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Probiotics and Their Potential Health Claims

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Many studies have attempted to identify specific positive health effects of probiotics. One of the challenges in generalizing health effects of probiotics is that different strains exert disparate effects on human health. As a result, the efficacy of one strain or species cannot necessarily be inferred from another. The objective of this review is to examine the current scientific literature that could be used as the basis for potential health claims. More specifically, this paper will review existing evidence of different probiotic strains to prevent and treat diarrhea, treat irritable bowel syndrome (IBS), treat inflammatory bowel disease, and prevent colon cancer. The strongest evidence is related to the use of Lactobacillus rhamnosus *GG in the prevention and treatment of rotavirus-associated diarrhea. Further examination of the literature also shows promise in the treatment of some forms of IBS with probiotics. Future studies that use consistent supplementation regimes will allow more definitive conclusions to be drawn on the effects of probiotics on IBS, inflammatory bowel disease, and colon cancer.*

Key words: colon cancer, diarrhea, inflammatory bowel disease, irritable bowel syndrome, probiotic bacteria

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INTRODUCTION

Many studies have attempted to identify specific positive health effects of probiotics. While Europe has embraced the idea of probiotic therapy, North America is slow to follow.[1] The objective of this review is to examine the current scientific literature that could be used as the basis for potential health claims. More specifically, this paper will review studies that report the efficacy of different probiotic strains to prevent and treat diarrhea, treat irritable bowel syndrome (IBS), treat inflammatory bowel disease (IBD), and prevent colon cancer.

Probiotics are defined as "live microorganisms [that] when administered in adequate amounts confer a health benefit on the host."[2] Probiotic bacteria either alone or in combination are sold in capsules or powders, or are used in the production of (or contained in) various fermented products. Table 1 lists common probiotic bacteria. Fermented milk products such as yogurt are the most familiar probiotic products, but other fermented foods have also been shown to have potential health benefits, and are therefore potential probiotics. Table 2 lists fermented foods that may be probiotics.[3]

One of the challenges in making generalized health claims on probiotics is that different strains of probiotic bacteria exert disparate effects on human health. Though the efficacy of one strain or species cannot necessarily be inferred from another, the general mechanisms by which they function to promote general gut health may be similar.[4] A large and diverse population of bacteria or microbiota resides in the gastrointestinal tract from the mouth to the anus. Some of the bacteria of this microbiotoa are beneficial to the host, while others are not. The numbers and types of bacteria are influenced by such factors as environment, age, gender, and diet. The human gut contains a balance of beneficial and pathogenic microorganisms.[5] This homeostasis of microorganisms is disrupted when there is an increase in pathogenic bacteria during antibiotic treatment, after some surgery and radiation procedures, and in some disease situations.[5] Generally, in adults, the microbial environment of the gut is relatively stable, particularly at the genus and species level, but dietary components can influence the numbers of particular bacteria.[6–8]

The addition of probiotics to the intestine may reestablish the colonic and intestinal microbial balance. Probiotics may restore balance to the intestinal microbiota population by changing the intestinal pH and producing

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Table 1. Bacteria That Have Been Tested for Their Probiotic Properties

Lactobacilli
Lactobacillus acidophilus spp.; *L. acidophilus* La-1
L. casei spp.; *L. rhamnosus* GG
L. reuteri
L. delbrueckii subsp. *bulgaricus*
L. bulgaricus
L. plantarum spp.; *L. plantarum 299v*
L. fermentum KLD
L. johnsonii
Bifidobacteria
Bifidobacterium bifidum
B. breve
B. infantis
B. longum
Other Bacteria
Enterococcus faecium
Escherichia coli Nissle 1917
Streptococcus salivarius subsp. *thermnophilus*
Yeasts
Saccharomyces boulardii

antimicrobial substances such as bacteriocins, organic acids, and hydrogen peroxide.[5,9,10] The increase in beneficial bacteria results in competition with pathogenic bacteria for nutrients, and thus survival. Experimental animal and human studies have shown that probiotics may reduce intestinal permeability, provide nutrition to the colonocytes by forming short-chain fatty acids and some amino acids, stimulate proliferation of colonocytes, and participate in the regulation of intestinal functions.[8,11–14] Probiotics have also been shown to positively affect immunoglobin production, antibody response, and other cellular immune responses that may contribute to good health and disease resistance.[15]

