Published in final edited form as:
Nutr Clin Care. 2004 ; 7(2): 56–68.

Probiotics and Medical Nutrition Therapy

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Abstract

Probiotics have been defined by The Food Agricultural Organization/World Health Organization (FAO/WHO) as "live microorganisms which when administered in adequate amounts confer a health benefit to the host." They have been used for centuries in the form of dairy-based fermented products, but the potential use of probiotics as a form of medical nutrition therapy has not received formal recognition. A detailed literature review (from 1950 through February 2004) of English-language articles was undertaken to find articles showing a relationship between probiotic use and medical conditions. Medical conditions that have been reportedly treated or have the potential to be treated with probiotics include diarrhea, gastroenteritis, irritable bowel syndrome, and inflammatory bowel disease (Crohn's disease and ulcerative colitis), cancer, depressed immune function, inadequate lactase digestion, infant allergies, failure-to-thrive, hyperlipidemia, hepatic diseases, *Helicobacter pylori* infections, genitourinary tract infections, and others. The use of probiotics should be further investigated for possible benefits and side-effects in patients affected by these medical conditions.

Keywords

probiotic; medical nutrition therapy; diet; disease

PROBIOTICS AND HEALTH

Probiotics are nonpathogenic organisms (yeast or bacteria, especially lactic acid bacteria) in foods that can exert a positive influence on the host's health.[1] The theory is that live microorganisms within food or in the form of a supplement improve the microbial balance of the intestinal tract.[2] The most commonly consumed probiotics are fermented dairy products such as yogurt and buttermilk. Probiotic therapy is not a new idea; it dates back almost 100 years to Elie Metchnikoff, who suggested that Bulgarian peasants lived longer lives because of their yogurt consumption. In the 1930s, a Japanese physician, Minoru Shirota, suggested that the right mix of bacteria in the gut could prevent disease. Miso soup, made from fermented soybean paste, is a staple of the Okinawan diet.

It has been suggested that disrupting the delicate balance in the gastrointestinal tract can contribute to diarrhea (antibiotic-associated diarrhea, traveler's diarrhea, intestinal infections),[1,3] gastroenteritis, constipation, irritable bowel syndrome, inflammatory bowel disease (Crohn's disease and ulcerative colitis), food allergies, and certain cancers.[4–6] On the contrary, a balanced or "normal" enteric flora may competitively exclude possible pathogenic organisms, stimulate the intestinal immune system,[7,8] and produce nutrients and other substances such as short-chain fatty acids, vitamins,[9] amino acids (arginine, cysteine, and glutamine), polyamines, growth factors, and antioxidants.[7]

PROBIOTIC SUPPLEMENTATION STUDIES

Studies show that commercial probiotic consumption often increases specific intestinal microflora, but usually not the total count of bacteria found in the intestine. It is also evident

in the majority of reported research cases that specific bacteria do not increase unless subjects consume very high dosages of probiotics in the form of supplements, not those naturally found in foods.

One of the early double-blind, placebo-controlled studies (20 men; 10/group) utilizing a commercially available probiotic was conducted by Spanhaak and associates,[10] who reported an increase in *Lactobacillus* count. Benno and Mitsuoka[11] reported that *Bifidobacterium longum* administered as a pharmaceutical in adults resulted in higher fecal bifidobacerial and lower clostridial counts, lower fecal pH, and lower fecal ammonia concentrations. A study of 64 adults by Ling et al.[12] showed that consumption of *Lactobacillus GG* resulted in higher fecal counts of *Lactobacillus GG*, decreased fecal beta-glucuronidase, nitroreductase, and glycocholic acid hydrolase activities. There was also a decrease in urinary p-cresol excretion, which is a product of colonic *Bacteriodes fragilis.* Studies in which bottle-fed infants were given an inoculum of *Bifidobacterium bifidum* and compared with control infants showed that *B. bifidum* did appear in the stools of infants in the treatment groups.[13,14]

SURVIVAL OF GASTROINTESTINAL MICROFLORA

The benefit of probiotics is based on the survival of these bacterial or yeast cultures in the gastrointestinal tract and the resulting effects they might generate to overall health. Studies evaluating how well probiotics fare through the gastrointestinal tract show that about 10–30% of probiotics survive. This depends on a number of variables, including the type of probiotic.[15,16]

