nupure probaflor ®

Study situation

Weiterführende Studien und Referenzen zu den in nupure probaflor® eingesetzen Inhaltsstoffen

Further studies and references to the ingredients used in nupure probaflor®

STUDY 01

1. Goldenberg JZ, et al.; Probiotics for the prevention of pediatric antibiotic-associated diarrhea, **https://www.ncbi.nlm.nih.gov/pubmed/31039287**

Abstract

BACKGROUND

Antibiotics alter the microbial balance commonly resulting in antibiotic-associated diarrhea (AAD). Probiotics may prevent AAD via providing gut barrier, restoration of the gut microflora, and other potential mechanisms of action.

OBJECTIVES

The primary objectives were to assess the efficacy and safety of probiotics (any specified strain or dose) used for the prevention of AAD in children.

SELECTION CRITERIA

Randomized, parallel, controlled trials in children (0 to 18 years) receiving antibiotics, that compare probiotics to placebo, active alternative prophylaxis, or no treatment and measure the incidence of diarrhea secondary to antibiotic use were considered for inclusion.

SEARCH METHODS

MEDLINE, Embase, CENTRAL, CINAHL, and the Web of Science (inception to 28 May 2018) were searched along with registers including the ISRCTN and Clinicaltrials.gov. We also searched the NICE Evidence Services database as well as reference lists from relevant articles.

DATA COLLECTION AND ANALYSIS

Study selection, data extraction, and risk of bias assessment were conducted independently by two authors. Dichotomous data (incidence of AAD, adverse events) were combined using a pooled risk ratio (RR) or risk difference (RD), and continuous data (mean duration of diarrhea) as mean difference (MD), along with corresponding 95% confidence interval (95% CI). We calculated the number needed to treat for an additional beneficial outcome (NNTB) where appropriate. For studies reporting on microbiome characteristics using heterogeneous outcomes, we describe the results narratively. The certainty of the evidence was evaluated using GRADE.

MAIN RESULTS

Thirty-three studies (6352 participants) were included. Probiotics assessed included Bacillus spp., Bifidobacterium spp., Clostridium butyricum, Lactobacilli spp., Lactococcus spp., Leuconostoc cremoris, Saccharomyces spp., orStreptococcus spp., alone or in combination. The risk of bias was determined to be high in 20 studies and low in 13 studies. Complete case (patients who did not complete the studies were not included in the analysis) results from 33 trials reporting on the incidence of diarrhea show a precise benefit from probiotics compared to active, placebo or no treatment control.

After 5 days to 12 weeks of follow-up, the incidence of AAD in the probiotic group was 8% (259/3232) compared to 19% (598/3120) in the control group (RR 0.45, 95% CI 0.36 to 0.56; I^2 = 57%, 6352 participants; NNTB 9, 95% CI 7 to 13; moderate certainty evidence). Nineteen studies had loss to follow-up ranging from 1% to 46%. After making assumptions for those lost, the observed benefit was still statistically significant using an extreme plausible intention-to-treat (ITT) analysis, wherein the incidence of AAD in the probiotic group was 12% (436/3551) compared to 19% (664/3468) in the control group (7019 participants; RR 0.61; 95% CI 0.49 to 0.77; P <0.00001; I^2 = 70%). An a priori available case subgroup analysis exploring heterogeneity indicated that high dose (≥ 5 billion CFUs per day) is more effective than low probiotic dose (< 5 billion CFUs per day), interaction P value = 0.01. For the high dose studies the incidence of AAD in the probiotic group was 8% (162/2029) compared to 23% (462/2009) in the control group (4038 participants; RR 0.37; 95% CI 0.30 to 0.46; P = 0.06; moderate certainty evidence). For the low dose studies the incidence of AAD in the probiotic group was 8% (97/1155) compared to 13% (133/1059) in the control group (2214 participants; RR 0.68; 95% CI 0.46 to 1.01; P = 0.02). Again, assumptions for loss to follow-up using an extreme plausible ITT analysis was statistically significant. For high dose studies the incidence of AAD in the probiotic group was 13% (278/2218) compared to 23% (503/2207) in control group (4425 participants; RR 0.54; 95% CI 0.42 to 0.70; P <0.00001; I^2 = 68%; moderate certainty evidence).

None of the 24 trials (4415 participants) that reported on adverse events reported any serious adverse events attributable to probiotics. Adverse event rates were low. After 5 days to 4 weeks follow-up, 4% (86/2229) of probiotics participants had an adverse event compared to 6% (121/2186) of control participants (RD 0.00; 95% CI -0.01 to 0.01; P < 0.00001; I^2 = 75%; low certainty evidence). Common adverse events included rash, nausea, gas, flatulence, abdominal bloating, and constipation.

After 10 days to 12 weeks of follow-up, eight studies recorded data on our secondary outcome, the mean duration of diarrhea; with probiotics reducing diarrhea duration by almost one day (MD -0.91; 95% CI -1.38 to -0.44; P <0.00001; low certainty evidence). One study reported on microbiome characteristics, reporting no difference in changes with concurrent antibiotic and probiotic use.

AUTHORS' CONCLUSIONS

The overall evidence suggests a moderate protective effect of probiotics for preventing AAD (NNTB 9, 95% CI 7 to 13). Using five criteria to evaluate the credibility of the subgroup analysis on probiotic dose, the results indicate the subgroup effect based on high dose probiotics (≥ 5 billion CFUs per day) was credible. Based on high-dose probiotics, the NNTB to prevent one case of diarrhea is 6 (95% CI 5 to 9). The overall certainty of the evidence for the primary endpoint, incidence of AAD, based on high dose probiotics was moderate due to the minor issues with risk of bias and inconsistency related to a diversity of probiotic agents used. Evidence also suggests that probiotics may moderately reduce the duration of diarrhea, a reduction by almost one day. The benefit of high dose probiotics (e.g. Lactobacillus rhamnosus orSaccharomyces boulardii) needs to be confirmed by a large well-designed multi-centered randomized trial. It is premature to draw firm conclusions about the efficacy and safety of 'other' probiotic agents as an adjunct to antibiotics in children. Adverse event rates were low and no serious adverse events were attributable to probiotics. Although no serious adverse events were observed among inpatient and outpatient children, including small studies conducted in the intensive care unit and in the neonatal unit, observational studies not included in this review have reported serious adverse events in severely debilitated or immuno-compromised children with underlying risk factors including central venous catheter use and disorders associated with bacterial/fungal translocation.

2. Allen SJ, et al.; Probiotics for treating acute infectious diarrhoea; **https://www.ncbi.nlm.nih.gov/pubmed/21069673**

Abstract

BACKGROUND:

Probiotics may offer a safe intervention in acute infectious diarrhoea to reduce the duration and severity of the illness.

OBJECTIVES:

To assess the effects of probiotics in proven or presumed acute infectious diarrhoea.

SEARCH STRATEGY

We searched the Cochrane Infectious Diseases Group's trials register (July 2010), the Cochrane Controlled Trials Register (The Cochrane Library Issue 2, 2010), MEDLINE (1966 to July 2010), EMBASE (1988 to July 2010), and reference lists from studies and reviews. We also contacted organizations and individuals working in the field, and pharmaceutical companies manufacturing probiotic agents.

SELECTION CRITERIA

Randomized and quasi-randomized controlled trials comparing a specified probiotic agent with a placebo or no probiotic in people with acute diarrhoea that is proven or presumed to be caused by an infectious agent.

DATA COLLECTION AND ANALYSIS

Two reviewers independently assessed the methodological quality of the trial and extracted data. Primary outcomes were the mean duration of diarrhoea, stool frequency on day 2 after intervention and ongoing diarrhoea on day 4. A random-effects model was used.