POTENTIAL HEALTH CLAIM #1: PROBIOTICS HELP TO PREVENT AND TREAT DIARRHEA

Most gastrointestinal infections affecting children in both developed and developing countries originate from rotavirus colonization of the gut.[9,16] Symptoms of infection by rotavirus manifest in gastroenteritis characterized by diarrhea and vomiting.[9] Currently, there is strong evidence indicating that *Lactobacillus casei (L. rhamnosus* L. GG) reduces the duration and severity of diarrhea associated with rotavirus in children.[9,17–19] Supplementation with this probiotic may elicit a general immune response, as well as increased IgA antibodies against rotavirus.[9,17] A recent meta-analysis by Van Niel et al.[16] of clinical trials involving children under 3 years of age indicates that oral administration of *Lactobacillus* spp. such as *L. acidophilus*, *L. rhamnosus*, *L. reuteri*, and *L. bulgaricus* results in a reduction in diarrhea duration by 0.7 days (CI 95% 0.3–1.2 days) and a decrease in diarrhea frequency by 1.6 stools (CI 95% 0.7–2.6 stools) after 2 days of treatment. In the studies examined, *L. rhamnosus* GG was used most frequently, and the dose prescribed most often was 10^{10} to 10^{11} CFU once to twice daily.[16] This meta-analysis was particularly persuasive because the trials examined were randomized, blinded, controlled trials.[16] Additionally, most of the trials were conducted in developed countries, which makes the results more relevant to the North American population.

There is also evidence that probiotics prevent the diarrhea that may occur due to antibiotic use. *Clostridium difficile* and *Klebsiella oxytoca* are two bacteria commonly thought to contribute to the occurrence of antibiotic-associated diarrhea (AAD) by playing a role in the pathogenesis of colonic lesions.[17–20] Decreases in the formation of colonic short-chain fatty acids and hyperosmolarity due to undigested carbohydrates are also thought to contribute to AAD.[21] Probiotics may be efficacious in preventing AAD by stabilizing the microbial population of the colon by restoring resident flora and by stimulating the immune system.[22] Stabilization of the microbial population will result in the production of short-chain fatty acids, specifically acetate, propionate, and butyrate, through fermentation of poly- and oligosaccharides, proteins, peptides, and glycoproteins.[13,23] Short-chain fatty acids are absorbed by diffusion, ion exchanges, or carrier-mediated exchanges.[24] Thus, their presence stimulates colonic water and sodium absorption, which allows for better stool formation.[24] Additionally, short-chain fatty acids provide nutrition to the colonocytes, resulting in stimulated proliferation.[13]

Saccharomyces boulardii yeast and *Lactobacillus* bacteria are the most popular probiotic microrganisms examined for the prevention of AAD.[22] Two recent, independently conducted meta-analyses suggest that the simultaneous administration of probiotics or probiotics plus antibiotics resulted in decreased side effects of antibiotic therapy.[22,25] Few studies reported on AAD duration and severity as an outcome measure. As summarized in Table 3, two of the four studies found that the duration and severity of AAD showed improvement after

Table 2. Some Foods That Contain or Are Produced by Potential Probiotic Bacteria

Food Product	Food Matrix
Yogurt	Milk
Kefir	Milk
Yakult	Milk
Miso	Soybean
Natto	Soybean
Tempeh	Soybean

Table 3. Trials Examining the Effect of Probiotic Therapy Supplemented As an Adjunct to Antibiotic Therapy on the Incidence, Duration, and Severity of Antibiotic-Associated Diarrhea (AAD)