Probiotic bacteria's survival in food products also varies according to strain differences, the product's storage conditions, the chemical composition of the product to which the probiotics are added, and other interactions between the components of the product.[17] Table 1[3,18] lists the most commonly used bacterial strains for probiotic purposes. Certain strains of lactic acid bacteria, such as *Lactobacillus plantarum* and *Lactobacillus rhamnosus*, have proved to be more effective in preserving the microbial balance of the colon, preserving the key nutrients produced by the bacteria, eliminating toxic components from food, protecting from decay, and obliterating pathogens.[7] In addition to the influence of various strains, several other characteristics essential for probiotics are adherence to cells, gastric acid and bile stability, production of antimicrobial substances, and activity against pathogenic bacteria.[19] Probiotics, regardless of their strain, must be resistant to acid pH and biliary acids in order to colonize the intestine.[3]

PROBIOTIC USE IN MEDICAL CONDITIONS

Even if the probiotics are viable, certain medical conditions and their relationships to probiotics are highly controversial. Their possible impact on gastrointestinal health is just beginning to be understood, and it must be remembered that multiple variables exist, along with the possibility of remission due to unknown factors. What follows is a brief review of the possible beneficial effect of probiotics on diarrhea, gastroenteritis, irritable bowel syndrome, inflammatory bowel disease (Crohn's disease and ulcerative colitis), cancer, the immune system, lactose digestion, infant allergies, failure-to-thrive, hyperlipidemia, hepatic disease, *Helicobacter pylori* infections, genitourinary tract infections, and other medical conditions (Table 2).[20]

DIARRHEA

Probiotics have been reported to treat three types of diarrhea: antibiotic-associated, traveler's, and infectious. The most common side effect of antibiotic therapy is diarrhea, which occurs in about 20% of patients due to a disruption in the balance of the endogenous flora in the colon.

[1,3] Antibiotic use can encourage the growth of pathogenic bacteria, specifically *Clostridium difficile* and *Klebsiella oxytoca.*[1,3] There have been several clinical trials attempting to determine the efficacy of administering probiotics to patients experiencing antibiotic-associated diarrhea (Table 3).[21] Three randomized, double-blind, controlled studies reduced the rate of occurrence of antibiotic-associated diarrhea using orally administered *Saccharomyces boulardii.* In animal models, *S. boulardii* has also been shown to decrease *C. difficile.*[3] *Lactobacillus rhamnosus* GG, another probiotic strain showing promise in treating AAD,[3,21] has been shown to colonize the colon of patients receiving erythromycin, penicillin, and ampicillin therapy.[3] The effects of other probiotic strains on antibiotic-associated diarrhea have been mixed. For example, Gotz et al. reported that a mixture of *Lactobacillus acidophilus* significantly prevented diarrhea, but two other studies show that the same mixture did not significantly prevent diarrhea (Table 3). Marteau et al. suggested that this could be due to differences in probiotic preparation and in Table 3[1] he shows a summary of different probiotics.[1,21]

Traveler's diarrhea also occurs in about half of the people who travel to underdeveloped or high-risk countries, and can range from mild to severe.[1] At least eight clinical trials have been conducted testing the use of orally administered probiotics to prevent traveler's diarrhea (Table 4).[1] A randomized study by Black and colleagues used a mixture of probiotic strains (*L. acidophilus, L. bulgaricus, B. bifidum, and S. thermophilus*) or a placebo to treat 94 Danish tourists traveling to Egypt for 2 weeks.[1,22,23] The incidence of traveler's diarrhea in the tourists was reduced significantly from 71% (placebo group) to 43% (probiotic group).[1,22,23] The oral administration of *L. rhamnosus* GG also resulted in a decreased occurrence of traveler's diarrhea, with the most significant study using 245 New Yorkers that traveled to a developing nation (3.9% probiotic group versus 7.4% placebo group).[1,24] Many other probiotic strains have had insignificant results (Table 4).[1]

The range of causes for intestinal infections causing diarrhea vary greatly. Some of the possible pathogens include *Shigella, Salmonella, Campylobacter, Colostridium difficile,* rotavirus, enterotoxigenic *Escherichia coli,* and *Helicobacter pylori.*[1,25] Infection with rotavirus is the most common cause of severe diarrhea in children, and probiotic therapy (*Lactobacillus GG*) has been shown to be effective in reducing the duration of rotavirus enteritis infection.[26] A meta-analysis suggested that *Lactobacillus* is an effective treatment for children with acute infectious diarrhea.[27]