MAIN RESULTS

Sixty-three studies met the inclusion criteria with a total of 8014 participants. Of these, 56 trials recruited infants and young children. The trials varied in the definition used for acute diarrhoea and the end of the diarrhoeal illness, as well as in the risk of bias. The trials were undertaken in a wide range of different settings and also varied greatly in organisms tested, dosage, and participants' characteristics. No adverse events were attributed to the probiotic intervention.Probiotics reduced the duration of diarrhoea, although the size of the effect varied considerably between studies.The average of the effect was significant for mean duration of diarrhoea (mean difference 24.76 hours; 95% confidence interval 15.9 to 33.6 hours; n=4555, trials=35) diarrhoea lasting ≥4 days (risk ratio 0.41; 0.32 to 0.53; n=2853, trials=29) and stool frequency on day 2 (mean difference 0.80; 0.45 to 1.14; n=2751, trials=20).The differences in effect size between studies was not explained by study quality, probiotic strain, the number of different strains, the viability of the organisms, dosage of organisms, the causes of diarrhoea, or the severity of the diarrhoea, or whether the studies were done in developed or developing countries.

AUTHORS' CONCLUSIONS

Used alongside rehydration therapy, probiotics appear to be safe and have clear beneficial effects in shortening the duration and reducing stool frequency in acute infectious diarrhoea. However, more research is needed to guide the use of particular probiotic regimens in specific patient groups.

STUDY 03

3. Zhang Y, Li L, Guo C, et al.; Effects of probiotic type, dose and treatment duration on irritable bowel syndrome diagnosed by Rome III criteria: a meta-analysis; https://www.ncbi.nlm.nih.gov/pubmed/27296254

Abstract

BACKGROUND:

Irritable bowel syndrome (IBS) is one of the most common functional gastroenterological diseases, affecting 11.2 % of people worldwide. Previous studies have shown that probiotic treatment may benefit IBS patients. However, the effect of probiotics and the appropriate type, dose, and treatment duration for IBS are still unclear. The aim of the current study was to assess the efficacy of different probiotic types, doses and treatment durations in IBS patients diagnosed by Rome III criteria via a meta-analysis of randomized controlled trials (RCTs).

METHODS:

Medline, EMBASE, and the Cochrane Central Register of Controlled Trials up to October 2015 were searched. RCTs including comparisons between the effects of probiotics and placebo on IBS patients diagnosed by Rome III criteria were eligible. Dichotomous data were pooled to obtain the relative risk (RR) with a 95 % confidence interval (CI), whereas continuous data were pooled using a standardized mean difference (SMD) with a 95 % CI.w

RESULTS

Twenty-one RCTs were included in this meta-analysis. Probiotic therapy was associated with more improvement than placebo administration in overall symptom response (RR: 1.82, 95 % CI 1.27 to 2.60) and quality of life (QoL) (SMD: 0.29, 95 % CI 0.08 to 0.50), but not in individual IBS symptoms. Single probiotics, a low dose, and a short treatment duration were more effective with respect to overall symptom response and QoL. No differences were detected in individual IBS symptoms in the subgroup analyses.

CONCLUSION:

Probiotics are an effective pharmacological therapy in IBS patients. Single probiotics at a low dose and with a short treatment duration appear to be more effective in improving overall symptom response and QoL, but more evidence for these effects is still needed.

STUDY 04

4. Ford AC, Quigley EM, Lacy BE, et al.; Efficacy of prebiotics, probiotics, and synbiotics in irritable bowel syndrome and chronic idiopathic constipation: systematic review and meta-analysis; https://www.ncbi.nlm.nih.gov/pubmed/25070051

Abstract

OBJECTIVES:

Irritable bowel syndrome (IBS) and chronic idiopathic constipation (CIC) are functional bowel disorders. Evidence suggests that disturbance in the gastrointestinal microbiota may be implicated in both conditions. We performed a systematic review and meta-analysis to examine the efficacy of prebiotics, probiotics, and synbiotics in IBS and CIC.

METHODS:

MEDLINE, EMBASE, and the Cochrane Controlled Trials Register were searched (up to December 2013). Randomized controlled trials (RCTs) recruiting adults with IBS or CIC, which compared prebiotics, probiotics, or synbiotics with placebo or no therapy, were eligible. Dichotomous symptom data were pooled to obtain a relative risk (RR) of remaining symptomatic after therapy, with a 95% confidence interval (CI). Continuous data were pooled using a standardized or weighted mean difference with a 95% CI.

RESULTS:

The search strategy identified 3,216 citations. Forty-three RCTs were eligible for inclusion. The RR of IBS symptoms persisting with probiotics vs. placebo was 0.79 (95% CI 0.70-0.89). Probiotics had beneficial effects on global IBS, abdominal pain, bloating, and flatulence scores. Data for prebiotics and synbiotics in IBS were sparse. Probiotics appeared to have beneficial effects in CIC (mean increase in number of stools per week=1.49; 95% CI=1.02-1.96), but there were only two RCTs. Synbiotics also appeared beneficial (RR of failure to respond to therapy=0.78; 95% CI 0.67-0.92). Again, trials for prebiotics were few in number, and no definite conclusions could be drawn.

CONCLUSIONS:

Probiotics are effective treatments for IBS, although which individual species and strains are the most beneficial remains unclear. Further evidence is required before the role of prebiotics or synbiotics in IBS is known. The efficacy of all three therapies in CIC is also uncertain.

STUDY 05

5. Hempel S, et al.; Safety of probiotics used to reduce risk and prevent or treat disease;
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4780970/

Abstract

DATA SOURCES

We searched 12 electronic databases, references of included studies, and pertinent reviews for studies addressing the safety of probiotics from database inception to August 2010 without language restriction.

OBJECTIVES

To catalog what is known about the safety of interventions containing Lactobacillus, Bifidobacterium, Saccharomyces, Streptococcus, Enterococcus, and/or Bacillus strains used as probiotic agents in research to reduce the risk of, prevent, or treat disease.

REVIEW METHODS

We identified intervention studies on probiotics that reported the presence or absence of adverse health outcomes in human participants, without restriction by study design, participant type, or clinical field. We investigated the quantity, quality, and nature of adverse events.

RESULTS

The search identified 11,977 publications, of which 622 studies were included in the review. In 235 studies, only nonspecific safety statements were made ("well tolerated"); the remaining 387 studies reported the presence or absence of specific adverse events. Interventions and adverse events were poorly documented. A number of case studies described fungemia and some bacteremia potentially associated with administered probiotic organisms. Controlled trials did not monitor routinely for such infections and primarily reported on gastrointestinal adverse events. Based on reported adverse events, randomized controlled trials (RCTs) showed no statistically significantly increased relative risk (RR) of the overall number of experienced adverse events (RR 1.00; 95% confidence interval [CI]: 0.93, 1.07, p=0.999); gastrointestinal; infections; or other adverse events, including seri-

ous adverse events (RR 1.06; 95% CI: 0.97, 1.16; p=0.201), associated with short-term probiotic use compared to control group participants; long-term effects are largely unknown. Existing studies primarily examined Lactobacillus alone or in combination with other genera, often Bifidobacterium. Few studies directly compared the safety among different intervention or participant characteristics. Indirect comparisons indicated that effects of delivery vehicles (e.g., yogurt, dairy) should be investigated further. Case studies suggested that participants with compromised health are most likely to experience adverse events associated with probiotics. However, RCTs in medium-risk and critically ill participants did not report a statistically significantly increased risk of adverse events compared to control group participants.

CONCLUSIONS

There is a lack of assessment and systematic reporting of adverse events in probiotic intervention studies, and interventions are poorly documented. The available evidence in RCTs does not indicate an increased risk; however, rare adverse events are difficult to assess, and despite the substantial number of publications, the current literature is not well equipped to answer questions on the safety of probiotic interventions with confidence.