	N	Age of Population	Study Design	Species	Dose (CFU)	Mode of Administration	AAD Incidence*	AAD Duration*	AAD Frequency*
Arvola et al.[27]	119	2 wks–12.8 yrs	Randomized, placebo-controlled	*Lactobacillus* GG	4×10^{10}	Capsule	3/61 vs. 9/58 $P < 0.05$	NS	NS
Vanderhoof et al.[28]	188	6 mos–10 yrs	Double-blind, randomized, placebo-controlled	*Lactobacillus* GG	1 to 2×10^{10}	Capsule	7/93 vs. 25/95 P = NA	4.7 days vs. 5.88 days $P = 0.05$	1.38 ± 0.070 (SEM)/d vs. 2.030 ± 0.130/d
McFarland et al.[29]	193	18–86 yrs	Double-blind, randomized, placebo-controlled	*Saccharomyces boulardii*	3×10^{10}	Capsule	7/97 vs. 14/96 $P = 0.02$	3.0 days vs. 4.0 days $P < 0.05$	NS
Beniwal et al.[30]	202	19–94 yrs	Randomized, open	*Lactobacillus acidophilus* *Lactobacillus bulgaricus* *Streptococcus thermophilus*	2.27×10^{8}	Yogurt	13/105 vs. 23/97 $P = 0.04$	NS	NS

*Treatment vs. placebo.
NA, not applicable; NS, not significant.

Table 4. Gastrointestinal Symptom Improvement in Trials Supplementing Probiotics in Patients with Irritable Bowel Syndrome (continues on facing page)

	N	Treatment Duration	Study Design	Species	Dose (CFU)
Nobaek et al.[34]	60	4 wks	Double-blind randomized, placebo-controlled	*Lactobacillus plantarum* 299v	2×10^{10}
Sen et al.[40]	12	4 wks	Double-blind, placebo-controlled	*L. plantarum* 299v	6.25×10^{9}
Halpern et al.[41]	18	6 wks	Double-blind randomized, placebo-controlled, crossover	*L. acidophilus* LB	2×10^{10}
Gade & Thorn[42]	54	4 wks	Double-blind randomized, placebo-controlled	*Enterococcus faecium*	NA
Niedzielin et al.[43]	40	4 wks	Randomized, placebo-controlled	*L. plantarum* 299v	2×10^{10}

*Treatment versus placebo.
†*P* values given after the treatment number represents significance of improvement in symptoms in the treatment group. *P* values given at the end of data represent significance of placebo vs. treatment.
NA, Not applicable; NS, not significant.

probiotic supplementation.[26–29] However, differences in the probiotics that were given, the size of the dosage, the species, and the mode of administration make it difficult to draw solid conclusions. Though the effectiveness of treatment of ADD by probiotics is promising, larger trials with standardized probiotic preparations would result in a clearer picture of the success of probiotic therapy.

Travelers' diarrhea affects 20% to 50% of travelers from industrialized countries who journey to tropical or semitropical areas.[9] Overall, there exists a paucity of studies that examine the prophylactic effect of probiotic supplementation on traveler's diarrhea. The preventative effect of probiotics on incidence seems to depend on both the bacterial strain and the destination of the traveler.[9,18] Though other bacteria have been studied, *Lactobacillus* bacteria are most commonly examined in the prevention of traveler's diarrhea. In one study, 245 travelers to developing countries were supplemented with *Lactobacillus* GG. The risk of diarrhea was reported to be 3.9% in those taking probiotics, compared with 7.4% in travelers who were taking the placebo ($P = 0.05$).[30] Another study in Austria found that 28.7% of participants who took *Saccharomyces boulardii* supplementation had diarrhea, compared with 39.1% in the placebo group ($P < 0.05$).[31] This study also found the prophylactic effect of *S. boulardii* to be dose dependent.[31] In contrast, Oksanen et al.[32] found that supplementation with *Lactobacillus* GG did not decrease the incidence of diarrhea in 820 participants at two holiday resorts in Turkey (46.5% placebo vs. 41.0% treatment; $P = 0.065$). Similarly, the consumption of 2.0×10^{11} CFU/d *L. acidophilus* LA or *L. fermentum* KLD for 3 weeks did not have any significant effect on the incidence of diarrhea in 282 soldiers sent to Belize.[33] Thus, the efficacy of probiotics in preventing travelers' diarrhea remains to be determined.

