. faecalis) for 2 wk, or those who did not take probiotics orally.

RESULTS: In culture supernatants, interferon-gamma (IFN-gamma) and interleukin (IL)-10 production increased, but IL-4 and tumor necrosis factor-alpha (TNF-alpha) production by PBMCs decreased after 1 and 2 wk of probiotic treatment. Flow cytometry was also performed on day 14 and detected enhanced expression of CD11b, HLA-DR, CD4, CD45RA, CD25, CD44 and CD69 in response to Bio-Three. Furthermore, IL-10 and IL-12 were upregulated in supernatants of monocyte-derived DCs, and IFN-gamma and IL-10 were enhanced in supernatants of CD4(+) T cells co-cultured with DCs.

CONCLUSION: Bio-Three appeared to stimulate the Th1 immune response, downregulate pro-inflammatory cytokines (TNF-alpha) and upregulate anti-inflammatory cytokine (IL-10). Probiotics could be effective in activation of PBMCs and DCs.