No significant benefit was seen regarding the use of *L. acidophilus* and *L. bulgaricus* for people with *E. coli* infection in a double-blind, placebo-controlled study.[28] Also, no benefit was seen with the use of *E. faecium* strain SF68 for adults with *Vibrio cholerae* and *E. coli* infection.[29] Upon colonization of the gastric mucosa, *H. pylori* infection can lead to gastritis, duodenal and gastric ulcers, and even some malignancies.[1,25] Some *Lactobacillus* strains have shown antagonistic actions against *H. pylori* in vitro[56,30] and in a gnotobiotic murine model.[31,32] The few human studies regarding *Lactobacillus* and *H. pylori* infection have had conflicting results.[25] Guandalini et al.[26] found that *Lactobacillus* GG helped their child subjects recover more rapidly from diarrhea caused by rotavirus enteritis; however, they also stated that information is limited as to the role of this probiotic in non-rotaviral diarrheal episodes.

GASTROENTERITIS

Inflammation of the mucous membrane of the intestines, or gastroenteritis, is the main cause of acute diarrhea, which generally lasts a few days.[1] The inflammation can result from viral pathogens, bacterial pathogens, or parasites; in children, however, it usually results from rotavirus infection. Oral rehydration therapy is the most common therapy, but does not reduce the duration of diarrhea.[1,3,25] Several controlled, randomized trials have shown a shortened

duration of rotavirus-associated diarrhea and gastroenteritis in infants with the use of probiotics, especially with *L. rhamnosus* GG (Table 5).[1,25] In addition, several nonrandomized trials have indicated a preventive effect of some fermented products on the incidence of diarrhea in children.[33,34] The results of adult gastroenteritis studies with probiotics have been less significant.[1]

IRRITABLE BOWEL SYNDROME

Symptoms most often associated with irritable bowel syndrome (IBS) may include, but are not limited to constipation and/or diarrhea, abdominal pain, flatulence, and bloating. In a randomized, controlled clinical trial conducted on 60 patients, Nobaek et al.[35] reported that orally administrated *L. plantarum* reduced pain and flatulence. In a small study of IBS sufferers given *L. plantarum*, participants demonstrated a small, yet significant decrease in abdominal pain.[36] Kim et al.[37] administered a probiotic formulation (VSL#3 twice daily for 8 weeks) to 25 patients with IBS in a randomized, controlled trial. There was a significant reduction in abdominal bloating, indicating that VSL#3 may assist patients with IBS.[37] In another study conducted by Brigidi et al.[38] 10 patients with IBS were given VSL#3, resulting in fecal microbiota showing increased concentrations of *Lactobacilli, Bifidobacteria, Streptococcus theromophilus*, and fecal beta-galactosidase.[38]

INFLAMMATORY BOWEL DISEASE

Inflammatory bowel disease (IBD) encompasses intestinal inflammatory diseases such as Crohn's disease and ulcerative colitis. These diseases all result from unknown origins, but intestinal flora disturbances[39,40] and a defective mucosal barrier[41] have been hypothesized as contributing factors. Intestinal infections sometimes mimic IBD symptoms but disappear with antibiotic therapy. There have been several IBD animal studies using probiotics with promising results[1,39]; however, only a few trials have been conducted in humans.[23,42] A study involving 14 children with Crohn's disease receiving *L. rhamnosus* GG found an increase in immunoglobulin A immune response.[43] This study has been criticized for its small sample size and short duration of 10 days. Additionally, *S. boulardii* has been shown to significantly reduce disease activity and the frequency of bowel movements in 20 Crohn's disease patients.[44] *S. boulardii* was also noted to reduce relapse rates and to extend remission time in patients with Crohn's disease.[45] Malchow[46] conducted a randomized, controlled clinical trial that involved 28 patients with Crohn's disease (only in the colon) who received either their standard treatment (glucocorticoids) plus a capsule containing a viable nonpathogenic *E. coli* strain Nissle 1917 or the steroid and a placebo. He found that administration of nonpathogenic *E. coli* reduced the risk for relapse and decreased the need for glucocorticoids.[46]

Further research is needed on probiotic treatments for ulcerative colitis.[23,25] A study by Venturi et al.[47] found that a combined probiotic preparation known as VSL#3 effectively maintained remission in mesalazine-intolerant ulcerative colitis patients. The VSL#3 preparation included four strains of lactobacilli, three strains of bifidobacteria, and *Streptococcus salivarius.* Gionchetti et al.[23] also used the VSL#3 combination in a study and found that it prevented the development of chronic pouchitis following pouch-anal anastomosis surgery treatment for ulcerative colitis.

