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Acidophilus Plus



This document contains peer reviewed studies that support ingredients found in Acidophilus Plus.

PEER REVIEWED STUDIES

Cognitive Health

Consumption of fermented milk product with probiotic modulates brain activity

ABSTRACT

Background & Aims:

Changes in gut microbiota have been reported to alter signaling mechanisms, emotional behavior, and visceral nociceptive reflexes in rodents. However, alteration of the intestinal microbiota with antibiotics or probiotics has not been shown to produce these changes in humans. We investigated whether consumption of a fermented milk product with probiotic (FMPP) for 4 weeks by healthy women altered brain intrinsic connectivity or responses to emotional attention tasks.

Methods:

Healthy women with no gastrointestinal or psychiatric symptoms were randomly assigned to groups given FMPP (n = 12), a nonfermented milk product (n = 11, controls), or no intervention (n = 13) twice daily for 4 weeks. The FMPP contained *Bifidobacterium animalis* subsp *Lactis*, *Streptococcus thermophilus*, *Lactobacillus bulgaricus*, and *Lactococcus lactis* subsp *Lactis*. Participants underwent functional magnetic resonance imaging before and after the intervention to measure brain response to an emotional faces attention task and resting brain activity. Multivariate and region of interest analyses were performed.

Results:

FMPP intake was associated with reduced task-related response of a distributed functional network (49% cross-block covariance; P = .004) containing affective, viscerosensory, and somatosensory cortices. Alterations in intrinsic activity of resting brain indicated that ingestion of FMPP was associated with changes in midbrain connectivity, which could explain the observed differences in activity during the task.

Conclusions:

Four-week intake of an FMPP by healthy

women affected activity of brain regions that control central processing of emotion and sensation.

Source

Tillisch K et al. Consumption of fermented milk product with probiotic modulates brain activity. Gastroenterol 144:1394-1401, 2013.

Digestive Health

Effect of feeding yogurt versus milk in children with acute diarrhea and carbohydrate malabsorption

ABSTRACT

Background:

The aim of this study was to compare the effect of infant formula and the same formula subjected to microbial fermentation (yogurt) on the duration of diarrhea in young children with acute watery diarrhea, with or without reducing substances in stools.

Methods:

One hundred twelve well-nourished children, aged 3 to 24 months, who were admitted to the hospital with acute watery diarrhea were included in a randomized trial. After appropriate rehydration, they were fed either an infant formula (group M, n = 56) or the same formula fermented with *Lactobacillus bulgaricus* and *Streptococcus thermophilus* (group Y, n = 56). The two feedings were comparable in lactose concentration (40 to 42 g/L), pH 4.5, flavor, and texture. The groups were subdivided into those with or without reducing sugars in stools at presentation. The presence of reducing sugars in stool was used as a marker of carbohydrate malabsorption.

Results:

Group M and group Y had comparable clinical characteristics at admission, including the number of patients with reducing sugars in stools (n = 31 in group M and 27 in group Y). The success rate (cessation of diarrhea and appropriate weight gain 7 days after enrollment into the study) was similar in both groups (82% in group M vs. 84% group Y). Clinical failure was 3.6% in both groups. The percentage of patients withdrawn from the study for

medical reasons (5.4% in group M vs. 7.1% in group Y) or withdrawn at the parents' request (8.9% in group M vs. 5.4% in group Y) was similar. Duration of diarrhea and number of stools were significantly less in group Y compared with group M. Forty-eight hours after inclusion, diarrhea was still present in 62% of group M versus in 35% of group Y (P < 0.002). In children with reducing sugars in stools, the rate of success (82%) was similar in groups M and Y, but the duration of diarrhea and number of stools per day were significantly decreased in group Y. Forty-eight hours after inclusion, diarrhea was still present in 75% of group M patients and in 20% of group Y patients who had reducing substances in the stool.

Conclusion:

Young children with acute watery diarrhea, without malnutrition or associated disease, can be equally well treated with feeding of either infant formula or yogurt. Yogurt feeding is associated with a clinically relevant decrease in stool frequency and duration of diarrhea in children who have reducing sugars in stools.

Source

Boudraa G, et al. Effect of feeding yogurt versus milk in children with acute diarrhea and carbohydrate malabsorption. J Pediatr Gastroenterol Nutr. 2001;33:307-313.

Effects of fermented milk containing *Lactobacillus acidophilus* C11285 and *Lactobacillus casei* in the prevention of antibiotic-associated diarrhea: a randomized, double blind, placebo-controlled trial

ABSTRACT

Background:

Antibiotic-associated diarrhea is an important problem in hospitalized patients. The use of probiotics is gaining interest in the scientific community as a potential measure to prevent this complication. The main objective of the present study was to assess the efficacy and safety of a fermented milk combining *Lactobacillus acidophilus* and *Lactobacillus casei* that is widely available in Canada, in the prevention of antibiotic-associated diarrhea.

Methods:

In this double-blind, randomized study, hospitalized patients were randomly assigned to receive either a lactobacilli-fermented milk or a placebo on a daily basis.