STUDY 06

6. Pattani R, et al.; Probiotics for the prevention of antibiotic-associated diarrhea and Clostridium difficile infection among hospitalized patients: systematic review and meta-analysis; https://www.ncbi.nlm.nih.gov/-pubmed/24348885

Abstract

BACKGROUND:

Antibiotic-associated diarrhea (AAD) and Clostridium difficile infection (CDI) are associated with high morbidity, mortality, and health care costs. Probiotics may mitigate the existing disease burden. We performed a systematic review and meta-analysis to evaluate the efficacy of co-administration of probiotics with antibiotics in preventing these adverse outcomes in adult inpatients.

METHODS:

Systematic searches of MEDLINE (1946 to May 2012), Embase (1980 to May 2012), and the Cochrane Central Register of Controlled Trials were undertaken on May 31, 2012, to identify relevant publications. We searched for randomized controlled trials, published in English, of adult inpatients who were receiving antibiotics and who were randomly assigned to co-administration of probiotics or usual care, with or without the use of placebo. Studies were included if they reported on AAD or CDI (or both) as outcomes. Data for predetermined criteria evaluating study characteristics, methods, and risk of bias were extracted. Trials were given a global rating of good, fair, or poor by at least 2 reviewers. Meta-analyses were performed using a random-effects model, and pooled relative risks (RRs) and 95% confidence intervals (CIs) were calculated.

RESULTS:

Sixteen trials met the criteria for inclusion in this review. Four studies were of good quality, 5 were of fair quality, and 7 were of poor quality. Pooled analyses revealed significant reductions in the risks of AAD (RR 0.61, 95% CI 0.47 to 0.79) and CDI (RR 0.37, 95% CI 0.22 to 0.61) among patients randomly assigned to co-administration of probiotics. The number needed to treat for benefit was 11 (95% CI 8 to 20) for AAD and 14 (95% CI 9 to 50) for CDI. With subgroup analysis, significant reductions in rates of both AAD and CDI were retained in the subgroups of good-quality trials, the trials assessing a primarily Lactobacillus-based probiotic formulation, and the trials for which the follow-up period was less than 4 weeks.

INTERPRETATION:

Probiotics used concurrently with antibiotics reduce the risk of AAD and CDI.

STUDY 07

7. Steed H, Macfarlane GT, Blackett KL, et al.; Clinical trial: the microbiological and immunological effects of synbiotic consumption—a randomized double-blind placebo-controlled study in active Crohn's disease; https://www.ncbi.nlm.nih.gov/pubmed/20735782

Abstract

BACKGROUND:

Crohn's disease is an inflammatory illness in which the immune response against gut microorganisms is believed to drive an abnormal immune response. Consequently, modification of mucosal bacterial communities, and the immune effects they elicit, might be used to modify the disease state.

AIM:

To investigate the effects of synbiotic consumption on disease processes in patients with Crohn's disease.

METHODS:

A randomized, double-blind placebo-controlled trial was conducted involving 35 patients with active Crohn's disease, using a synbiotic comprising Bifidobacterium longum and Synergy 1. Clinical status was scored and rectal biopsies were collected at the start, and at 3- and 6-month intervals. Transcription levels of immune markers and mucosal bacterial 16S rRNA gene copy numbers were quantified using real-time PCR.

RESULTS:

Significant improvements in clinical outcomes occurred with synbiotic consumption, with reductions in both Crohn's disease activity indices (P = 0.020) and histological scores (P = 0.018). The synbiotic had little effect on mucosal IL-18, INF-gamma and IL-1beta; however, significant reductions occurred in TNF-alpha expression in synbiotic patients at 3 months (P = 0.041), although not at 6 months. Mucosal bifidobacteria proliferated in synbiotic patients.

CONCLUSION:

Synbiotic consumption was effective in improving clinical symptoms in patients with active Crohn's disease.

8. Molin, G. ; The Role of Lactobacillus plantarum in Foods and in Human Health; In: Farnworth, E.R. (Ed), Handbook of Fermented Functional Foods.
9. Aguirre, M. & Collins, M.D. (1993); Lactic acid bacteria and human clinical infections; J. Appl. Bact. 75:95-107.
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11. Salminen S., von Wright, A., Morelli, L., Marteau, P., Brassart, D., de Vos, W.M., Fonden, R., Saxelin, M., Collins, K., Mogensen, G., Birkeland, S.-E. & Mattila- Sandholm, T. (1998); Demonstration of safety of probiotics-a review; https://www.ncbi.nlm.nih.gov/pubmed/9849787

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.

12. Borriello, S.P., Hammes, W.P., Holzapfel, W., Marteau, P., Schrezenmeir, J., Vaara, M. & Valtonen, V. (2003); Safety of probiotics that contain lactobacilli or bifidobacteria; https://www.ncbi.nlm.nih.gov/pubmed/12627362

Abstract

Lactobacilli and bifidobacteria are extremely rare causes of infection in humans, as are probiotics based on these organisms. This lack of pathogenicity extends across all age groups and to immunocompromised individuals. Strains used for new probiotics should be chosen from the commensal flora of humans and should not

carry intrinsic resistance to antibiotics that would prevent treatment of a rare probiotic infection. Vigilance regarding the detection of possible rare cases of infection due to probiotics should be maintained, and isolates should be sent to reference centers for molecular characterization and confirmation.

STUDY 13

13. Salminen, M.K., Tynkkynen, S., Rautelin, H., Saxelin, M., Vaara, M., Ruutu, P., Seppo Sarna, S., Valtonen, V. & Järvinen, A. (2002); Lactobacillus Bacteremia during a Rapid Increase in Probiotic Use of Lactobacillus rhamnosus GG in Finland; https://www.ncbi.nlm.nih.gov/pubmed/12410474

Abstract

Lactobacilli supposedly have low pathogenicity; they are seldom detected in blood culture. Lactobacillus rhamnosus GG, which originates indigenously in the human intestine, became available for use as a probiotic in 1990 in Finland. We evaluated the possible effects of the increased probiotic use of L. rhamnosus GG on the occurrence of bacteremia due to lactobacilli. Lactobacilli were isolated in 0.02% of all blood cultures and 0.2% of all blood cultures with positive results in Helsinki University Central Hospital and in Finland as a whole, and no trends were seen that suggested an increase in Lactobacillus bacteremia. The average incidence was 0.3 cases/100,000 inhabitants/-year in 1995-2000 in Finland. Identification to the species level was done for 66 cases of Lactobacillus bacteremia, and 48 isolates were confirmed to be Lactobacillus strains. Twenty-six of these strains were L. rhamnosus, and 11 isolates were identical to L. rhamnosus GG. The results indicate that increased probiotic use of L. rhamnosus GG has not led to an increase in Lactobacillus bacteremia.

STUDIES 14, 15, 16

14. Mogensen, G., Salminen, S., O'Brien, J., Ouwehand, A.C., Holzapfel, W., Shortt, C., Fonden, R., Miller, G.D., Donohue, D., Playne, M., Crittenden, R., Salvadori, B. & Zink, R. (2002); Inventory of microorganisms with a documented history of safe use in food; Bulletin of the International Dairy Federation. 377:10-19

15. List of taxonomic units proposed for QPS status; http://www.efsa.europa.eu/EFSA/Scientific_Opinion/sc_op_ej587_qps_en.pdf.

