# Summary of Clinical / Preclinical Studies


## *MasterFlora* Acidophilus May Help:

- CONSTIPATION
- DIARRHEA
- LACTOSE INTOLERANCE
- CHOLESTEROL REDUCTION
- YEAST INFECTION
- IMMUNE SYSTEM ENHANCEMENT
- CANCER SUPPRESSION
- REDUCTION OF ANTIBIOTIC SIDE EFFECTS

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| MasterFlora | |
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| **SOURCE** | **SUMMARY** |
| **CONSTIPATION PREVENTION/TREATMENT** | |
| Ouwehand AC, Lagstrom H, Suomalainen T, Salminen S., Effect of probiotics on constipation, fecal azoreductase activity and fecal mucin content in the elderly., Ann. Nutr. Metab., 2002; 46(3-4): 159. | RESULTS: The subjects receiving the *L. rhamnosus*/*P. freudenreichii*-supplemented juice exhibited a 24% increase in defecation frequency. However, no reduction in laxative use was observed. The fecal azoreductase activity was also significantly reduced in this group. No changes in fecal pH or mucin excretion were observed. CONCLUSION: Some relief from constipation may be observed with the combination of *L. rhamnosus*/*P. freudenreichii*. This probiotic combination also reduced fecal enzyme activity. |
| Salminen S, Salminen E., Lactulose, lactic acid bacteria, intestinal microecology and mucosal protection. Scand. J. Gastroenterol. Suppl., 1997; 222: 45. | Lactulose promotes the growth of lactic acid bacteria and bifidobacteria and, more specifically, Lactobacillus acidophilus in the colon. Lactulose and lactulose-containing products fermented with lactic acid bacteria lower colonic pH balancing intestinal microecology and normalizing intestinal transit. In animal studies, lactulose promotes a mainly Gram-positive faecal microflora, but large doses of lactulose may be associated with transient diarrhoea. Our studies indicate that lactulose with lactic acid bacteria effectively relieves constipation in human volunteers. |
| Alm L., Acidophilus milk for therapy in gastrointestinal disorders. Nahrung., 1984; 28(6-7): 683. | A new developed Acidophilus milk has been introduced as therapy in different disorders of the gastrointestinal tract. The milk contains acid resistant tribes of L. acidophilus and is fortified with vitamins, its fat content is low. The passage of alive L. acidophilus could be proved. The preparation showed a clear response in patients suffering from intestinal disorders due to an application of antibiotics and in patients with constipations. |
| **DIARRHEA PREVENTION/TREATMENT** | |
| Black, F.T., Anderson, P.L., Orskov J., Orskov, F., Gaarslev, K. and Laulund, S. Prophylactic Efficacy of Lactobacilli on Traveler's Diarrhea. 1989. Travel Medicine. 333- 335. | One capsule containing a lyophilized mixture of *Lactobacillus acidophilus, Bifidobacterium lactis, Streptococcus thermophilus* and *Lactobacillus bulgaricus* administered three times daily significantly reduced the frequency of diarrhea (p=0.019) compared to the placebo. This gives a protection rate of 39.4% against travelers' diarrhea in Egypt. |
| Saaverda, J.M., Bauman, N.A., Oung, I., Perman, J.A., and Yolken, R.H. Feeding of *Bifidobacterium bifidum* and *Streptococcus thermophilus* to infants in hospital for prevention of diarrhea and shedding of rotavirus. 1994. The Lancet. 344: 1046-1048. | The supplementation of infant formula with *B. bifidum* and *S. thermophilus* can significantly reduce the incidence of acute diarrhea (p=0.035) and rotavirus shedding (p+0.025) in infants admitted to hospital. |