Although the evidence supporting the prevention of travelers' diarrhea by probiotics is weak, there seems to be an overall protective effect on the prevention and treatment of diarrhea from AAD, with especially strong evidence on the efficacy of *Lactobacillus* in treating diarrhea from rotavirus infection. Further investigation will allow the determination of ideal species and dosages for the treatment of diarrhea from different causes, as well as the mechanisms through which they act.

POTENTIAL HEALTH CLAIM #2: PROBIOTICS CAN BE USED TO TREAT IRRITABLE BOWEL SYNDROME

IBS is the most frequent diagnosis for gastroenterological disorders, affecting 11% to 14% of the North American population.[34–36] IBS is characterized by abdominal pain, flatulence, and irregular bowel movements. The onset of IBS may be subtle, with symptoms presented over a period of time, or acute, with the development of persistent symptoms after a bout of gastroenteritis.[37] The etiology of IBS is unclear, but may include genetic susceptibility, behavioral factors, and stress factors.[38] Though the causes of IBS have not been fully elucidated, the increased gas production accompanying the syndrome is suspected to be a result of a perturbed intestinal microbial population.[18,39] More specifically, IBS has been associated with lower *Lactobacilli* and *Bifidobacteria* colonies and increases in anaerobic *Clostridium* spp. in place of anaerobic *Bacteriodes* spp. and *Bifidobacterium* spp.[39,40] The onset of symptoms has been associated with lactose and sucrose consumption.[39] However, the ingestion of specific foods, such as those

Mode of Administration	Flatulence*	Abdominal Pain*	Stool Frequency, Consistency, Constipation*	Overall GI Symptoms*
Rosehip drink	44% vs. 18% ($P < 0.05$)†	36% ($P = 0.0004$) vs. 18% (P = NS)	Improved compared with placebo ($P = 0.06$)	44% vs. 26.6% ($P = 0.06$)
Rosehip drink	NS	NA	NS	NA
Capsule	NA	NA	NA	50% vs. 5.6% ($P = 0.018$)
Capsule	NS	NS	NS	81% vs. 41% ($P = 0.002$)
Rosehip drink	55.6% vs. 33.3% (P = NA)	100% vs. 42.1% ($P = 0.0012$)	NA	45% vs. 15% ($P < 0.0001$)

containing lactose and sucrose, is only thought to relate to symptom onset by providing a nutritional source for the overgrown pathogenic microbial population.[39]

Early clinical trials on patients with IBS have suggested supplementation with probiotics as a promising therapy (Table 4). A randomized, double-blind, crossover study showed that the ingestion of 2×10^{10} CFU/d of heat-killed *L. acidophilus* for 42 days by 18 IBS patients resulted in symptom improvement ($P = 0.018$).[41] In this trial, symptom improvement was assessed based on a questionnaire measuring abdominal pain, bloating or gas, daily number of stools, consistency, mucus content, and general physical state.[41] Since the questionnaires were self-administered, further studies with more measurable criteria need to be conducted. Supplementation of a group of 54 men and women who had suffered from IBS for an average of 7 years showed that 81% of patients receiving *Enterococcus faecium* showed an improvement in symptoms according to overall physician assessment, compared with only 41% of those who received the placebo ($P = 0.002$).[42]

More recently, scientists have looked to *L. plantarum* 299v supplementation as a means to treat IBS. In all three studies described, the *L. plantarum* 299v was provided through a fruit drink called Pro Viva (Probi AB, Ltd., Sweden). The drink provided 5×10^7 CFU/mL of *L. plantarum*.[34,40,43] In a double-blind, placebo-controlled, crossover trial, 12 patients with IBS were given 125 mL/d of Pro Viva for 4 weeks, and there were no differences in indicators of colonic fermentation or IBS symptoms between the treatment and placebo groups.[40] When the dose of *L. plantarum* was doubled (250 mL/d of the probiotic drink) in another placebo-controlled, double-blind study of 40 IBS patients over 4 weeks, abdominal pain was significantly better resolved in the treatment group compared with the placebo group ($P = 0.0012$).[43] A larger study, 4 weeks in duration and also double-blind and placebo controlled, randomized 60 patients with IBS into treatment or placebo groups.[34] Patients in the treatment group were given 400 mL of the probiotic drink.[34] Self-administered questionnaires indicated that the treatment group experienced decreased pain and flatulence compared with the placebo groups ($P < 0.01$).[34]

Despite the fact that these clinical trials indicate the effectiveness of probiotic treatment, the different preparation, species, and dosages used make it difficult to answer the question of whether probiotics have a truly beneficial effect on IBS.