16. Daniel,C., Poiret, S., Goudercourt, D., Dennin,V., Leyer, G. & Pot, B. (2006); Selecting Lactic Acid Bacteria for Their Safety and Functionality by Use of a Mouse Colitis Model; https://www.ncbi.nlm.nih.gov/pubmed/16957197

Abstract

Studies showed that specific probiotics might provide therapeutic benefits in inflammatory bowel disease. However, a rigorous screening of new probiotics is needed to study possible adverse interactions with the host, particularly when intended for administration to individuals with certain health risks. In this context, the objective of this study was to investigate the role of three lactobacilli (LAB) on intestinal inflammation and bacterial translocation using variations of the mouse model of 2,4,6-trinitrobenzene sulfonic acid (TNBS)-induced acute colitis. We first compared the in vitro ability of LAB to survive gastrointestinal tract (GIT) conditions and their ability to persist in the GIT of mice following daily oral administration. As a control, we included a nonprobiotic Lactobacillus paracasei strain, previously isolated from an endocarditis patient. Feeding high doses of LAB strains to healthy and to TNBS-treated mice did not induce any detrimental effect or abnormal translocation of

the bacteria. Oral administration of Lactobacillus salivarius Ls-33 had a significant preventive effect on colitis in mice, while Lactobacillus plantarum Lp-115 and Lactobacillus acidophilus NCFM did not. None of the three selected LAB strains translocated to extraintestinal organs of TNBS-treated mice. In contrast, L. paracasei exacerbated colitis under severe inflammatory conditions and translocated to extraintestinal organs. This study showed that evaluations of the safety and functionality of new probiotics are recommended. We conclude that not all lactobacilli have similar effects on intestinal inflammation and that selected probiotics such as L. salivarius Ls-33 may be considered in the prevention or treatment of intestinal inflammation.

STUDY 17

17. Collado, M.C., Meriluoto, J. & Salminen, S. (2007); Adhesion and aggregation properties of probiotic and pathogen strains; https://link.springer.com/article/10.1007/s00217-007-0632-x

Abstract

Autoaggregation has been correlated with adhesion, which is known to be a prerequisite for colonization and infection of the gastrointestinal tract by many pathogens. The coaggregation properties of probiotic strains with pathogens as well as their ability to displace pathogens are of importance for therapeutic manipulation of the aberrant intestinal microbiota. Consequently, the ability to aggregate and coaggregate are desirable properties for probiotics in health-promoting foods. Aggregation assays and bacterial adhesion to hydrocarbons (BATH test) demonstrated significant differences in cell surface properties among the tested commercial probiotic strains. Hydrophobicity increased when the cells were heat-inactivated. All probiotic strains tested showed aggregation abilities with the pathogen strains tested, but the results were strain-specific and dependent on time and incubation conditions. Our results indicate that the ability to autoaggregate, together with cell-surface hydrophobicity and coaggregation abilities with pathogen strains can be used for preliminary screening in order to identify potentially probiotic bacteria suitable for human or animal use.

STUDY 18

18. Collado, M.C., Meriluoto, J. & Salminen, S. (2007); Role of commercial probiotic strains against human pathogen adhesion to intestinal mucus; https://www.ncbi.nlm.nih.gov/pubmed/17897389

Abstract

AIMS:

The aims of this study present were to assess and to evaluate in vitro the abilities of commercial probiotic strains derived from fermented milk products and related sources currently marketed in European countries, to inhibit, compete and displace the adhesion of selected potential pathogens to immobilized human mucus.

METHODS AND RESULTS:

The adhesion was assessed by measuring the radioactivity of bacteria adhered to the human mucus. We tested 12 probiotic strains against eight selected pathogens. All strains tested were able to adhere to mucus. All probiotic strains tested were able to inhibit and displace ($P<0.05$) the adhesion of Bacteroides, Clostridium, Staphylococcus and Enterobacter. In addition, the abilities to inhibit and to displace adhered pathogens depended on both the probiotic and the pathogen strains tested suggesting that several complementary mechanisms are implied in the processes.

CONCLUSIONS:

Our results indicate the need for a case-by-case assessment in order to select strains with the ability to inhibit or displace a specific pathogen. Probiotics could be useful to correct deviations observed in intestinal microbiota associated with specific diseases and also, to prevent pathogen infections.

SIGNIFICANCE AND IMPACT OF THE STUDY:

The competitive exclusion properties of probiotics as well as their ability to displace and inhibit pathogens are the most importance for therapeutic manipulation of the enteric microbiota. The application of such strategies could contribute to expand the beneficial properties on human health against pathogen infection.

STUDIES 19, 20, 21, 22, 24

19. Cori, C.F. & Cori, G.T. (1929); Glycogen formation in the liver from D- and L-lactic acid; J. Biol. Chem. 81, 389-403.
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24. Foligne, B., Nutten, S., Grangette, C., Dennin, V., Goudercourt, D., Poiret, S., Dewulf, J., Brassart, D., Mercenier, A. & Pot, B. (2007); Correlation between in vitro and in vivo immunomodulatory properties of lactic acid bacteria; https://www.ncbi.nlm.nih.gov/pubmed/17226902

Abstract

AIM:

To investigate the correlation between in vitro and in vivo immunomodulation potential of the probiotic strain and its ability to prevent experimental colitis in mice.

METHODS:

In vitro immunomodulation was assessed by measuring interleukin (IL)-12p70, IL-10, tumor necrosis factor alpha (TNFalpha) and interferon gamma (IFNgamma) release by human peripheral blood mononuclear cells (PBMCs) after 24 h stimulation with 13 live bacterial strains. A murine model of acute TNBS-colitis was next used to evaluate the prophylactic protective capacity of the same set of strains.

RESULTS:

A strain-specific in vivo protection was observed. The strains displaying an in vitro potential to induce higher levels of the anti-inflammatory cytokine IL-10 and lower levels of the inflammatory cytokine IL-12, offered the best protection in the in vivo colitis model. In contrast, strains leading to a low IL-10/IL-12 cytokine ratio could not significantly attenuate colitis symptoms.

CONCLUSION:

These results show that we could predict the in vivo protective capacity of the studied lactic acid bacteria (LAB) based on the cytokine profile we established in vitro. The PBMC-based assay we used may thus serve as a useful primary indicator to narrow down the number of candidate strains to be tested in murine models for their anti-inflammatory potential.

STUDY 25

25. Delcour, J., Ferain, T., Deghorain, M., Palumbo, E. & Hols, P. (1999); The biosynthesis and functionality of the cellwall of lactic acid bacteria; https://www.ncbi.nlm.nih.gov/pubmed/10532377

Abstract

The cell wall of lactic acid bacteria has the typical gram-positive structure made of a thick, multilayered peptidoglycan sacculus decorated with proteins, teichoic acids and polysaccharides, and surrounded in some species by an outer shell of proteins packed in a paracrystalline layer (S-layer). Specific biochemical or genetic data on the biosynthesis pathways of the cell wall constituents are scarce in lactic acid bacteria, but together with genomics information they indicate close similarities with those described in Escherichia coli and Bacillus subtilis, with one notable exception regarding the peptidoglycan precursor. In several species or strains of enterococci and lactobacilli, the terminal D-alanine residue of the muramyl pentapeptide is replaced by D-lactate or D-serine, which entails resistance to the glycopeptide antibiotic vancomycin. Diverse physiological functions may be assigned to the cell wall, which contribute to the technological and health-related attributes of lactic acid bacteria. For instance, phage receptor activity relates to the presence of specific substituents on teichoic acids and polysaccharides; resistance to stress (UV radiation, acidic pH) depends on genes involved in peptidoglycan and teichoic acid biosynthesis; autolysis is controlled by the degree of esterification of teichoic acids with D-alanine; mucosal immunostimulation may result from interactions between epithelial cells and peptidoglycan or teichoic acids.