Results:

Among 89 randomized patients, antibiotic-associated diarrhea occurred in seven of 44 patients (15.9%) in the lactobacilli group and in 16 of 45 patients (35.6%) in the placebo group (OR 0.34, 95% CI 0.125 to 0.944; $P=0.05$). The median hospitalization duration was eight days in the lactobacilli group, compared with 10 days in the placebo group ($P=0.09$). Overall, the lactobacilli-fermented milk was well tolerated.

Conclusion:

The daily administration of a lactobacilli-fermented milk was safe and effective in the prevention of antibiotic-associated diarrhea in hospitalized patients.

Source

Bradsoliel M, et al. Effects of fermented milk containing *Lactobacillus acidophilus* C11285 and *Lactobacillus casei* in the prevention of antibiotic-associated diarrhea: a randomized, double blind, placebo-controlled trial. *Can J Gastroenterol.* 2007 Nov; 21

In vitro analysis of probiotic strain combinations to inhibit pathogen adhesion to human intestinal mucus

ABSTRACT

We evaluated the ability of commercial probiotic strains (*Lactobacillus rhamnosus* GG, *L. rhamnosus* LC705, *Bifidobacterium breve* 99, and *Propionibacterium freudenreichii* ssp. *shermanii* JS) to adhere alone or in different combinations to immobilized mucus. Probiotic combinations were clearly able to enhance the adhesion of *L. rhamnosus* GG, *L. rhamnosus* LC705, and *P. freudenreichii* ssp. *shermanii* JS. For *L. rhamnosus* GG and *P. freudenreichii* JS, all the combinations significantly improved adhesion to intestinal mucus, from 29.7 to 34.9% and from 1.9 to 2.3%, respectively. The adhesion of *L. rhamnosus* LC705 was improved from 0 to 46.4%. The adhesion of

B. breve 99 was improved only in combination with *L. rhamnosus* GG and *P. freudenreichii* JS. Our results suggest that probiotic combinations could increase the beneficial health effects as compared with individual strains. Combinations of probiotic strains may therefore have synergistic adhesion effects, and such combinations also should be assessed in clinical studies

Source

Collado MC, Meriluoto J, and Selaminen S. In vitro analysis of probiotic strain combinations to inhibit pathogen adhesion to human intestinal mucus. *Food Rsrch Intl.* 2007 June; 40(5): 629-636

Probiotics in prevention of antibiotic associated diarrhoea: meta-analysis

ABSTRACT**Objective:**

To evaluate efficacy of probiotics in prevention and treatment of diarrhoea associated with the use of antibiotics.

Design:

Meta-analysis; outcome data (proportion of patients not getting diarrhoea) were analysed, pooled, and compared to determine odds ratios in treated and control groups.

Identification:

Studies identified by searching Medline between 1966 and 2000 and the Cochrane Library. Studies reviewed Nine randomised, double blind, placebo controlled trials of probiotics.

Results:

Two of the nine studies investigated the effects of probiotics in children. Four trials used a yeast (*Saccharomyces boulardii*), four used lactobacilli, and one used a strain of enterococcus that produced lactic acid. Three trials used a combination of probiotic strains of bacteria. In all nine trials, the probiotics were given in combination with antibiotics and the control groups received placebo and antibiotics. The odds ratio in favour of active treatment over placebo in preventing diarrhoea associated with antibiotics was 0.39 (95% confidence interval 0.25 to 0.62; $P<0.001$) for the yeast and 0.34 (0.19 to 0.61; $P<0.01$ for

lactobacilli. The combined odds ratio was 0.37 (0.26 to 0.53; $P<0.001$) in favour of active treatment over placebo.

Conclusion:

The meta-analysis suggests that probiotics can be used to prevent antibiotic associated diarrhoea and that *S. boulardii* and lactobacilli have the potential to be used in this situation. The efficacy of probiotics in treating antibiotic associated diarrhoea remains to be proved. A further large trial in which probiotics are used as preventive agents should look at the costs of and need for routine use of these agents.

Source

D'Souza AL, et al. Probiotics in prevention of antibiotic associated diarrhoea: meta-analysis. *BMJ.* 2002;324:1361

Probiotics—Compensation for Lactase Insufficiency

ABSTRACT

Yogurt and other conventional starter cultures and probiotic bacteria in fermented and unfermented milk products improve lactose digestion and eliminate symptoms of intolerance in lactose maldigesters. These beneficial effects are due to microbial beta-galactosidase in the (fermented) milk product, delayed gastrointestinal transit, positive effects on intestinal functions and colonic microflora, and reduced sensitivity to symptoms. Intact bacterial cell walls, which act as a mechanical protection of lactase during gastric transit, and the release of the enzyme into the small intestine are determinants of efficiency. There is a poor correlation between lactose maldigestion and intolerance; in some studies, low hydrogen exhalation without significant improvement of clinical symptoms was observed. Probiotic bacteria, which by definition target the colon, normally promote lactose digestion in the small intestine less efficiently than do yogurt cultures. They may, however, alleviate clinical symptoms brought about by undigested lactose or other reasons.

Source

deVrese M, et al. *Probiotics— Compensation for Lactase Insufficiency. Am J Clin Nutr.* 2001;421S-429S

“Probiotic” remedies are not what they seem**ABSTRACT****Objective:**

To assess whether commercially prepared probiotic products contain viable organisms, as claimed by their manufacturers, particularly whether products labeled as containing *Lactobacillus* did so. To identify and quantify as many species as feasible and to compare them with the contents listed on labels.