CANCER

Probiotics have been found by several researchers to decrease fecal concentrations of enzymes and secondary bile salts, and reduce absorption of harmful mutagens that may contribute to colon carcinogenesis.[48] Other studies suggest that normal intestinal flora can influence carcinogenesis by producing enzymes (glycosidase, B-glucuronidase, azoreductase, and nitroreductase) that transform precarcinogens into active carcinogens.[12,49–52] Certain

probiotics may protect the host from this activity. *L. acidophilus* and *L. casei* supplementation in humans helped to decrease levels of these enzymes, as shown by fecal specimens.[53–55] In animal studies, the bacterial enzymes aforementioned have been suppressed with the administration of *Lactobacillus GG*.[45] Other lactic acid bacteria have shown similar results; however, the relationship between enzyme activity and cancer risk needs further investigation.

Certain studies have shown an effect of probiotics on tumor growth. Burns and Rowland[56] suggested that increasing the amount of lactic acid bacteria in the colon decreases the ability of microflora to produce carcinogens. A randomized, controlled study by Aso and Akazan[57] of 48 Japanese patients demonstrated that the recurrence of bladder tumors was delayed with daily intake of *L. casei.* They performed another study that was larger (125 patients) and placebo-controlled, and found that *L. casei* reduced the recurrence of tumors in all patients except those with more than one recurrent tumor.[58] The hypothesis is that lactobacilli might bind mutagenic compounds in the intestine, which would reduce the absorption of these harmful mutagens.[59] A short-term study has confirmed this hypothesis by measuring the excretion of mutagens in urine after consumption of hamburger meals supplemented with *L. acidophilus*.[60] In an animal model with dimethylhydrazine (DMH)-induced colon cancer, it was shown that *Lactobacillus* GG significantly reduced the incidence of colon tumors.[61] Lactic acid bacteria administered to animals have been shown to prevent carcinogen-induced preneoplastic tumors and lesions.[62] Hirayama et al.[63] found that lactic acid bacteria reduced the growth and viability of the HT-29 human colon cancer line. A review article by Vanderhoof[64] describes a study using two carcinogens to test the effects of probiotics on the prevention of DNA damage in an animal model. The carcinogens used were N-methyl-N-nitro-N-nitrosoguanidine (MNNG) and DMH, Several probiotic strains were tested in this study, including *L. gasseri, L. confusus, S. thermophilus, B. breve, B. longum,* and *L. acidophilus.* All of the strains showed an antigenotoxic effect after MNNG administration.[64] Similar studies have shown that pretreatment with *L. acidophilus, L. confusus, L. gasseri, B. longum,* and *B. breve* inhibited DNA damage from DMH, but that only one of four *S. thermophilus* strains and only one of three *L. delbrueckeii* strains were protective.[48] Another study found that all five of the lactic acid bacteria strains that they tested inhibited the growth of the MCF7 breast cancer cell line, although *B. infantis* and *L. acidophilus* were the most effective.[65]

Several mechanisms have been proposed as to how lactic acid bacteria may inhibit colon cancer; these include: enhancing the host's immune response, altering the metabolic activity of the intestinal microflora, binding and degrading carcinogens, producing antimutagenic compounds, and altering the physiochemical conditions in the colon.[63] Studies have suggested that the host's immune response may be stimulated by *B. infantis*, leading to tumor suppression or regression.[63] The metabolic activity of the intestinal microflora may also be altered with administration of lactic acid bacteria. Goldin and Gorbach[66] studied the effect of *L. acidophilus* on three bacterial enzymes (β-glucoronidase, nitroreductase, and azoreductase) in 21 volunteers for 10 days, *L. acidophilus* reduced the activity of the carcinogen-releasing bacterial enzymes. Binding and degrading carcinogens may be possible by lactic acid bacteria supplementation. The production of antimutagenic compounds in the colon has been demonstrated with *B. longum* administration in rats. Azomethane-induced colon tumor development was also suppressed with a decrease in colonic mucosal cell proliferation and tumor ornithine decarboylase and ras-p21 activities.[63] The alteration of the physicochemical conditions in the colon may influence colon cancer, and Modler et al.[67] suggest that reducing the intestinal pH may prevent the growth of putrefactive bacteria. In a 3-month study, *L. acidophilus* and *B. bifidum* were administered to patients with colonic adenomas. The result was a decrease in fecal pH and cell proliferative activity in the upper colon.[68] The mechanisms of the links of probiotics to antitumor activity are not completely clear, but offer useful potential material for future cancer studies.