STUDY 26

26. Aagaard K, Petrosino J, Keitel W, Watson M, Katancik J, Garcia N, Patel S, Cutting M, Madden T, Hamilton H, Harris E, Gevers D, Simone G, McInnes P, Versalovic J.; The Human Microbiome Project strategy for comprehensive sampling of the human microbiome and why it matters; https://www.ncbi.nlm.nih.gov/pubmed/23165986

Abstract

The Human Microbiome Project used rigorous good clinical practice standards to complete comprehensive body site sampling in healthy 18- to 40-yr-old adults, creating an unparalleled reference set of microbiome specimens. To ensure that specimens represented minimally perturbed microbiomes, we first screened potential participants using exclusion criteria based on health history, including the presence of systemic diseases (e.g., hypertension, cancer, or immunodeficiency or autoimmune disorders), use of potential immunomodulators, and recent use of antibiotics or probiotics. Subsequent physical examinations excluded individuals based on body mass index (BMI), cutaneous lesions, and oral health. We screened 554 individuals to enroll 300 (149 men and 151 women, mean age 26 yr, mean BMI 24 kg/m, 20.0% racial minority, and 10.7% Hispanic). We obtained specimens from the oral cavity, nares, skin, gastrointestinal tract, and vagina (15 specimens from men and 18 from women). The study evaluated longitudinal changes in an individual's microbiome by sampling 279 participants twice (mean 212 d after the first sampling; range 30-359 d) and 100 individuals 3 times (mean 72 d after the second sampling; range 30-224 d). This sampling strategy yielded 11,174 primary specimens, from which 12,479 DNA samples were submitted to 4 centers for metagenomic sequencing. Our clinical design and well-defined reference cohort has laid a foundation for microbiome research.

27. McFarland LV; Use of probiotics to correct dysbiosis of normal microbiota following disease or disruptive events: a systematic review; https://www.ncbi.nlm.nih.gov/pubmed/25157183

Abstract

OBJECTIVE:

To assess the evidence for the claim probiotics can correct dysbiosis of the normal microbiota resulting from disease or disruptive events.

SETTING:

Systematic review of published clinical trials of patients receiving a probiotic intervention for the prevention or treatment of various diseases.

DATA SOURCES:

Sources searched (1985-2013): PubMed, EMBASE, Cochrane Database of Systematic Reviews, CINAHL, AMED and ISI Web of Science. Three on-line clinical trial registries were searched: Cochrane Central Register of Controlled trials, MetaRegister of Controlled Trials and National Institutes of Health.

REVIEW METHODS:

Included studies were randomised clinical trials of probiotic interventions having microbiological assays. Studies were evaluated following Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines for specific probiotic strains. A standard data extraction form was used to collect the raw data.

RESULTS:

The review of the literature found three distinct study designs: model A (restoration) assayed patients enrolled with a healthy, undisturbed microbiota and then assayed postdisruptive event and probiotic therapy; model B (alteration) assayed patients with pre-existing disrupted microbiota and then postprobiotic therapy; model C (no dysbiosis) assayed volunteers with no disruptive event prebiotic and postprobiotic. From a total of 63 trials, 83% of the probiotic products using model A restored the microbiota, 56% using model B improved the microbiota and only 21% using model C had any effect on microbiota. Clinical efficacy was more commonly associated with strains capable of restoration of the normal microbiota.

OUTCOME MEASURES:

The primary outcome is the degree of microbiota correction by specific probiotic strains. Secondary outcome was the association between the degree of dysbiosis correction and clinical efficacy.

CONCLUSIONS:

The ability to assess the degree of dysbiosis improvement is dependent on the enrolled population and the timing of microbiological assays. The functional claim for correcting dysbiosis is poorly supported for most probiotic strains and requires further research.

28. World Health Organization & Food and Agriculture Organization of the United Nations; Probiotics in food: Health and nutritional properties and guidelines for evaluation; FAO Food and Nutrition paper 85 2006; page 2.

29. Stamatova I, Meurman JH; Probiotics: Health benefits in the mouth; https://www.ncbi.nlm.nih.gov/pubmed/20178208

Abstract

Probiotics or health-beneficial bacteria have only recently been introduced in dentistry and oral medicine after years of successful use in mainly gastro-intestinal disorders. The concept of bacteriotherapy and use of health-beneficial micro-organisms to heal diseases or support immune function was first introduced in the beginning of the 20th century. Later the concept lead to the development of modem dairy industry and even today most probiotic strains are lactobacilli or bifidobacteria used in milk fermentation. The mechanisms of probiotic action are mainly unknown but the inter-microbial species interactions are supposed to play a key role in this together with their immuno-stimulatory effects. The introduction of probiotic bacteria in the mouth calls for ascertainment of their particular safety. Since acid production from sugar is detrimental to teeth, care must be taken not to select strains with high fermentation capacity. The first randomized controlled trials have nevertheless shown that probiotics may control dental caries in children due to their inhibitory action against cariogenic streptococci. Less evidence exists on their role in periodontal disease or oral yeast infections. Furthermore the best vehicles for oral probiotic applications need to be assessed. So far mainly dairy products have been investigated but other means such as probiotics in chewing gums or lozenges have also been studied. From the clinical practitioner's point of view direct recommendations for the use of probiotics cannot yet be given. However, scientific evidence so far indicates that probiotic therapy may be a reality also in dentistry and oral medicine in the future.

30. Gareau MG, Sherman PM, Walker WA; Probiotics and the gut microbiota in intestinal health and disease; https://www.ncbi.nlm.nih.gov/pubmed/20664519

Abstract

The use of probiotics is increasing in popularity for both the prevention and treatment of a variety of diseases. While a growing number of well-conducted, prospective, randomized, controlled, clinical trials are emerging and investigations of underlying mechanisms of action are being undertaken, questions remain with respect to the specific immune and physiological effects of probiotics in health and disease. This Review considers recent advances in clinical trials of probiotics for intestinal disorders in both adult and pediatric populations. An overview of recent in vitro and in vivo research related to potential mechanisms of action of various probiotic formulations is also considered.

STUDY 31

31. Bermudez-Brito M, Plaza-Díaz J, Muñoz-Quezada S, Gómez-Llorente C, Gil A, 2012; Probiotic mechanisms of action; https://www.ncbi.nlm.nih.gov/pubmed/23037511

Abstract

Probiotics are live microorganisms that provide health benefits to the host when ingested in adequate amounts. The strains most frequently used as probiotics include lactic acid bacteria and bifidobacteria. Probiotics have demonstrated significant potential as therapeutic options for a variety of diseases, but the mechanisms responsible for these effects have not been fully elucidated yet. Several important mechanisms underlying the antagonistic effects of probiotics on various microorganisms include the following: modification of the gut microbiota, competitive adherence to the mucosa and epithelium, strengthening of the gut epithelial barrier and modulation of the immune system to convey an advantage to the host. Accumulating evidence demonstrates that probiotics communicate with the host by pattern recognition receptors, such as toll-like receptors and nucleotide-binding oligomerization domain-containing protein-like receptors, which modulate key signaling pathways, such as nuclear factor-κB and mitogen-activated protein kinase, to enhance or suppress activation and influence downstream pathways. This recognition is crucial for eliciting measured antimicrobial responses with minimal inflammatory tissue damage. A clear understanding of these mechanisms will allow for appropriate probiotic strain selection for specific applications and may uncover novel probiotic functions. The goal of this systematic review was to explore probiotic modes of action focusing on how gut microbes influence the host.

STUDY 32

32. de Almada CN, de Almada CN, Martinez RCR, Sant Ana A de S; Characterization of the intestinal microbiota and its interaction with probiotics and health impacts; https://www.ncbi.nlm.nih.gov/pubmed/25895093

Abstract

The gastrointestinal tract (GIT) is a dynamic microecosystem containing a diversified microbiota of about 500-1000 different microbial species. Humans depend on their intestinal microbiota to carry out vital functions, and thus, equilibrium among intestinal groups of microorganisms is essential. In this review article, the use of traditional and molecular methods is discussed for the characterization of the intestinal microbiota, as well as its interaction with probiotics and their effects on health. An improved knowledge on intestinal microbiota composition and diversity and how changes in this microecosystem can cause or are associated with diseases remains far from being completely understood. Therefore, a better understanding of the GIT microbial populations is crucial, which will certainly contribute to the development of new strategies for the prevention and/or treatment of several diseases. The manipulation of the GIT microbiota by probiotics consumption is an interesting approach to maintain and restore human health.