Design:

Randomized, double-blind trial.

Identification:

Community hospital in Chilliwack, BC.

Main Outcome Measures:

Trial of 10 randomly chosen brands of probiotic preparations bought over-the-counter in British Columbia's lower mainland. Only products claiming to contain *Lactobacillus* were included in this study. Viable organisms in each probiotic brand and quantities of *Lactobacillus* in each product.

Results:

None of the 10 products tested matched their labeled microbiologic specifications. Two brands grew nothing aerobically or anaerobically. No *Lactobacillus* grew in five brands, although their labels stated that this was the main species. Eight brands contained viable cells, but only 10% of the number stated by their manufacturers.

Conclusion:

Most product labels did not adequately identify or quantify microbes. Use of probiotics should not be recommended at this time.

Source

Hamilton-Miller JM, Shah S, and Smith CT. “Probiotic” remedies are not what they seem. *BMJ.* 1996 January 6; 312(7022): 55–56

Effect of lactic acid bacteria on the intestinal production of lactate and short-chain fatty acids, and the absorption of lactose**ABSTRACT**

The characteristic fermentation pattern seen with specific saccharides in incubations with pure cultures of *Lactobacillus acidophilus* and *Bifidobacterium bifidum* disappeared when incubated in 16.7% fecal homogenate. The productions of lactate and short-chain fatty acids in mixed bacterial-fecal incubations were similar to productions in fecal homogenates without *L. acidophilus* and *B. bifidum* and were mainly associated with the specific mono-, di-, and polysaccharides added to the incubate. *B. bifidum* was cultured from ileostomic contents in eight of nine ileostomists after oral administration (2.4×10^{10} cells), but did not influence the concentrations and productions of DL-lactate and short-chain fatty acids in the ileostomic outputs and incubates. Large amounts of ingested lactic acid bacteria (4.2×10^{10} cells) did not ameliorate lactose malabsorption measured by the breath-hydrogen test in 12 lactose malabsorbers. This study shows that ingested lactic acid bacteria are indeed present in the colon, but it does not support the theory that they change the pattern of colonic fermentation or the degree of intestinal lactose malabsorption.

Source

Hove H, Nordgaard-Andersen I, and Mortensen PB. *Effect of lactic acid bacteria on the intestinal production of lactate and short-chain fatty acids, and the absorption of lactose. Am J Clin Nutr.* 1994;59: 74-79

Review article: The use of biotherapeutic agents in the prevention and treatment of gastrointestinal disease**ABSTRACT**

There is presently a lack of well conducted clinical trials demonstrating any significant benefits of probiotics in humans. With the exception of diarrhoea due to rotavirus infection in children there is little evidence from randomized, double-blind,

placebo-controlled studies that bacterial probiotics have a significant beneficial action in preventing diarrhoea of any cause. The yeast *Saccharomyces boulardii* has been shown to be of benefit in the prevention of antibiotic-associated diarrhoea but not in preventing infection with *Clostridium difficile*. *S. boulardii* may also be of benefit in preventing relapse of *C. difficile* infection. Because of the simplicity of in vitro systems and some animal models, beneficial characteristics of probiotics such as the ability of bacteria to bind to epithelial surfaces are not always transferable to humans. Thus any postulated benefit from consumption of probiotic bacteria should only be accepted as fact after testing in clinical studies. This review outlines our present knowledge of the mode of action of probiotics and presents the data from clinical trials on their use.

Source

Lewis SJ and Freedman AR. *Review article: The use of biotherapeutic agents in the prevention and treatment of gastrointestinal disease. Aliment Pharmacol Ther.* 1998 Sep;12(9):807-22.

Lactobacilli in relation to human ecology and antimicrobial therapy**ABSTRACT**

The establishment of lactobacilli in the gastrointestinal tract is believed to contribute to the stabilization of the microflora of healthy subjects and to exert beneficial effects on the host. Because of these proposed healthful properties, several *Lactobacillus* species have been used especially to prevent gastrointestinal disturbances. Though there have been several studies of the possible beneficial effects of lactobacilli in humans, there is still no conclusive evidence for the therapeutic value of these microorganisms.

Source

Lidbeck A and Nord C E. *Lactobacilli in relation to human ecology and antimicrobial therapy. Intl J Tissue React.* 1991;13(2):115-22.

Meta-analysis of Probiotics for the Prevention and Treatment of Acute Pediatric Diarrhea

ABSTRACT

Context:

Antibiotic-associated diarrhea (AAD) is a common complication of most antibiotics and *Clostridium difficile* disease (CDD), which also is incited by antibiotics, is a leading cause of nosocomial outbreaks of diarrhea and colitis. The use of probiotics for these two related diseases remains controversial.

Objective:

To compare the efficacy of probiotics for the prevention of AAD and the treatment of CDD based on the published randomized, controlled clinical trials.

Data Sources:

PubMed, Medline, Google Scholar, NIH registry of clinical trials, metaRegister, and Cochrane Central Register of Controlled Trials were searched from 1977 to 2005, unrestricted by language. Secondary searches of reference lists, authors, reviews, commentaries, associated diseases, books, and meeting abstracts.