POTENTIAL HEALTH CLAIM #3: PROBIOTICS CAN BE USED TO TREAT INFLAMMATORY BOWEL DISEASE

IBD is a general term for diseases that result in chronic and recurring inflammation of the digestive tract. More specifically, IBD encompasses ulcerative colitis, Crohn's disease, and pouchitis, which manifest as inflammation of the large intestine, the digestive tract, or the ileal reservoir, respectively.[18] It is estimated that up to 3.6 million people are affected by IBD in the United States and Europe alone.[44] Recently, it has been indicated that the incidence of ulcerative colitis and Crohn's disease has increased in all age groups with the exception of children under 11 years of age and adults over 80.[45] The peak incidence of IBD occurs between 20 and 30 years of age.[46] Although environmental and genetic etiologies have been implied, the extent to which they are associated with IBD incidence is unclear. Although the etiology of the disease is not definitive, evidence suggests that an imbalance of intestinal bacteria, more spe-

cifically overgrowth of entero-adhesive and entero-emorrhagic *Escherichia coli* and low levels of *Bifidobacteria*, may initiate and perpetuate the inflammation that characterizes these diseases.[18,47,48] Additionally, by invading tight junctions between epithelial cells, pathogenic bacteria may disrupt the barrier function of the gut, resulting in translocation of pathogenic bacteria, which causes an inflammatory immune response.[49] Probiotics likely decrease disease activity and increase remission through decreasing pathogenic bacterial growth by lowering gut pH, enhancing barrier function to prevent the invasion of tight junctions, and stimulating nonspecific and specific immune responses.[50] An in vitro study also indicated that probiotics may decrease adhesion and invasion of epithelial cells.[51] Despite a lack of human trials, studies show that probiotics may play a role in maintenance of IBD remission.[18]

Two large human studies and one smaller study compared the effects of the *E. coli* Nissle strain and mesalazine on ulcerative colitis at a daily dose of 5×10^{10} CFU.[52–54] The rate of relapse of patients taking the traditional mesalazine therapy was comparable to the rate of relapse of those treated with *E. coli*.[52–54] However, the larger trial that lasted one year found that patients in both the mesalazine and *E. coli* treatment groups had high relapse rates of about 70%.[52] Thus, although both treatments produced comparable results, neither was effective in preventing disease relapse.

Another probiotic, *Bifidobacteria*, has also been shown to be effective in maintaining remission when taken as fermented milk as an adjunct to ulcerative colitis therapy. Two studies supplemented a commercial fermented milk product with about 1×10^{10} CFU of *B. breve*, *B. bifidum*, and *L. acidophillus* as an adjunct to regular ulcerative colitis therapy.[46,55] The year-long study found that supplementation was successful in maintaining ulcerative colitis remission.[46] Supplementation over 12 weeks in the second trial found a possible beneficial effect in treating active ulcerative colitis, as shown by lower clinical activity index, endoscopic, and histological scores ($P < 0.05$).[55] However, although the trials were conducted at two separate institutions, only about 20 patients were used in each study.

Probiotics have also been shown to be effective in the prevention of relapse in Crohn's disease (Table 5). Significantly fewer patients relapsed after 6 months of combined treatment with *S. boulardii* and mesalazine (6.25%) compared with those taking mesalazine alone (37.5%) ($P = 0.04$).[56] Treatment effectiveness was further emphasized in a shorter, 7-week trial supplementing *S. boulardii*.[57] This trial found a significant reduction in disease symptoms in patients with Crohn's disease ($P < 0.05$).[57] Trials examining the potential of other probiotics also found effectiveness in therapies that used *E. coli*

Table 5. Trials Examining the Effect of Probiotic Therapy in the Prevention of Relapse of Crohn's Disease.