STUDY 33

33. Sengupta R, Altermann E, Anderson RC, McNabb WC, Moughan PJ, Roy NC.; The Role of Cell Surface Architecture of Lactobacilli in Host-Microbe Interactions in the Gastrointestinal Tract; https://www.hindawi.com/journals/mi/2013/237921/

Abstract

Lactobacillus species can exert health promoting effects in the gastrointestinal tract (GIT) through many mechanisms, which include pathogen inhibition, maintenance of microbial balance, immunomodulation, and enhancement of the epithelial barrier function. Different species of the genus Lactobacillus can evoke different responses in the host, and not all strains of the same species can be considered beneficial. Strain variations may be related to diversity of the cell surface architecture of lactobacilli and the bacteria's ability to express certain surface components or secrete specific compounds in response to the host environment. Lactobacilli are known to modify their surface structures in response to stress factors such as bile and low pH, and these adaptations may help their survival in the face of harsh environmental conditions encountered in the GIT. In recent years, multiple cell surface-associated molecules have been implicated in the adherence of lactobacilli to the GIT lining, immunomodulation, and protective effects on intestinal epithelial barrier function. Identification of the relevant bacterial ligands and their host receptors is imperative for a better understanding of the mechanisms through which lactobacilli exert their beneficial effects on human health.

STUDY 34

34. Teanpaisan R, Piwat S, Dahlén G.; Inhibitory effect of oral Lactobacillus against oral pathogens; https://www.ncbi.nlm.nih.gov/pubmed/21801186

Abstract

AIMS:

To determine the inhibitory effect of oral Lactobacillus against putative oral pathogens.

METHODS AND RESULTS:

Total 357 strains comprising 10 species of oral Lactobacillus, Lactobacillus fermentum (195), Lactobacillus salivarius (53), Lactobacillus casei (20), Lactobacillus gasseri (18), Lactobacillus rhamnosus (14), Lactobacillus paracasei (12), Lactobacillus mucosae (12), Lactobacillus oris (12), Lactobacillus plantarum (11) and Lactobacillus vaginalis (10) were used as producer strains. Inhibitory effect against a panel of indicators, periodontitis- and caries-related pathogens, was assessed. Most oral Lactobacillus was able to inhibit the growth of both periodontitis- and caries-related pathogens. The strongest inhibitory activity was associated with Lact. paracasei, Lact. plantarum, Lact. rhamnosus, Lact. casei and Lact. salivarius. Lactobacillus SD1-SD6, representing the six species with the strong inhibitory effect, inhibited growth of Streptococcus mutans ATCC 25175 in the biofilm model. Also, it was demonstrated that growth of Strep. mutans was inhibited in a mixture with Lact. paracasei SD1. The inhibition was enhanced in acidic condition and 5% glucose.

CONCLUSIONS:

The results have shown that oral Lactobacillus SD1-SD6 showed a strong inhibitory effect against Strep. mutans and Streptococcus sobrinus, as well as, Gram-negative periodontal pathogens Porphyromonas gingivalis and Aggregatibacter actinomycetemcomitans.

SIGNIFICANCE AND IMPACT OF THE STUDY:

The results indicated that Lactobacillus may be of benefit as probiotics for the prevention of oral diseases.

35. Mousavi E, Makvandi M, Teimoori A, Ataei A, Ghafari S, Najafian M, Ourang Z, Samarbaf-Zadeh A.; In vitro adherence of Lactobacillus strains isolated from the vaginas of healthy Iranian women.; https://www.ncbi.nlm.nih.gov/pubmed/27562422

Abstract

BACKGROUND:

The lactobacilli are a part of the bacterial flora of the human vagina. Detection of normal Lactobacillus species in the vaginas of healthy women in different geographical locations, and evaluation of their specific properties, can aid in the selection of the best species for preventing sexually transmitted diseases in the future. This study was performed to isolate and identify the Lactobacillus species in the vaginas of healthy women and to evaluate the adherence of these lactobacilli to Vero and HeLa cell lines.

METHODS:

The study included 100 women. Bacteria were isolated from healthy women and purified. Phenotypic and biochemical tests were performed to identify the lactobacilli. The Lactobacillus species were detected by molecular methods using polymerase chain reaction amplification of the full length of the 16S rDNA of the isolated bacteria. Several isolates of each species were then selected to study their adherence to Vero and HeLa cell lines.

RESULTS:

Among the 50 samples taken from healthy women meeting the inclusion criteria, Lactobacillus species were identified in 33 (66%) samples. Of these lactobacilli, 14 isolates were Lactobacillus crispatus, six (18.2%) were Lactobacillus gasseri, nine (27%) were Lactobacillus rhamnosus, and the rest were either Lactobacillus salivarius (6%) or Lactobacillus plantarum (6%). L. rhamnosus showed the greatest adhesion to the cells when compared to the other tested species. All the lactobacilli isolated in this study showed a smaller capacity for cell adherence when compared with control species.

CONCLUSION:

L. crispatus, L. rhamnosus, and L. gasseri were the dominant Lactobacillus species in the vaginas of healthy women in Iran. L. rhamnosus attached more readily to the cells than did the other species; therefore, this isolate is a good candidate for further studies on the potential health benefits and application of lactobacilli as probiotics.

36. Haghshenas B, Nami Y, Haghshenas M, Abdullah N, Rosli R, Radiah D, Khosroushahi AY.; Bioactivity characterization of Lactobacillus strains isolated from dairy products; https://www.ncbi.nlm.nih.gov/pubmed/26219634

Abstract

This study aimed to find candidate strains of Lactobacillus isolated from sheep dairy products (yogurt and ewe colostrum) with probiotic and anticancer activity. A total of 100 samples were randomly collected from yogurt and colostrum and 125 lactic acid bacteria were isolated. Of these, 17 Lactobacillus strains belonging to five species (L. delbrueckii, L. plantarum, L. rhamnosus, L. paracasei, and L. casei) were identified. L. plantarum 17C and 13C, which isolated from colostrums, demonstrated remarkable results such as resistant to low pH and high concentrations of bile salts, susceptible to some antibiotics and good antimicrobial activity that

candidate them as potential probiotics. Seven strains (1C, 5C, 12C, 13C, 17C, 7M, and 40M), the most resistant to simulated digestion, were further investigated to evaluate their capability to adhere to human intestinal Caco-2 cells. L. plantarum 17C was the most adherent strain. The bioactivity assessment of L. plantarum 17C showed anticancer effects via the induction of apoptosis on HT-29 human cancer cells and negligible side effects on one human epithelial normal cell line (FHs 74). The metabolites produced by this strain can be used as alternative pharmaceutical compounds with promising therapeutic indices because they are not cytotoxic to normal mammalian cells.