Study Selection:

Trials were included in which specific probiotics given to either prevent or treat the diseases of interest. Trials were required to be randomized, controlled, blinded efficacy trials in humans published in peer-reviewed journals. Trials that were excluded were pre-clinical, safety, Phase 1 studies in volunteers, reviews, duplicate reports, trials of unspecified probiotics, trials of prebiotics, not the disease being studied, or inconsistent outcome measures. Thirty-one of 180 screened studies (totally 3,164 subjects) met the inclusion and exclusion criteria.

Data Extraction:

One reviewer identified studies and abstracted data on sample size, population characteristics, treatments, and outcomes.

Data Synthesis:

From 25 randomized controlled trials (RCTs), probiotics significantly reduced the relative risk of AAD (RR = 0.43, 95% CI 0.31, 0.58, $p < 0.001$). From six randomized trials, probiotics had significant efficacy for CDD

(RR = 0.59, 95% CI 0.41, 0.85, $p = 0.005$).

Conclusion:

A variety of different types of probiotics show promise as effective therapies for these two diseases. Using meta-analyses, three types of probiotics (*Saccharomyces boulardii*, *Lactobacillus rhamnosus* GG, and probiotic mixtures) significantly reduced the development of antibiotic-associated diarrhea. Only *S. boulardii* was effective for CDD.

Source

McFarland LV, Elmer GW and McFarland M. Meta-analysis of Probiotics for the Prevention and Treatment of Acute Pediatric Diarrhea. Internl J Probiotics Prebiotics. 2006; 1: 63-76

Association of dietary patterns with cancer recurrence and survival in patients with stage III colon cancer

ABSTRACT

Context:

Dietary factors have been associated with the risk of developing colon cancer but the influence of diet on patients with established disease is unknown.

Objective:

To determine the association of dietary patterns with cancer recurrences and mortality of colon cancer survivors.

Design, Setting, and Patients

Prospective observational study of 1009 patients with stage III colon cancer who were enrolled in a randomized adjuvant chemotherapy trial (CALGB 89803) between April 1999 and May 2001. Patients reported on dietary intake using a semiquantitative food frequency questionnaire during and 6 months after adjuvant chemotherapy. We identified 2 major dietary patterns, prudent and Western, by factor analysis. The prudent pattern was characterized by high intakes of fruits and vegetables, poultry, and fish; the Western pattern was characterized by high intakes of meat, fat, refined grains, and dessert. Patients were followed up for cancer recurrence or death.

Main Outcome Measures:

Disease-free survival, recurrence-free survival,

and overall survival by dietary pattern.

Results:

During a median follow-up of 5.3 years for the overall cohort, 324 patients had cancer recurrence, 223 patients died with cancer recurrence, and 28 died without documented cancer recurrence. A higher intake of a Western dietary pattern after cancer diagnosis was associated with a significantly worse disease-free survival (colon cancer recurrences or death). Compared with patients in the lowest quintile of Western dietary pattern, those in the highest quintile experienced an adjusted hazard ratio (AHR) for disease-free survival of 3.25 (95% confidence interval [CI], 2.04-5.19; P for trend $< .001$). The Western dietary pattern was associated with a similar detriment in recurrence-free survival (AHR, 2.85; 95% CI, 1.75-4.63) and overall survival (AHR, 2.32; 95% CI, 1.36-3.96), comparing highest to lowest quintiles (both with P for trend $< .001$). The reduction in disease-free survival with a Western dietary pattern was not significantly modified by sex, age, nodal stage, body mass index, physical activity level, baseline performance status, or treatment group. In contrast, the prudent dietary pattern was not significantly associated with cancer recurrence or mortality.

Conclusion:

Higher intake of a Western dietary pattern may be associated with a higher risk of recurrence and mortality among patients with stage III colon cancer treated with surgery and adjuvant chemotherapy. Further studies are needed to delineate which components of such a diet show the strongest association.

Source

Meyerhardt, JA, et al. Association of dietary patterns with cancer recurrence and survival in patients with stage III colon cancer. The Journal of the American Medical Association; August 2007, Vol. 298, Number 7, pp 754 to 764

Oral supplementation with lactic acid bacteria during intake of clindamycin

ABSTRACT

Objective:

To study the effect of administration of clindamycin with or without supplementation of the intestinal microflora with *Bifidobacterium bifidum* and *Lactobacillus acidophilus*.

Methods:

Twenty-three healthy subjects received clindamycin by mouth for 7 days. Eleven of the subjects also received capsules containing lyophilized *L. acidophilus* and *B. bifidum* for 14 days. The other 12 subjects received placebo.

Results:

There was a marked decrease in total numbers of anaerobic bacteria during the administration of clindamycin. In the lactic acid bacteria-supplemented group, a tendency towards delayed reduction and earlier increase in bifidobacteria was observed, and two of 11 subjects (18%) were colonized with *Clostridium difficile*, in comparison with five of 12 (41%) in the placebo group. The total number of microorganisms was significantly higher in the lactic acid bacteria-supplemented group than in the placebo group ($p=0.02$) 4 days after the end of clindamycin administration. The difference was mainly due to higher counts of *Escherichia coli* and enterococci. Mean levels of other enterobacteria increased less in the lactic acid bacteria-supplemented group than in the placebo group between days 0 and 14.