IMPROVED IMMUNE SYSTEM

Probiotics have also been shown to influence several aspects of immune function. In animal and human studies with different bacteria treatments (*L. casei, L. acidophilus,* or *B. bifidus*), an enhanced secretory immunoglobulin (Ig) A production was observed.[70] *L. casei* is most effective in stimulating secretory Ig A[70] and increasing the systemic immune response in malnourished animals.[71] Another study showed that mice fed lactic acid bacteria had higher splenocyte proliferation in response to mitogens for T and B cells.[69,72] Several studies have shown that probiotics (*L. casei, L. rhamnosus* GG, and other strains) can affect cytokine production.[69] In addition, several studies have shown that probiotics promote a nonspecific immune response by enhancing phagocytosis of pathogens.[69] The mechanisms by which probiotics affect the immune system and its responses are still yet to be determined.

IMPROVED LACTOSE DIGESTION

It is well established that lactose is digested better in fermented dairy foods such as yogurt than in non-fermented dairy products.[73–78] Despite being studied extensively, the mechanisms involved have not clearly been deciphered. The viability of lactic acid bacteria has been proposed to be involved with this improved digestibility because pasteurization is known to reduce lactose digestibility. [1,74,76,78] In 1991, Martini and colleagues[79] proposed that the improved digestibility was partially due to the activity of bacterial enzymes (β-galactosidases) produced from the two lactic acid bacteriums used to ferment milk to yogurt (*Streptococcus salivarius* subsp *thermophilus* and *Lactobacillus delbrueckii* subsp *bulgaricus*). Bacterial enzymes synthesized from these bacteria are thought to be responsible for the improved lactose digestion.[80,81] Researchers hypothesized that different strains and species of lactic acid bacteria would digest lactose more or less efficiently due to their varying activity of bacterial enzymes. When they tested different yogurts on seven lactase-deficient subjects, they found that all yogurts improved lactose digestion (despite their varying bacterial enzyme activity), but that different lactic acid bacteria strains resulted in different levels of improved lactose digestion. For example, *B. bifidus* milk gave the subjects only minimal improvement, while *L. bulgaricus* milk resulted in almost complete lactose digestion.[79]

INFANT ALLERGIES

Alverez first suggested in 1939 that poi be used as a substitute food for allergic people.[82] Poi is a potential probiotic found in the Pacific Islands made from the starchy corm of the Taro plant. During World War II, many military-associated people used poi as a substitute starch for people allergic to cereal or grain.[83] Later, Dr. Jerome Glaser, a pediatrician and allergist visiting Hawaii in 1961, observed that many infants in Hawaii were provided poi, especially infants with allergies or gastrointestinal problems.[84] He suggested that infants allergic to cereal could use poi as a substitute. Glaser reported that 19 rice-fed babies and 28 poi-fed babies had similar growth curves over a 2-month period. He also noted that only three of the 22 poi-fed babies (14%) had hematocrits that were 30 or less, compared with three out of 11 rice-fed infants (27%). Roth et al.[85] supported Glaser's findings when they concluded that poi was definitely well tolerated by babies, showing that poi may be regarded as a useful alternative when there is a family history of cereal allergy. Later, a study by Kalliomaki et al.[86] found that expectant mothers given a capsule of *Lactobacillus GG* for 2 weeks prior to delivery followed by their infants receiving the same capsule from birth to age 6 months resulted in half of the experimental infants developing eczema during that time period. The occurrence of eczema in infancy is a good indicator that a food allergy will develop later in childhood. These positive research results have prompted some researchers to suggest that probiotics might be a novel approach to treating food allergies.[87]

FAILURE-TO-THRIVE

A few studies on the use of poi and failure-to-thrive were completed, but they date back to the mid 1960s. Glaser et al.[84] reported that 12 preterm infants consumed poi and thrived as well as other preterm infants (of comparable weight and size). A case study of a failure-to-thrive premature infant weighing 1500 grams noted that the infant was on various formulas but gained only 100 grams in 54 days. The infant's test results were all negative, including gastrointestinal x-rays, sweat electrolytes, carbohydrate utilization tests, and blood chemistry tests. She responded positively when provided poi and was able to maintain a healthy weight (2250 to 2500 grams). The authors therefore reported that poi could be safely recommended as a food for any very young infant, but some doctors question this because it is not sterilized.[84] These studies also occurred more than 50 years ago, and recommendations for future probiotic research would include studies with failure-to-thrive infants.