STUDY 37

37. Plaza-Diaź J, Fernández-Caballero JÁ, Chueca N, García F, Gómez-Llorente C, Sáez-Lara MJ, Fontana L, Gil Á.; Pyrosequencing Analysis Reveals Changes in Intestinal Microbiota of Healthy Adults Who Received a Daily Dose of Immunomodulatory Probiotic Strains.; https://www.ncbi.nlm.nih.gov/pubmed/26016655

Abstract

The colon microbiota plays a crucial role in human gastrointestinal health. Current attempts to manipulate the colon microbiota composition are aimed at finding remedies for various diseases. We have recently described the immunomodulatory effects of three probiotic strains (Lactobacillus rhamnosus CNCM I-4036, Lactobacillus paracasei CNCM I-4034, and Bifidobacterium breve CNCM I-4035). The goal of the present study was to analyze the compositions of the fecal microbiota of healthy adults who received one of these strains using high-throughput 16S ribosomal RNA gene sequencing. Bacteroides was the most abundant genus in the groups that received L. rhamnosus CNCM I-4036 or L. paracasei CNCM I-4034. The Shannon indices were significantly increased in these two groups. Our results also revealed a significant increase in the Lactobacillus genus after the intervention with L. rhamnosus CNCM I-4036. The initially different colon microbiota became homogeneous in the subjects who received L. rhamnosus CNCM I-4036. While some orders that were initially present disappeared after the administration of L. rhamnosus CNCM I-4036, other orders, such as Sphingobacteriales, Nitrospirales, Desulfobacterales, Thiotrichales, and Synergistetes, were detected after the intervention. In summary, our results show that the intake of these three bacterial strains induced changes in the colon microbiota.

STUDY 38

38. Kumar A, Kumar D.; Development of antioxidant rich fruit supplemented probiotic yogurts using free and microencapsulated Lactobacillus rhamnosus culture; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4711432/

The present study reports the preparation of probiotic yogurt using Lactobacillus rhamnosus. The standard starter cultures used for yogurt fermentation were Streptococcus thermophilus and Lactobacillus delbrueckii subsp. bulgaricus and obtained from NDRI, Karnal, India. The prepared yogurt was supplemented with fruit pulp (10 % w/v) of apricot, raspberries, plum and jamun. These fruits were rich in antioxidant property as observed by DPPH, nitric oxide radical scavenging and ferric reducing antioxidant power assay methods. The probiotic yogurt products were prepared using free, alginate (2 %) and carrageenan (2 %) encapsulated probiotic L. rhamnosus culture. The microencapsulated beads were characterized by FTIR and alginate beads with bacteria showed characteristic wavelength major at 1424 and 1033 nm. The acidity increased (0.40 ± 0–0.76 ± 0.01 %) and pH of yogurts decreased (4.63 ± 0.06 – 2.83 ± 0.03) during storage. Probiotic L. rhamnosus count decreased during storage and alginate microencapsulated probiotic culture was more stable (8.85 ± 0.01 – 4.35 ± 0.03 log CFU/g) as compared with carrageenan encapsulated (8.79 ± 0.01 –2.56 ± 0.04 log CFU/g) and free culture (8.90 ± 0.01 – 2.26 ± 0.03 log CFU/g). The antioxidant power of fruits supplemented probiotic yogurts decreased successively during storage up to 15 days

STUDY 39

39. Azat R, Liu Y, Li W, Kayir A, Lin D.-B., Zhou W.-W., Zheng X.-D.; Probiotic properties of lactic acid bacteria isolated from traditionally fermented Xinjiang cheese; https://www.ncbi.nlm.nih.gov/pubmed/27487805

Abstract

Six lactic acid bacterial (LAB) strains were isolated from traditionally fermented Xinjiang cheese and evaluated for functional and probiotic properties and potentials as starter cultures. The isolated six LAB strains comprised Lactobacillus rhamnosus (one strain), Lactobacillus helveticus (one strain), and Enterococcus hirae (four strains). All of the six strains were tolerant to acidic and bile salt conditions. Among which, the L. rhamnosus R4 strain showed more desirable antimicrobial, auto-aggregation, and hydrophobic activity. In addition, the strain L. rhamnosus R4 exhibited the highest level of free radical scavenging activity (53.78% of 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radicals and 45.79% of hydroxyl radicals). L. rhamnosus R4 also demonstrated cholesterol and triglyceride degradation by 50.97% and 28.92%, respectively. To further examine the health-promoting effects of these LAB strains on host lifespan, Caenorhabditis elegans was used as an in vivo model. Worms fed LAB as a food source had significant differences in lifespan compared to those fed Escherichia coli OP50 (as a negative control). Feeding of L. rhamnosus R4 extended the mean lifespan of C. elegans by up to 36.1% compared to that of the control. The results suggest that the strains isolated from Xinjiang fermented dairy products have high potential as starter cultures in the cheese industry.

STUDY 40

40. Hauser G, Salkic N, Vukelic K, JajacKnez A, Stimac D.; Probiotics for Standard Triple Helicobacter pylori Eradication: A Randomized, Double-blind, Placebo-controlled Trial.; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4603068/

Abstract

The primary objective in the study is determination of efficacy of probiotic preparation as a supportive therapy in eradication of Helicobacter pylori.

The study was multicenter, prospective, randomized, placebo controlled, and double-blind. The subjects first filled out a specially designed questionnaire to assess the severity of the 10 symptoms, which can be related to eradication therapy to be monitored during the trial. Each subject then received 28 capsules of probiotic preparation or matching placebo capsules, which they were supposed to take over the following 14 days, twice a day, at least 2 hours prior to or after the antibiotic therapy administration.

A total of 804 patients were enrolled in the trial, of which 650 (80.85%) were included in the analysis. The results show a significantly larger share of cured subjects in the probiotic arm versus the placebo arm (87.38% vs 72.55%; P < 0.001). Additionally, presence and intensity of epigastric pain, bloating, flatulence, taste disturbance, loss of appetite, nausea, vomiting, heartburn, rash, and diarrhea were monitored over the study period. At 15 days postinclusion, probiotic treatment was found superior to placebo in 7 of 10 mentioned symptoms. Average intensity for symptoms potentially related to antibiotic therapy was significantly higher in the placebo group, 0.76 vs 0.55 (P < 0.001).

Adding probiotics to the standard triple therapy for H pylori eradication significantly contributes to treatment efficacy and distinctly decreases the adverse effects of therapy and the symptoms of the underlying disease.

STUDY 41

41. Sanchez, M, Darimont C, Panahi S, Drapeau V, Marette A, Taylor VH, Doré J, Tremblay A.; Effects of a Diet-Based Weight-Reducing Program with Probiotic Supplementation on Satiety Efficiency, Eating Behaviour Traits, and Psychosocial Behaviours in Obese Individuals.; https://www.ncbi.nlm.nih.gov/pubmed/28294985

Abstract

This study evaluated the impact of probiotic supplementation (Lactobacillus rhamnosus CGMCC1.3724 (LPR)) on appetite sensations and eating behaviors in the context of a weight-reducing program. Obese men (n = 45) and women (n = 60) participated in a double-blind, randomized, placebo-controlled trial that included a 12-week weight loss period (Phase 1) based on moderate energy restriction, followed by 12 weeks of weight maintenance (Phase 2). During the two phases of the program, each subject consumed two capsules per day of either a placebo or a LPR formulation (10 mg of LPR equivalent to 1.6 108 CFU/capsule, 210 mg of oligofructose, and 90 mg of inulin). The LPR supplementation increased weight loss in women that was associated with a greater increase in the fasting desire to eat (p = 0.03). On the other hand, satiety efficiency (satiety quotient for desire to eat) at lunch increased (p = 0.02), whereas disinhibition (p = 0.05) and hunger (p = 0.02) scores decreased more in the LPR-treated women, when compared with the female control group. Additionally, the LPR female group displayed a more pronounced decrease in food craving (p = 0.05), and a decrease in the Beck Depression Inventory score (p = 0.05) that was significantly different from the change noted in the placebo group (p = 0.02), as well as a higher score in the Body Esteem Scale questionnaire (p = 0.06). In men, significant benefits of LPR on fasting fullness and cognitive restraint were also observed. Taken together, these observations lend support to the hypothesis that the gut-brain axis may impact appetite control and related behaviors in obesity management.