	N	Treatment Duration	Study Design	Species	Dose (CFU)	Mode of Administration	Rate of Relapse*	Time to Relapse (weeks)*
Guslandi et al.[56]	32	24 wks	Randomized	*Saccharomyces boulardii*	NA	Capsule	1/16 vs. 6/16 ($P = 0.04$)	NA
Plein & Hotz[57]	20	7 wks	Double-blind, randomized, placebo-controlled	*S. boulardii*	1.5×10^{10}	Capsule	Improvement in bowel movement and BEST index scores 107 ± 85 (SD) points vs. 180 ± 61 points ($P < 0.05$)	
Helmut[58]	28	52 wks	Randomized, placebo-controlled	*Escherichia coli* Nissle	5×10^9	Capsule	3/10 vs. 7/10 (P = NS)	NA
Schultz et al.[60]	11	24 wks	Randomized, placebo-controlled	*Lactobacillus* GG	2×10^9	Capsule	3/5 vs. 2/4 (P = NS)	16 ± 4 (SD) vs. 12 ± 4.3 ($P = 0.05$)

*Treatment versus placebo.
NA, Not applicable; NS, not significant.

Nissle or *Lactobacillus*. More specifically, a 12-month supplementation with *E. coli* Nissle 1917 strain at 5×10^{10} CFU reduced relapse in Crohn's disease patients compared with the placebo (30% vs. 70%, respectively).[58] However, the small number of patients used in this trial did not show these differences to be significant. In vitro experiments conducted by Boudeau et al.[59] indicated that *E. coli* Nissle 1917 may help to reduce relapse in Crohn's disease patients by competing with pathogenic *E. coli* strains for adhesion to intestinal epithelial cells, thereby preventing their invasion.[59] Trials examining the effectiveness of other probiotics such as *Lactobacillus* also found significantly improved well-being, decreased gastrointestinal symptoms, and increased maintenance of remission in Crohn's disease patients.[17,60]

Pouchitis occurs when there is a nonspecific inflammation of the ileal pouch reservoir that is created surgically after an ileal-anal anastomosis.[61, 62] The etiology of pouchitis is unknown. It has been shown that remission produced by broad-spectrum antibiotics following surgery can be extended by the use of VSL#3, a mixture of eight bacteria (*L. casei*, *L. plantarum*, *L. acidophilus*, *L. delbrueckii* subsp. *bulgaricus*, *B. longum*, *B. breve*, *B. infantis*, and *S. salivarius* subsp. *thermophilus*) given at a dose of 6 g/d providing 3×10^{12} CFU of viable lyophilized bacteria.[35] However, the protective effect of the probiotic bacteria disappeared when the treatment was stopped.[35] Another study conducted by the same group gave VSL#3 to patients with pouchitis at the same dose for 1 year or until relapse.[36] It was observed that significantly more patients on the VSL#3 treatment were able to maintain antibiotic-introduced remission compared with the placebo group given maize ($P < 0.001$).[36] Several studies have shown that probiotic bacteria often pass through the GI tract without colonization; the probiotic bacteria cannot be found in fecal samples soon after the termination of ingestion.[63] The inability of probiotic bacteria to colonize the GI tract was evident in a trial conducted by Kuisma et al.,[37] in which only 40% of patients consuming *Lactobacillus* GG supplements providing 1 to 2×10^{10} CFU/d were colonized.[37] In this trial, no differences were found in disease activity between treatment and placebo groups.[37]

Probiotics seem to be effective in the treatment of some forms of IBD. However, too few clinical trials have been conducted for a definitive conclusion to be drawn. Future trials may continue to show probiotics as a promising therapy to IBD.