Conclusion:

The recolonization with aerobic and anaerobic microorganisms was faster in the lactic acid bacteria-supplemented group than in the placebo group. This may be of importance in preventing colonization with *C. difficile*.

Source

Nord CE, et al. Oral supplementation with lactic acid bacteria during intake of clindamycin. *Clin Microbio & Infect.* 1997;3(1): 124-132

Hydrogen excretion upon ingestion of dairy products in lactose-intolerant male subjects: importance of the live flora

ABSTRACT

Objective:

To assess the effects of the ingestion of milk,

yoghurt (10(8) bacteria/ml), heat-treated yoghurt (<15 bacteria/ml) and two products obtained by dilution of yoghurt with heat-treated product (10(6) and 10(5) bacteria/ml) on hydrogen production and symptoms of lactose intolerance in lactose malabsorbers.

Design:

Double-blind, randomised cross-over design.

Setting:

The study was performed in the phase 1 clinical unit of OPTIMED, Nancy, France.

Subjects:

Twenty-four male lactose malabsorbers were selected for the study.

Interventions:

Hydrogen production and adverse events were followed during 8 h after ingestion of the products.

Results:

The results clearly demonstrate that ingestion of yoghurt with 10(8) bacteria/ml leads to lower H(2) excretion and complaints than the other products. Results observed with the products containing a reduced population of live flora remain better than those observed with milk.

Conclusion:

The importance of a high population of the live flora is underlined.

Source

Pelletier X, Laure-Boussuge S, Donazzolo Y. Hydrogen excretion upon ingestion of dairy products in lactose-intolerant male subjects: importance of the live flora. *Eur J Clin Nutr.* 2001;55:509-512.

Clostridium difficile pilot study: effects of probiotic supplementation on the incidence of C. difficile diarrhoea

ABSTRACT

Colonic infection with *Clostridium difficile*, leading to pseudomembranous colitis, is a common complication of antibiotic therapy, especially in elderly patients. It has been suggested that non-pathogenic probiotic bacteria might prevent the development and recurrence of *C. difficile* infection. This double-blind, placebo-controlled study examines the role of probiotic administration in the

prevention of *C. difficile*-associated diarrhoea (CDAD) in elderly patients receiving antibiotic therapy. Consecutive patients (150) receiving antibiotic therapy were randomised to receive either a probiotic containing both *Lactobacillus* and *Bifidobacterium* or placebo for 20 days. Upon admission to hospital, bowel habit was recorded and a faecal sample taken. Trial probiotic or placebo was taken within 72 h of prescription of antibiotics, and a second stool sample was taken in the event of development of diarrhoea during hospitalisation or after discharge. Of the randomised patients, 138 completed the study, 69 with probiotics in conjunction with antibiotics and 69 with antibiotics alone. On the basis of development of diarrhoea, the incidence of samples positive for *C. difficile*-associated toxins was 2.9% in the probiotic group compared with 7.25% in the placebo-control group. When samples from all patients were tested (rather than just those developing diarrhoea) 46% of probiotic patients were toxin-positive compared with 78% of the placebo group.

Source

Plummer S, et al. *Clostridium difficile* pilot study: effects of probiotic supplementation on the incidence of *C. difficile* diarrhoea. *Int Microbiol.* 2004;7:59-62.

Fermented milks, probiotic cultures, and colon cancer

ABSTRACT

Colorectal cancer (CRC) is a major cause of death from cancer in the Western world. Approximately 70% of CRC is associated with environmental factors, probably mainly the diet. There is interest in the potential protective role of fermented milks containing probiotic cultures against CRC. This article analyzes the existing data from human, animal, and in vitro studies that explore whether consumption of milks fermented with probiotic cultures could play a role in colon cancer risk reduction. Cohort studies have failed to detect significant effects, but most case-control studies favor a protective role of fermented milks against colon cancer. Interventional studies have shown a shift of intermediate markers of CRC risk in human

subjects from a high- to low-risk pattern after ingestion of fermented milks or probiotics. Animal studies consistently show a reduction in chemically induced colorectal tumor incidence and aberrant crypt formation accompanying probiotic administration. In vitro studies also provide evidence of protection, and permit a better understanding of active compounds involved, and of the mechanisms underlying their anticarcinogenic effects. Probiotics may beneficially modulate several major intestinal functions: detoxification, colonic fermentation, transit, and immune status, which may accompany the development of colon cancer. Although the evidence is not conclusive and much further research is required, the data reviewed constitute a promising body of evidence supporting the protective role of milks fermented with probiotic cultures in colon cancer risk reduction.