HYPERLIPIDIMIA

Human and animal studies have suggested that the use of dairy products fermented with probiotics (lactic acid bacteria and bifidobacteria) may reduce serum lipid levels.[78,88–93] Two studies with normal-lipidemic subjects reported that probiotic administration resulted in a reduction in serum triglycerides (19% and 27%, respectively), along with slight changes in serum total and LDL cholesterol.[94] The proposed mechanism by which probiotics may decrease serum cholesterol is suggested to be related to the fermentation of indigestible dietary carbohydrates. Products of bacterial fermentation, specifically short-chain fatty acids, may inhibit cholesterol synthesis in the liver and/or cause the mobilization of plasma cholesterol to the liver.[94] Some gastrointestinal bacteria may also prevent cholesterol absorption by deconjugating bile salts that then affect cholesterol metabolism. Taranto et al.[95] reported that administration of *Lactobacilllus reuteri* was effective in preventing hypercholesterolemia in mice. In addition, he observed a decrease in total cholesterol (22%) and triglycerides (33%), as well as a 17% increase in the ratio of HDL to LDL. In a study conducted by Usman and Hosono,[96] *Lactobacillus gasseri* was shown to lower serum lipids in hypercholesterolemic rats receiving nonfermented milk produced from *L. gasseri.* Total cholesterol and LDL levels by 42 and 64%, respectively.

HEPATIC DISEASES

Mechanisms by which probiotics may treat hepatic encephalopathy have been suggested to include the following: (1) decreased portal blood ammonia by reduced bacterial urease activity, decreased pH due to less ammonia absorption, less intestinal permeability and improved gut epithelium; (2) decreased inflammation and oxidative stress due to reduced ammonia and toxins; and (3) reduced uptake of other toxins.[97] Solga[97] reported that the probiotic combination of VSL#3 reduced stool urease activity and pH, altered the production of short-chain fatty acids, and decreased inflammation in colonic cells.

Probiotics may also be effective in treating nonalcoholic fatty liver disease (NAFLD). Li et al.[98] studied the effects of VSL#3 on 48 ob/ob mice with NAFLD. The results were an improved liver histology, decreased total fatty acid content of the liver, and reduced serum ALT levels.

HELICOBACTER PYLORI INFECTIONS

Studies suggest that probiotics, especially lactic acid bacteria, could be effective in the treatment and prevention of *Helicobacter pylori*, the bacteria cited as a causative agent of ulcers. In vitro studies have suggested that lactic acid bacteria may inhibit or kill *H. pylori* by acting as a bactericide.[99,100] Bifidobacteria and *B. subtilis* may inhibit the growth or attachment of *H. pylori.*[101] Cruchet et al.[99] conducted a double-blind, randomized, controlled

clinical trial to investigate the effects of *H. pylori* colonization in children given *Lactobacillus johnsonii* La 1, which interfered with *H. pylori* colonization by restricting the size of the pathogen's population and delaying colonization. Sakamoto et al.[102] also found that *H. pylori* could be eradicated in gnotobiotic murine models administered *Lactobacillus gasseri* OLL 2716(LG21). Possible mechanisms by which *L. salivarius* eradicates *H. pylori* include the ability of the former to bind to gastric epithelial cells, to produce a high quantity of lactic acid, and to proliferate rapidly.[31] Bhatia et al.[103] suggested the mechanism by which *L. acidophilus* may inhibit *H. pylori* is through the production of lactic acid.