POTENTIAL HEALTH CLAIM #4: PROBIOTICS CAN BE USED TO PREVENT COLON CANCER

Bacteria have enzymatic activity that can be detrimental to health; some enzymes (e.g., β-glucuronidase, β-glucosidase, nitroreductase) cause the formation of carcinogens in digesta as it passes down the gastrointestinal tract. Feeding probiotic bacteria has been shown to reduce the activity of several bacteria that have been implicated in the long-term development of intestinal/colon cancer.[55,64–66] In addition, metabolites produced by probiotics (such as short-chain fatty acids) alter digesta pH and thus can also have a protective effect. The short-chain fatty acid butyrate is important in the metabolism of intestinal cells. Bacteriocins produced by some probiotic bacteria can reduce the number of pathogenic bacteria. Table 6 provides a summary of the enzymes that have been shown to change with probiotic supplementation.[67,68]

Data from two large epidemiological studies did not show any association between the consumption of milk and fermented dairy products and the risk of colon cancer.[69] In addition, the intake of fermented dairy products in a trial conducted in elderly people in the Netherlands revealed similar negative results, in that the intake of fermented dairy products was not shown to be associated with the risk of colon cancer.[70] Despite these negative results, a 28% decrease in mutagens contained in feces was found in one human clinical trial after the consumption of fried meat and *L. acidophilus* fermented milk ($P < 0.02$).[71] Furthermore, studies in rats given *L. bulgaricus* and *B. longum* resulted in reduced incidence and number of induced colonic tumors.[72,73] A trial in which DMH dihydrocloride was used to induce colorectal cancer in mice supplemented with yogurt containing 6×10^9 CFU of *L. bulgaricus* and *S. thermophilus* showed inhibition of tumor progression and promotion.[74] Another study found that supplementation of mini pigs with *L. johnsonii* and *L. reuteri* resulted in decreases in fecal bacterial enzymes ($P < 0.05$).[75] Overall, these studies indicate the possible existence of anticarcinogenic properties of probiotics. However, there is a general lack of human trials that confirm these positive results.

CONCLUSION

This review of the scientific literature of health benefits of probiotics indicates that, at this time, there are not enough data to support health claims. The strongest evidence is related to the use of *L. rhamnosus* GG in the

Table 6. Fecal Enzymes Shown to Change upon Probiotic Supplementation

Change	Enzyme
Decrease	β-Glucuronidase
Decrease	Nitroreductase
Decrease	Azoreductase
Decrease	Detoxifying enzyme activity
Increase	Glutathione S-transferase

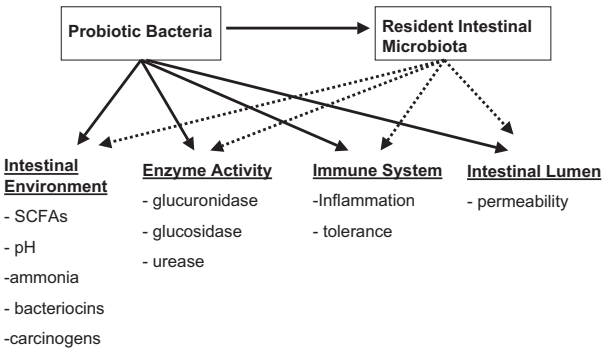

Figure 1. Mechanisms by which probiotic bacteria may effectively prevent and treat gastrointestinal disorders.

prevention and treatment of rotavirus-associated diarrhea. Further examination of the literature also shows promise in the treatment of some forms of IBS with probiotics.

Figure 1 summarizes the mechanisms by which probiotics may effectively prevent and treat gastrointestinal disorders. Probiotics can act directly or they can act through changes brought about to the existing intestinal microbiota. When positive results are obtained with probiotic treatment, it is difficult to identify which mechanism(s) is being affected. Probiotic bacteria may compete with resident intestinal microbiota to influence the intestinal environment; the activity of glucuronidase, glucosidase, and urease enzymes; immune system inflammation and tolerance; or intestinal lumen permeability. Although probiotics are likely to be effective in treating gut-associated disorders, it is difficult to draw conclusions from many studies examining the therapeutic use of probiotics because the strains and dosages used vary greatly. Future studies using consistent supplementation regimes will allow more definitive conclusions to be elicited on the effects of probiotics on IBS, IBD, and colon cancer.

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