Source

Saikali J. *Fermented milks, probiotic cultures, and colon cancer. Nutr and Cancer. 2004; 49:14-24.*

Demonstration of safety of probiotics— a review

ABSTRACT

Probiotics are commonly defined as viable microorganisms (bacteria or yeasts) that exhibit a beneficial effect on the health of the host when they are ingested. They are used in foods, especially in fermented dairy products, but also in pharmaceutical preparations. The development of new probiotic strains aims at more active beneficial organisms. In the case of novel microorganisms and modified organisms the question of their safety and the risk to benefit ratio have to be assessed. Lactic acid bacteria (LAB) in foods have a long history of safe use. Members of the genera *Lactococcus* and *Lactobacillus* are most commonly given generally-recognised-as-safe (GRAS) status whilst members of the genera *Streptococcus* and *Enterococcus* and some other genera of LAB contain some opportunistic pathogens. Lactic acid bacteria are intrinsically resistant to many antibiotics. In many cases resistances are not, however, transmissible, and the species are also

sensitive to many clinically used antibiotics even in the case of a lactic acid bacteria-associated opportunistic infection. Therefore no particular safety concern is associated with intrinsic type of resistance. Plasmid-associated antibiotic resistance, which occasionally occurs, is another matter because of the possibility of the resistance spreading to other, more harmful species and genera. The transmissible enterococcal resistance against glycopeptide antibiotics (vancomycin and teicoplanin) is particularly noteworthy, as vancomycin is one of the last effective antibiotics left in the treatment of certain multidrug-resistant pathogens. New species and more specific strains of probiotic bacteria are constantly identified. Prior to incorporating new strains into products their efficacy should be carefully assessed, and a case by case evaluation as to whether they share the safety status of traditional food-grade organisms should be made. The current documentation of adverse effects in the literature is reviewed. Future recommendations for the safety of already existing and new probiotics will be given.

Source

Salminen S, et al. *Demonstration of safety of probiotics—a review. Int J Food Microbiol. 1998 Oct 20;44(1-2):93-106.*

A randomized trial of *Lactobacillus acidophilus* BG2FO4 to treat lactose intolerance

ABSTRACT

Background:

Lactose intolerance is the most common disorder of intestinal carbohydrate digestion. *Lactobacillus acidophilus* BG2FO4 is a strain of lactobacilli with properties of marked intestinal adherence and high beta-galactosidase activity.

Objective:

This study was designed to determine whether oral feeding of *Lactobacillus acidophilus* BG2FO4 leads to a lactose-tolerant state.

Design:

We studied 42 subjects with self-reported lactose intolerance and performed

breath-hydrogen tests to determine whether they were lactose maldigesters. Subjects with established lactose maldigestion (n = 24) were invited to be randomly assigned to an omeprazole-treated (hypochlorhydric) group or a non-omeprazole-treated group, but 6 subjects chose not to participate.

All randomly assigned subjects (n = 18) ingested *Lactobacillus acidophilus* BG2FO4 twice per day for 7 d and stool samples were collected. Breath-hydrogen tests were performed and symptom scores were recorded at baseline and after lactobacilli ingestion.

Results:

Lactose maldigestion was established in 24 of 42 subjects (57%) with self-reported lactose intolerance. In 18 lactose-maldigesting subjects, overall hydrogen production and symptom scores after ingestion of *Lactobacillus acidophilus* BG2FO4 were not significantly different from baseline values. Live *Lactobacillus acidophilus* BG2FO4 was recovered in stool samples from 7 subjects.

Conclusion:

Lactose intolerance is overreported in subjects with gastrointestinal symptoms after lactose ingestion. Treatment of lactose-maldigesting subjects with and without hypochlorhydria with *Lactobacillus acidophilus* BG2FO4 for 7 d failed to change breath-hydrogen excretion significantly after lactose ingestion.

Source

Saltzman JR, et al. *A randomized trial of Lactobacillus acidophilus BG2FO4 to treat lactose intolerance. Am J Clin Nutr. 1999;69: 140-146.*

Healthy Pregnancy

Gut microbiota composition is associated with body weight, weight gain and biochemical parameters in pregnant women

ABSTRACT

Obesity is associated with complications during pregnancy and increased health risks in the newborn. The objective of the present

study was to establish possible relationships between gut microbiota, body weight, weight gain and biochemical parameters in pregnant women. Fifty pregnant women were classified according to their BMI in normal-weight (n 34) and overweight (n 16) groups. Gut microbiota composition was analysed by quantitative real-time PCR in faeces and biochemical parameters in plasma at 24 weeks of pregnancy. Reduced numbers of Bifidobacterium and Bacteroides and increased numbers of Staphylococcus, Enterobacteriaceae and Escherichia coli were detected in overweight compared with normal-weight pregnant women. E. coli numbers were higher in women with excessive weight gain than in women with normal weight gain during pregnancy, while Bifidobacterium and Akkermansia muciniphila showed an opposite trend. In the whole population, increased total bacteria and Staphylococcus numbers were related to increased plasma cholesterol levels. Increased Bacteroides numbers were related to increased HDL-cholesterol and folic acid levels, and reduced TAG levels. Increased Bifidobacterium numbers were related to increased folic acid levels. Increased Enterobacteriaceae and E. coli numbers were related to increased ferritin and reduced transferrin, while Bifidobacterium levels showed the opposite trend. Therefore, gut microbiota composition is related to body weight, weight gain and metabolic biomarkers during pregnancy, which might be of relevance to the management of the health of women and infants.

Source

Santacruz A, Gut microbiota composition is associated with body weight, weight gain and biochemical parameters in pregnant women. *Br J Nutr.* 2010 Jul;104(1):83-92.