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| Gonzalrez, S., Albarracin, G., Locascio de Ruiz Pesce, M., Male, M., Apella, M.C., Pesce de Ruiz Holgado, A. and Oliver, G. 1990. Prevention of Infantile Diarrhea by Fermented Milk. Microbiologie-Aliments-Nutrition. 8: 349-354. | Significant difference between the two groups were noted after treatment with respect to the development of diarrhea and weight gain. These data suggest that fermented milk can be used in the prevention of gastrointestinal disorders in children of high risk populations. Furthermore, the gain of weight in children receiving fermented milk was twice that of controls. |
| Gionchetti P, Rizzello F, Venturi A, Campieri M. Probiotics in infective diarrhoea and inflammatory bowel diseases. J Gastroenterol Hepatol 2000 May;15(5):489-93 | Experimental and clinical studies suggest that there are potential therapeutic roles for probiotics in the treatment of inflammatory bowel diseases. This review focuses on the available data concerning the mechanisms of action of probiotics, and on the results from clinical studies using probiotics to treat infective diarrhoea and inflammatory bowel disease. |
| **LACTOSE INTOLERANCE PREVENTION/TREATMENT** | |
| Virta, P., Otterstrom, K., Niemi, L., Wieser-Aho, M.T., Lahteenmaki, A.L. and Leppanen, T. The Effect of a Preparation Containing Freeze-Dried Lactic Acid Bacteria on Lactose Intolerance. 1993. Pilot study performed by Pharmacia, Finland. | Individuals taking capsules containing *Lactobacillus acidophilus, Bifidbacterium lactis (bifidum), Streptococcus thermophilus* and *Lactobacillus bulgaricus* showed a decrease in the symptoms caused by lactose intolerance although the subjects are lactose containing food. |
| Noh, D.O. and Gilliland, S.E. Influence of Bile on Cellular Integrity and β-galactosidase Activity of Lactobacillus acidophilus. 1993. J. Dairy Sci. 76(5): 1253-1259. | The influence of bile on β-galactosidase activity, cellular integrity, cellular retention of β-galactosidase, and cellular permeability of five strains of *Lactobacillus acidophilus* were tested. It was concluded that, in the presence bile, the permeability of cells of L. acidophilus increased, permitting more substrate to enter the cells, thus increasing the β-galactosidase activity of the whole cells. |
| Lin. M.Y., Savaiano, D. and Harlander, S. Influence of Nonfermented Dairy Products containing Bacteria Starter Cultures on Lactose Mal-digestion in Humans. 1991. J. Dairy Sci. 74: 87-95. | Only one strain, L. acidophilus, which demonstrated low bile resistance and intermediate β-galactosidase activity, was capable of significantly decreasing breath hydrogen values when 108 CFU/ml of milk was consumed |

| **CHOLESTEROL REDUCTION** | |
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| Kiessling G, Schneider J, Jahreis G. Long-term consumption of fermented dairy products over 6 months increases HDL cholesterol. Eur. J. Clin. Nutr., 2002; 56(9): 843. | OBJECTIVE: Assessment of the hypocholesterolaemic effect of yoghurt supplemented with *Lactobacillus acidophilus* and *Bifidobacterium longum* in women. SUBJECTS: Twenty-nine healthy women, aged 19-56 y. Fifteen of these were normocholesterolaemic and 14 women were hypercholesterolaemic. RESULTS: The mean serum concentration of total cholesterol and the LDL cholesterol was not influenced by the synbiotic (P>0.05). The HDL concentration increased significantly by 0.3 mmol/l (P=0.002). The ratio of LDL/HDL cholesterol decreased from 3.24 to 2.48 (P=0.001). CONCLUSIONS: The long-term daily consumption of 300 g yoghurt over a period of 21 weeks (control and synbiotic) increased the serum concentration of HDL cholesterol and lead to the desired improvement of the LDL/HDL cholesterol ratio. |
| Pereira DI, Gibson GR. Cholesterol assimilation by lactic acid bacteria and bifidobacteria isolated from the human gut. Appl. Environ. Microbiol., 2002; 68(9): 4689. | The objective of this study was to evaluate the effect of human gut-derived lactic acid bacteria and bifidobacteria on cholesterol levels in vitro. C A comparative evaluation regarding the in vitro cholesterol reduction abilities of these strains along with commercial probiotics was undertaken. The degree of acid and bile tolerance of strains was also evaluated. The human isolate *L. fermentum* was able to maintain viability for 2 h at pH 2 and to grow in a medium with 4,000 mg of bile acids per liter. This strain was also able to remove a maximum of 14.8 mg of cholesterol per g (dry weight) of cells from the culture medium and therefore was regarded as a candidate probiotic. |
| Grill JP, Cayuela C, Antoine JM, Schneider F. Effects of Lactobacillus and Bifidobacterium on cholesterol. Lett. Appl. Microbiol., 2000; 31(2): 154 | To determine the validity of the hypothesis of assimilation and/or precipitation of cholesterol by Lactobacillus and Bifidobacterium species, culture were undertaken in TPY medium containing oxgall or taurocholic acid. In the case of growing cells, both strains were able to remove cholesterol in the presence of bile salts. Nevertheless, the behaviour was different according to the kind of bile salt. In the presence of taurocholic acid, the removal of cholesterol was due to both bacterial uptake and precipitation. In the presence of Oxgall, bacterial uptake and precipitation were observed for Lactobacillus but only precipitation occurred for Bifidobacterium. |
| Gilliland, S.E. and Walker, D.K. Factors to consider when selecting a culture of *Lactobacillus acidophilus* as a dietary adjunct to produce a hypocholesterolemic effect in humans. 1990. J. Dairy Sci. 73: 905. | Data from this study suggest that several *Lactobacillus acidophilus* strains could be the culture of choice from among those tested for use as a dietary adjunct to provide benefit in helping control cholesterol levels. |