GENITOURINARY TRACT INFECTIONS

It has been suggested that some probiotics may be of benefit in the treatment and prevention of genitourinary tract infections such as vaginitis, urinary tract infections, and bacterial vaginosis.[104–108] According to Reid and Burton[105], the probiotic *Lactobacillus* has the potential to prevent infections of the urogenital and intestinal tracts. Instillation of *Lactobacillus* GR-1 and B-54 or RC-14 directly into the vagina and oral ingestion of the probiotic have been shown to reduce the risk of urinary tract infections by creating a healthier environment within the vaginal flora. Specifically, lactic acid bacteria may protect and treat genitourinary infections because they are easily cultivated, non-pathogenic, population stable, and can adhere to vaginal epithelial cells,[109] forming a protective barrier to prevent colonization of pathogenic bacteria.[110]

OTHER POSSIBLE USES OF PROBIOTICS

Other health conditions that may benefit from probiotic consumption include hypertension,[111–115] illness-related weight-loss,[116,117] and alcohol-induced liver damage.[20,118] Takano[111] suggested that probiotics can be used to treat hypertension when he reported that bioactive peptides produced from the proteolytic action of probiotic bacteria on casein—the protein found in milk—during milk fermentation may be able to lower the blood pressure of hypertensive individuals. Evidence to support his findings can be found in animal studies by Nakamura et al.[112,113] and one human study by Hata et al.,[114] which found that the dairy-based fermentation of milk by *Saccharomyces cerevisiae* and *Lactobacillus helveticus* resulted in the formation of two tripeptides that may have a role in lowering blood pressure. These two tripeptides, valine-proline-proline and isoleucine-proline-proline, act as angiotensin-I-converting enzyme inhibitors (ACE inhibitors) to lower blood pressure. Kalliomaki et al.[86] reported that perinatal administration of probiotics resulted in less atopic eczema in at-risk infants. These potential other benefits of probiotics remain inconclusive and controversial.

CONCLUSION

Probiotics may play a beneficial role in several medical conditions, including diarrhea, gastroenteritis, irritable bowel syndrome, and inflammatory bowel disease (Crohn's disease and ulcerative colitis), cancer, depressed immune function, inadequate lactase digestion, infant allergies, failure-to-thrive, hyperlipidemia, hepatic diseases, *Helicobacter pylori* infections, genitourinary tract infections, and others, all of which are suggested by certain research studies to improve with the use of probiotics. Probiotics should be further investigated for their possible benefits to patients affected by these and possibly other medical conditions. At the same time, the potential for negative side effects from probiotics should also be researched. The correct combination and concentration of gastrointestinal microflora is determined by nature and numerous interdependent variables. Changing one factor such as concentration and trying to "optimize" nature's delicately balanced gastrointestinal environment may very well be altering a condition that nature never intended to alter. The short- and long-term effects of this change may be difficult to evaluate given the multifactorial nature of the gastrointestinal environment.

Acknowledgements

This research was supported by a Research Centers in Minority Institutions award, P20 RR11091, from the National Center for Research Resources, National Institutes of Health. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NCRR/NIH. A grant from the USDA-CSREES (Cooperative State Research, Education, and Extension Service) also supported this research.

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Table 1

Commonly Used Bacterial Strains for Probiotic Purposes

Lactobacillus **Species**	***Bifidobacterium*** **Species**	**Other Lactic Acid Bacteria**	**Non-Lactic Acid Bacteria**
L. acidophilus	*B. adolescentis*	*Enterococcus faecium*	*Bacillus subtilis*
L. bulgaricus	*B. animalis*	*Streptococcus thermophilus*	*Escherichia coli strain nisslle*
L. casei	*B. bifidum*		*Saccharomyces boulardii*
L. rhamnosus GG	*B. breve*		*Saccharomyces cerevisiae*
L. plantarum	*B. infantis*		
	B. longum		
	B. thermophilus		

From reference [3] and [18]

Table 2

Possible Probiotic Benefits (adapted from Goldin[20])

Intestinal Disorders
Diarrhea
Antibiotic-associated
Traveler's
Pathogen-induced or infectious
Gastroenteritis
Irritable bowel syndrome
Inflammatory bowel disease
Crohn's disease
Ulcerative colitis
Pouchitis
Lactase digestion
Other Medical Disorders
Cancer
Helicobacter pylori infections
Hepatic diseases
Hyperlipidemia
Genitourinary tract infections
Improved immune function
Food substitute in allergies
Nutritional Supplement for Weight Gain
Faliure-to-thrive
Cancer cachexia
AIDS
Pancreatitis/cystic fibrosis
Inflammatory bowel disease