Immune Health

Probiotic agents and infectious diseases: a modern perspective on a traditional therapy

ABSTRACT

There is an increasing scientific and commercial interest in the use of beneficial microorganisms, or "probiotics," for the

prevention and treatment of disease. The microorganisms most frequently used as probiotic agents are lactic-acid bacteria such as *Lactobacillus rhamnosus* GG (LGG), which has been extensively studied in recent literature. Multiple mechanisms of action have been postulated, including lactose digestion, production of antimicrobial agents, competition for space or nutrients, and immunomodulation. We have reviewed recent studies of probiotics for the treatment and control of infectious diseases. Studies of pediatric diarrhea show substantial evidence of clinical benefits from probiotic therapy in patients with viral gastroenteritis, and data on LGG treatment for *Clostridium difficile* diarrhea appear promising. However, data to support use of probiotics for prevention of traveler's diarrhea are more limited. New research suggests potential applications in vaccine development and prevention of sexually transmitted diseases. Further studies are needed to take full advantage of this traditional medical approach and to apply it to the infectious diseases of the new millennium.

Source

Alvarez-Olmos MI, Oberhelman RA. Probiotic agents and infectious diseases: a modern perspective on a traditional therapy. *Clin Infect Diseases.* 2001;32(11):1567-1576.

Enhancement of immunity in the elderly by dietary supplementation with the probiotic Bifidobacterium lactis

ABSTRACT

Background:

The aging process can lead to a decline in cellular immunity. Therefore, the elderly could benefit from safe and effective interventions that restore cellular immune functions.

Objective:

We determined whether dietary supplementation with the known immunostimulating probiotic Bifidobacterium lactis HN019 could enhance aspects of cellular immunity in elderly subjects.

Design:

Thirty healthy elderly volunteers (age range: 63-84 y; median: 69 y) participated in a

3-stage dietary supplementation trial lasting 9 wk. During stage 1 (run-in), subjects consumed low-fat milk (200 mL twice daily for 3 wk) as a base-diet control. During stage 2 (intervention), they consumed milk supplemented with B. lactis HN019 in a typical dose (5 x 10¹⁰ organisms/d) or a low dose (5 x 10⁹ organisms/d) for 3 wk. During stage 3 (washout), they consumed low-fat milk for 3 wk. Changes in the relative proportions of leukocyte subsets and ex vivo leukocyte phagocytic and tumor-cell-killing activity were determined longitudinally by assaying peripheral blood samples.

Results:

Increases in the proportions of total, helper (CD4(+)), and activated (CD25(+)) T lymphocytes and natural killer cells were measured in the subjects' blood after consumption of B. lactis HN019. The ex vivo phagocytic capacity of mononuclear and polymorphonuclear phagocytes and the tumoricidal activity of natural killer cells were also elevated after B. lactis HN019 consumption. The greatest changes in immunity were found in subjects who had poor pretreatment immune responses. In general, the 2 doses of B. lactis HN019 had similar effectiveness.

Conclusion:

B. lactis HN019 could be an effective probiotic dietary supplement for enhancing some aspects of cellular immunity in the elderly.

Source

Gill HS, et al. Enhancement of immunity in the elderly by dietary supplementation with the probiotic Bifidobacterium lactis. *Am J Clin Nutr.* 2001; 74:833-836

Probiotic Effects on Cold and Influenza-Like Symptom Incidence and Duration in Children

ABSTRACT

Objective:

Probiotic consumption effects on cold and influenza-like symptom incidence and duration were evaluated in healthy children during the winter season.

Methods:

In this double-blind, placebo-controlled study, 326 eligible children (3-5 years of age) were assigned randomly to receive placebo (N = 104), *Lactobacillus acidophilus* NCFM (N = 110), or *L. acidophilus* NCFM in combination with *Bifidobacterium animalis* subsp. *lactis* Bi-07 (N = 112). Children were treated twice daily for 6 months.

Results:

Relative to the placebo group, single and combination probiotics reduced fever incidence by 53.0% (P = .0085) and 72.7% (P = .0009), coughing incidence by 41.4% (P = .027) and 62.1% (P = .005), and rhinorrhea incidence by 28.2% (P = .68) and 58.8% (P = .03), respectively. Fever, coughing, and rhinorrhea duration was decreased significantly, relative to placebo, by 32% (single strain; P = .0023) and 48% (strain combination; P < .001). Antibiotic use incidence was reduced, relative to placebo, by 68.4% (single strain; P = .0002) and 84.2% (strain combination; P < .0001). Subjects receiving probiotic products had significant reductions in days absent from group child care, by 31.8% (single strain; P = .002) and 27.7% (strain combination; P < .001), compared with subjects receiving placebo treatment.

Conclusion:

Daily dietary probiotic supplementation for 6 months was a safe effective way to reduce fever, rhinorrhea, and cough incidence and duration and antibiotic prescription incidence, as well as the number of missed school days attributable to illness, for children 3 to 5 years of age.