| YEAST INFECTION PREVENTION/TREATMENT | |
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| Elmer GW, Surawicz CM, McFarland LV., Biotherapeutic agents: A neglected modality for the treatment and prevention of selected intestinal and vaginal infections. JAMA., 1996. 20; 275(11): 870. | OBJECTIVE: To evaluate the potential of biotherapeutic agents (microorganisms with therapeutic properties) for the prevention and/or treatment of selected intestinal and vaginal infections. CONCLUSIONS: There is now evidence that administration of selected microorganisms is beneficial in the prevention and treatment of certain intestinal and, possibly, treatment of vaginal infections. In an effort to decrease the reliance on antimicrobials, the time has come to carefully explore the therapeutic applications of biotherapeutic agents. |
| Jack, M. Wood, B.J.B. and Berry, D.R. Evidence for the Involvement of Thiocyanate in the Inhibition of *Candida albicans* by *Lactobacillus acidophilus*. 1990. Microbios. 62: 37-46. | *Lactobacillus acidophilus* has been found to inhibit Candida albicans when grown on MRS agar plates. The addition of sodium thiocyanate to the agar was found to increase the inhibition of offered by the lactobacillus. The results indicate the hydrogen peroxide produced by the lactobacillus is being used to convert the thiocyanate to hypothicyanate which is more toxic. |
| Hansen, B.W.L. *Candida albican*'s vaginitis: Treatment of Candida albican's vaginitis with *Lactobacillus acidophilus*. 1987. Monthly Publication for the Practical Medical Profession. December: 877-879. | This investigation showed an effect at 73% on the patients treated with *Lactobacillus acidophilus* at the control after 14 days of treatment. |
| Hallen, A., Jarstrand, C., and Pahlson, C. Treatment of Bacterial Vaginosis with Lactobacilli. Sexually Transmitted Diseases. May-June 1992. | In a double blind, placebo controlled study, 16 out of 28 women who were treated with *Lactobacillus acidophilus* had normal vaginal wet smears. None of the 29 women treated with placebo were affected. This is statistically significant ($p<0.05$). |
| Hiton, E., Isenburg, H.D., Alpenstein, P., France, K. and Brenstein. Ingestion of yogurt containing Lactobacillus acidophilus as prophylaxis for candidal vagintis. 1992. Am. Int. Medicine. 116: 353-357. | Daily ingestion of 8 ounces of yogurt containing *Lactobacillus acidophilus* decreased both candidal colonization and infection. |
| **IMMUNE SYSTEM ENHANCEMENT** | |
| Schiffrin, E.J., Rochat, F., Link-Amster, H., Aeschlimann, J.M. and Donnet-Hughcs, A. Immunomodulation of Human Blood Cells Following the Ingestion of Lactic Acid Bacteria. 1995. J. Dairy Sci. 78: 491-497. | Nonspecific, anti-infective mechanisms of defense can be enhanced by the ingestion of specific lactic acid bacteria strains. These strains can by used as nutritional supplements to improve the immune function of particular age groups, i.e., the neonate or the elderly, for which these functions are diminished. |