Table 3

Clinical Trials Showing Significant Therapeutic Effects of Probiotics in Prevention of Antibiotic-associated Diarrhea (from Marteau et al.[1])

Study	Antibiotic	Probiotic	Study Size	Blind Study	Probiotic Group vs. Control Group
Gotz, 1979	Ampicillin	*Lactobacillus acidophilus* + *Lactobacillus bulgaricus*	98	Yes	8.3% vs. 21%
Clements, 1983	Neomycin	*L. acidophilus* + *L. bulgaricus*	39	No	20% vs. 42%
Witsell, 1995	Amoxicillin-clavulanate	*L. acidophilus* + *L. bulgaricus*	27	No	Positive*
Borgia, 1982	Antituberculous	*Enterococcus faecium SF68*	200	No	5% vs. 18%
Wunderlich, 1989	Miscellaneous	*E. faecium SF68*	45	Yes	8.7% vs. 27.2%
Colombel, 1987	Erythromycin	*Bifidobacterium longum*	10	Yes	Positive*
Siitonen, 1990	Erythromycin	*Lactobacillus rhamnosus GG*	16	No	Positive*
Young, 1997	Miscellaneous	*L. rhamnosus GG*	188	No	17% vs. 48%
Orrhage, 1994	Clindamycin	*B. longum* + *Lactobacillus*	10	Yes	Positive*
Adam, 1977	β-lactamins or tetracyclins	*Saccharomyces boulardii*	388	Yes	4.5% vs. 17.5%
Surawicz, 1989	Miscellaneous	*S. boulardii*	180	Yes	9.5% vs. 21.8%
McFarland, 1995	β-lactamins	*S. boulardii*	193	Yes	7.2% vs. 14.6%

*The authors reported a positive effect of the probiotic but did not provide the percentage of subjects with antibiotic-associated adverse effects in the two groups.

Table 4

Clinical Trials of Probiotics Used to Prevent Traveler's Diarrhea (from Marteau et al.[1])

Study	Probiotic	Study Size	Probiotic Group vs. Control Group
Pozo-Olano, 1978	*Lactobacillus acidophilus* + *Lactobacillus bulgaricus*	50	35% vs. 29% (NS)
Kollaritsch, 1983	Lactobacilli	212	55% vs. 51% (NS)
Katelaris, 1995	*Lactobacillus fermentum strain KLD*	282	23.8% vs. 23.8% (NS)
Katelaris, 1995	*L. acidophilus*	282	25.7% vs. 23.8% (NS)
Black, 1989	*L. acidophilus* + *Streptococcus thermophilus* + *Bifidobacterium bifidum* + *L. bulgaricus*	81	43% vs. 71% ($P = 0.02$)
Kollaritsch von, 1993	*Saccharomyces boulardii*	1016	28.7% vs. 39.1% ($P < 0.05$)
Oksanea 1990	*Lactobacillus rhamnosus GG*	756	41% vs. 46.5% ($P = 0.065$)
Hilton, 1997	*L. rhamnosus GG*	245	3.9%/day vs. 7.4%/day ($P = 0.05$)

Table 5

Clinical Trials on Infants Showing Significant Therapeutic Effects of Probiotics Used in Acute Gastroenteritis (from Marteau et al.[1])

Study	Disorder	Probiotic	Study Size
Curative Treatment			
Isolaurl, 1991	Rotavirus-associated diarrhea	*Lactobacillus rhamnosus GG*	71
Kaila, 1992		*L. rhamnosus GG*	39
Majamaa, 1995		*L. rhamnosus GG*	49
Isolaurl, 1994		*L. rhamnosus GG*	42
Sugita 1994		*L. casei Shirota*	32
Raza, 1995	Gastroenteritis	*L. rhamnosus GG*	32
Pant, 1996		*L. rhamnosus GG*	26
Guarino, 1997		*L. rhamnosus GG*	100
Shornikova, 1997		*L. rhamnosus GG*	123
Guandalini, 2000		*L. rhamnosus GG*	287
Bellomo, 1980*		*Enterococcus faecium SF68*	104
Chapoy, 1966		*Saccharomyces boulardii*	38
Shornikova 1997		*L. reuteri*	66
Prevention			
Saavedra, 1994	Acute diarrhea or rotavirus	*Bifidobacterium bifidum* + *Streptococcus thermophllus*	55

* G. Boudraa, unpublished results, 1996.