Source

Letr GJ, et al. *Probiotic Effects on Cold and Influenza-Like Symptom Incidence and Duration in Children*. *Pediatrics*. 2009 Aug;124(2):e172-9. Epub 2009 Jul 27

Different effects of probiotic species/strains on infections in preschool children: A double-blind, randomized, controlled study

ABSTRACT

Treatment and prevention of pediatric infectious diseases of three commercial probiotic products were evaluated by a

double-blind, randomized, controlled trial. Test subjects under age 5, 1062 in total, were distributed randomly into four groups. This investigation showed that *L. casei* rhamnosus can control bacterial, viral and respiratory infections; a multi-species probiotic reduced gastrointestinal disease significantly. Long-term consumption of *L. rhamnosus* T cell-1 decreased the incidence of bacterial infection.

Source

Lin JS, et al. *Different effects of probiotic species/strains on infections in preschool children: A double-blind, randomized, controlled study*. *Vaccine*. 2009 Feb 11; 27(7):1073-9

Probiotics that modify disease risk

ABSTRACT

Probiotics are defined as live bacterial preparations with clinically documented health effects in humans. Probiotics have specific properties and targets in the human intestinal tract and intestinal microbiota. Each probiotic strain, independent of its genus and species is unique and, thus, the properties and the human health effects of each strain have to be assessed in a case-by-case manner. Understanding the mechanisms by which probiotics influence the normal intestinal microbiota and counteract aberrancies in microbiota would facilitate the use of probiotics for both dietary management and reduction in risk of specific diseases. Development of intestinal microbiota is an important factor affecting the health of the newborn. Recent studies suggest that specific bacterial components, especially the bifidobacteria, have a key impact on development of a healthy balanced infant microbiota. The composition of infant and child intestinal microbiota may become aberrant and thus influence the development of diarrheal, inflammatory, and allergic diseases. Based on this understanding, positive health effects of probiotics have been reported in the management of diarrheal, inflammatory, and allergic diseases in infants. Most recently, a reduction in risk of atopic diseases followed early administration of specific probiotics.

Source

Salminen SJ, Gueimonde M, Isolauri E. *Probiotics that modify disease risk*. *J of Nutr*. 2005;135(5):1294-1298.

Skin Health

Prospective, randomized, open-label trial comparing the safety, efficacy, and tolerability of an acne treatment regimen with and without a probiotic supplement and minocycline in subjects with mild to moderate acne

ABSTRACT

Background:

Systemic antibiotics are an effective treatment for acne vulgaris. However, intolerable side effects may invariably occur.

Objective:

To determine whether probiotics reduce the side effects imparted by systemic antibiotics while working synergistically with the latter in treating inflammatory acne.

Methods:

Forty-five 18- to 35-year-old females were randomly assigned to one of three arms in this prospective, open-label study. Group A received probiotic supplementation, whereas group B received only minocycline. Group C was treated with both probiotic and minocycline. Clinical and subjective assessments were completed at baseline and during the 2-, 4-, 8-, and 12-week follow-up visits.

Results:

All patients demonstrated a significant improvement in total lesion count 4 weeks after treatment initiation (p < .001), with continued improvement seen with each subsequent follow-up visit (p < .01). At the 8- and 12-week follow-up visits, group C had a significant decrease in total lesion count versus groups A (p < .001) and B (p < .01). Two patients (13%) from group B failed to complete the study secondary to vaginal candidiasis.

Conclusion:

Probiotics may be considered a therapeutic option or adjunct for acne vulgaris by providing a synergistic antiinflammatory effect with systemic antibiotics while also

reducing potential adverse events secondary to chronic antibiotic use.

Source

Jung GW et al. Prospective, randomized, open-label trial comparing the safety, efficacy, and tolerability of an acne treatment regimen with and without a probiotic supplement and minocycline in subjects with mild to moderate acne. J Cutan Med Surg 17:114-

Sports Nutrition

Reversal of fatigued athletes of a defect in interferon-gamma secretion after administration of lactobacillus acidophilus

IFNgamma concentrations in healthy control athletes after the one month course of L acidophilus demonstrated in man the capacity for this probiotic to enhance the mucosal IFNgamma concentration.

Conclusion:

This is the first evidence of a T cell defect in fatigued athletes, and of its reversal following probiotic therapy.

Source

Clancy, R. Reversal of fatigued athletes of a defect in interferon-gamma secretion after administration of lactobacillus acidophilus.. British Journal of Sports Medicine, 40, 351-354.

ABSTRACT

Background:

Fatigue and impaired performance in athletes is well recognised and has been loosely linked to “overtraining”. Reduced concentration of IgA in the saliva and increased shedding of Epstein Barr virus (EBV) have been associated with intense training in elite athletes.

Objective:

To determine whether athletes presenting with fatigue and impaired performance had an immune defect relevant to defective containment of EBV infection, and whether a probiotic preparation (Lactobacillus acidophilus) shown to enhance mucosal immunity in animal models could reverse any detected abnormality.

Results:

The fatigued athletes had clinical characteristics consistent with re-activation of EBV infection and significantly ($p = 0.02$) less secretion of interferon (IFN) gamma from blood CD4 positive T cells. After one month of daily capsules containing 2×10^{10} colony forming units of L acidophilus, secretion of IFNgamma from T cells had increased significantly ($p = 0.01$) to levels found in healthy control athletes. A significant ($p = 0.03$) increase in salivary