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| Miettinen, M., Vuopio-Varkila, J., Varkila, K. Production of human tumor necrosis factor alpha, interleukin-6 and interleukin-10 is induced by lactic acid bacteria. 1996. Inf. and Immun. 64(12): 5403-5405. | The production of tumor necrosis factor alpha, IL-6 and in some cases, IL-10 was induced in amounts even greater than those obtained with lipopolysaccharide as a stimulant. The results suggest that the lactic acid bacteria can stimulate nonspecific immunity. |
| Perdigon, G., Alvarez, S., Nader de Macias, M.E., Roux, M.E., and Pesce de Ruiz Holgado, A. The Oral Administration of Lactic Acid Bacteria Increase the Mucosal Intestinal Immunity in Response to Enteropathogens. 1990. Journal of Food Protection. 53(5): 404-410. | It is suggested that the oral feeding with *L. casei* or *S. thermophilus* could be used as an immunobiological method in controlling and preventing enteric disorders in humans and veterinary, *L. casei* being better, because it induces specific local response very important in the host defense against pathogens. |
| Perdigon., G.,. Nader de Macia, M., Alvarez, S., Oliver, G., Pesce de Ruiz Holgado, A. Prevention of gastrointestinal infection using immunobiological methods with milk fermented with *Lactobacillus casei* and *Lactobacillus acidophilus*, Journal of Dairy Research. 1990.57:255-264. | The results suggest that the augmentation of resistance to salmonella caused by the treatment with L. casei and L. acidophilus fermented milk was due to the anti-salmonella protective immunity mainly mediated by the mucosal tissue. Milk fermented with this mixture could be used as an immunobiological method to prevent gastrointestinal infection. |
| Perigon, G., Alvarez, S., Medici, M. and Pesce de Ruiz Holgado, A. Influence of the Use of *Lactobacillus casei* as an Oral Adjuvant on the Levels of Secretary Immuglobulin A During an Infection with Salmonella typhimurium. 1993. Food & Agricultural Immunology. 5. 27-37. | It seems likely that *L. casei* stimulated the T- and/or B-cells, enhancing the number of B cells that enter the IgA cycle and thus increasing the synthesis of immunoglobulin A. This stimulation is apparently closely related to the *L. casei* dose. |
| Nader de Macias, M.E., Romero, C., Apella, M.C., Gonzalez, S.N. and Oliver, G. 1993. Prevention of Infection Produced by *Escherichia coli* and Listeria Monocytogenes by Feeding Milk Fermented with Lactobacilli. Journal of Food Protection. 56 (5): 401-405. | Colonization of the liver and spleen by *E. coli* was markedly inhibited by pretreatment with fermented milk; the pathogen was not detected on the 5th day post-challenge. In the Listeria challenged mice, the pathogen was present in 1 to 2 log units lower than the control up to the 10th day. The levels of antipathogen sera and intestinal antibodies were 2 to 4 times higher in the treated mice, with lower values in the Listeria treated mice. The mechanisms of protection in both types of infections were discussed. The results obtained suggested that milk fermented with *L. casei* and *L. acidophilu*s could be used as a prophylactic against selected infections. |

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| Perigon, G., Alvarez, S., Gobbato, N., de Budeguer, M.V. and Pesce de Ruiz Holgado, A. Comparative Effect of the Adjuvant Capacity of *Lactobacillus casei* and Lipopolysaccharide on the Intestinal Secretary Antibody Response and Resistance to Salmonella Infection in Mice. 1995. Food & Agricultural Immunology. 7: 283-294. | The authors believe that viable *L. casei*, by either itself or associated with LPS (the most important structure of the Gram-negative enteropathogen cell wall), administered at adequate doses, might act as a useful adjuvant in the mucosa by protecting the host from infections. |
| Perigon, G., Alvarez, S. and Pesce de Ruiz Holgado, A. Immuno-adjuvant activity of oral *Lactobacillus casei*: influence of dose on the secretary immune response and protective capacity in intestinal infections. 1991. Journal of Dairy Research. 58: 485-496. | These results show that *L. casei* plays an important role in the prevention of enteric infection. A low dose being enough for protection against intestinal infection by increasing IgA secretion into the intestinal lumen, thus providing adequate defenses for the mucosal surface. A previously administered dose of this magnitude could therefore be used as an oral adjuvant in preventing enteric infections. |
| Perdigon, G., Nader de Macias, M.E., Alvarez, S., Medici, M., Oliver, G. and de Ruiz Holgado, A.P. Effect of a Mixture of *Lactobacillus casei* and *Lactobacillus acidophilus* Administered Orally on the Immune System in Mice. 1986. Journal of Food Protection. 49(12): 986-989. | On 8 consecutive days, groups of 32-40 Swiss albino mice were fed skim milk containing 1.2 X $10^9$ cells of *Lactobacillus acidophilus* and *L. casei* cells (equivalent to 100 micro gram protein). Enzymatic activity of peritoneal macrophages in the experimental mice was 1.5-3.5 times higher than in macrophages from control mice fed on milk without added lactobacilli. In vitro phagocytic activity of peritoneal macrophages was 1.5-2.0 times higher in mice fed the lactobacillus mixture than in control mice. Enhancement of the immune response by oral administration of a mixture of *L. casei* and *L. acidophilus* appears to be greater than that obtained by either organism used alone. |
| **CANCER SUPPRESSION** | |
| Kim, H.Y. Bae, H.S. and Back, Y.J. In-vivo Antitumor Effects of Lactic Acid Bacteria on Sarcoma 180 and Mouse Lewis Lung Carcinoma. 1991. Journal of Korean Cancer. 23: 188-195. | Seven lactic acid bacteria were administered intraperitoneally and the antitumor effect were measured by the increase of body weights and mean survival days. *L. casei* group was more effective than any other group. Mean survival days of *L. casei* group were longer than 43.3 days, while the control group was only 26.9 days. |
| Biffi, A., Coradini, D., Larsen, R., Riva, L. DiFronzo, G. Antiproliferative Effect of Fermented Milk on the Growth of a Human Breast Cancer Cell Line. 1997. Nutrition and Cancer. 28(1): 93-99 | Although the mechanism of the antitumor activity is not clear, the present study suggests the potentiality offered by fermented milk, with *L. acidophilus* and *B. lactis*, as producers of compounds with antiproliferative activity useful in the prevention and therapy of solid tumors like breast cancer. |

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| Perdigon, G., Alvarez, S., Nader de Macias, M.E., Margini, R.A., Oliver, G. and de Ruiz Holgado, A.P. Lactobacilli administered orally induce release of enzymes from peritoneal macrophages in mice. 1986. Milchwissenschaft. 41(6): 344-348. | The effect of *Lactobacillus casei*, *L. bulgaricus* and *L. acidophilus* on the growth of transplantable allogenic and syngenic mouse tumors by intraperitoneal treatment with these lactobacilli was demonstrated. A significant inhibition of tumor cells proliferation was observed. |
| Perdigon, G., Eugenia de Jorrat, M., Valdez, J.C., de Budeguer, M. and Oliver, G. Cytolytic Effect of the Serum of Mice Fed with *Lactobacillus casei* on tumor cells. 1995. Microbiologie-Alimenmts-Nutrion. 13: 15-24. | It was concluded that cells belonging to the immune system, activated by *L. casei*, may be responsible for the antitumoral effect exerted by *L. casei.* |
| **REDUCTION OF ANTIBIOTIC SIDE EFFECTS** | |
| Black, F.T., Einarsson, K., Lidbeck, A., Orrhage, K. and Nord, C.E. Effect of Lactic Acid Producing Bacteria on the Human Intestinal Microflora during Ampicillin Treatment. 1991. Scand. J. Infect. Dis. 23: 247-254. | 20 healthy volunteers participated in a double blind study concerning the effect of lactic acid bacterial on the intestinal microfloral during ampicillin treatment. 10 volunteers received 550 mg ampicillin tablets t.i.d. together with capsules containing lactic acid producing bacteria (*Lactobacillus acidophilus* and *Bifidobacterium bifidum*) for 7 days, and the other 10 volunteers were given 500 mg ampicillin tablets together with placebo capsules t.i.d. 7 days. The volunteers receiving lactic acid bacteria were recolonized slightly faster than those having placebo. |
| Nord, C.E., Lidbeck, A., Orrhange, K. and Sjostedt, S. Oral supplementation with lactic acid bacteria during intake of clindamycin. 1997. Clinical Microbiology and Infection. 3(1). | In a double blind randomized study, 23 healthy subjects were divided into two groups.During the second week in the group receiving the lactic acid bacterial supplement the mean level of the total number of aerobic microorganisms was significantly increased compared to the placebo group ($p=0.05$). In the lactic acid bacteria group, the reduction in bifidobacteria during clindamycin administration tended to be delayed ($p=0.08$) as well as the enhancement afterwards accelerated. No difference in lactobacilli was detected. |