42. EFSA BIOHAZ Panel (EFSA Panel on Biological Hazards), Ricci A, Allende A, Bolton D, Chemaly M, Davies R, Girones R, Koutsoumanis K, Herman L, Lindqvist R, Nørrung B, Robertson L, Ru G, Sanaa M, Simmons M, Skandamis P, Snary E, Speybroeck N, Ter Kuile B, Threlfall J, Wahlström H, Cocconcelli PS, Klein G (deceased), Peixe L, Maradona MP, Querol A, Suarez JE, Sundh I, Vlak J, Correia S and Fernández Escámez PS, 2017.; Statement on the update of the list of QPS-recommended biological agents intentionally added to food or feed as notified to EFSA 5: suitability of taxonomic units notified to EFSA until September 2016. EFSA Journal 2017;15(3):4663, 20 pp.

43. Pendharkar S, Brandsborg E, Hammarström L, Marcotte L, Larsson P.-G.; Vaginal colonisation by probiotic lactobacilli and clinical outcome in women conventionally treated for bacterial vaginosis and yeast infection; https://www.ncbi.nlm.nih.gov/pubmed/26137971

Abstract

BACKGROUND:

The aim of this study was to investigate the colonisation by lactobacilli and clinical outcome in women with bacterial vaginosis (BV) and recurrent vulvovaginal candidiasis (R-VVC) receiving antibiotic or anti-fungal treatment in combination with the probiotic EcoVag® capsules.

METHODS:

A total of 40 Scandinavian women diagnosed with BV or VVC on the basis of Amsel's criteria or clinical symptoms were consecutively recruited in two pilot open label clinical trials. In trial I, women with BV were treated with clindamycin and metronidazole followed by vaginal EcoVag® capsules, containing Lactobacillus rhamnosus DSM 14870 and Lactobacillus gasseri DSM 14869, for 5 consecutive days after each antibiotic treatment. In trial II, women were recruited in three groups as follows: women with BV receiving clindamycin and metronidazole treatment together with a prolonged administration of EcoVag® (10 consecutive days after each antibiotic treatment followed by weekly administration of capsules for next four months), women with R-VVC receiving extended fluconazole and EcoVag® treatment, and women receiving extended fluconazole treatments only. The difference in frequency of isolation of EcoVag® strains or other lactobacilli between groups was compared by Fisher's exact test.

RESULTS:

The 6-month cure rate for BV was 50 % in trial I while both the 6- and 12-month cure rates were 67 % in trial II. The 6- and 12-month cure rates for VVC were 100 % and 89 % in women receiving fluconazole and EcoVag®, and 100 % and 70 % in women receiving fluconazole only. The frequency of isolation of any Lactobacillus species during the course of the study was associated with cure of BV in trial I and II, whereas the frequency of isolation of EcoVag® strains was significantly associated with the cure of BV in trial II only. As previously observed, a change in sexual partner was associated with relapse of BV with an Odds ratio of 77 (95 % CI: 2.665 to 2225).

CONCLUSIONS:

The study suggests that the treatment with antibiotics or anti-fungal medication in combination with EcoVag® capsules provide long-term cure against BV and R-VVC as compared to previous reports.

STUDY 44

44. Gad M, Ravn P, Søborg DA, Lund-Jensen K, Ouwehand AC, Jensen SS.; Regulation of the IL-10/IL-12 axis in human dendritic cells with probiotic bacteria; https://www.ncbi.nlm.nih.gov/pubmed/21707779

Abstract

In this study, we have used monocyte-derived dendritic cells (DCs) to design a screening model for the selection of microorganisms with the ability to suppress DC-secreted IL-12p70, a critical cytokine for the induction of T-helper cell type 1 immune responses under inflammatory conditions. By the treatment of DCs with cocktails containing TLR agonists and proinflammatory cytokines, the cells increased the secretion of the Th1-promoting cytokine IL-12p70. Clinically used probiotics were tested for their IL-10- and IL-12p70-stimulating properties in immature DCs, and showed a dose-dependent change in the IL-10/IL-12p70 balance. Lactobacillus acidophilus NCFM(™) and the probiotic mixture VSL#3 showed a strong induction of IL-12p70, whereas Lactobacillus salivarius Ls-33 and Bifidobacterium infantis 35624 preferentially induced IL-10. Escherichia coli Nissle 1917 induced both IL-10 and IL-12p70, whereas the probiotic yeast Saccharomyces boulardii induced low levels of cytokines. When combining these microorganisms with the Th1-promoting cocktails, E. coli Nissle 1917 and B. infantis 35624 were potent suppressors of IL-12p70 secretion in an IL-10-independent manner, indicating a suppressive effect on Th1-inducing antigen-presenting cells. The present model, using cocktail-stimulated DCs with potent IL-12p70-stimulating capacity, may be used as an efficient tool to assess the anti-inflammatory properties of microorganisms for potential clinical use.

STUDY 45

45. Foligne B, Zoumpopoulou G, Dewulf J, Younes AB, Chareyre F, Sirard J.-C., Pot B, Grangette C. A; Key Role of Dendritic Cells in Probiotic Functionality.; https://www.ncbi.nlm.nih.gov/pubmed/17375199

Abstract

BACKGROUND:

Disruption of the intestinal homeostasis and tolerance towards the resident microbiota is a major mechanism involved in the development of inflammatory bowel disease. While some bacteria are inducers of disease, others, known as probiotics, are able to reduce inflammation. Because dendritic cells (DCs) play a central role in regulating immune responses and in inducing tolerance, we investigated their role in the anti-inflammatory potential of probiotic lactic acid bacteria.

METHODOLOGY/PRINCIPAL FINDINGS:

Selected LAB strains, while efficiently taken up by DCs in vitro, induced a partial maturation of the cells. Transfer of probiotic-treated DCs conferred protection against 2, 4, 6-trinitrobenzenesulfonic acid (TNBS)-induced colitis. Protection was associated with a reduction of inflammatory scores and colonic expression of pro-inflammatory genes, while a high local expression of the immunoregulatory enzyme indolamine 2, 3 dioxgenase (IDO) was observed. The preventive effect of probiotic-pulsed DCs required not only MyD88-, TLR2- and NOD2-dependent signaling but also the induction of CD4+ CD25+ regulatory cells in an IL-10-independent pathway.

CONCLUSIONS/SIGNIFICANCE:

Altogether, these results suggest that selected probiotics can stimulate DC regulatory functions by targeting specific pattern-recognition receptors and pathways. The results not only emphasize the role of DCs in probiotic immune interactions, but indicate a possible role in immune-intervention therapy for IBD.

STUDY 46

46. Dardmeh F, Nielsen HI, Alipour H, Kjærgaard B, Brandsborg E, Gazerani P. Potential Nociceptive Regulatory Effect of Probiotic Lactobacillus rhamnosus PB01 (DSM 14870) on Mechanical Sensitivity in Diet-Induced Obesity Model; https://www.ncbi.nlm.nih.gov/pubmed/27647980

Abstract

Treatments for obesity have been shown to reduce pain secondary to weight loss. Intestinal microbiota, as an endogenous factor, influences obesity and pain sensitivity but the effect of oral probiotic supplementation on musculoskeletal pain perception has not been studied systematically. The present study examined the effect of a single daily oral dose (1 × 10(9) CFU) of probiotics (Lactobacillus rhamnosus PB01, DSM14870) supplement on mechanical pain thresholds in behaving diet-induced obese (DIO) mice and their normal weight (NW) controls. The mice (N = 24, 6-week-old male) were randomly divided into four groups on either standard or high fat diet with and without probiotic supplementation. Both DIO and NW groups with probiotic supplementation maintained an insignificant weight gain while the control groups gained significant weight (P < 0.05). Similarly, both DIO and NW probiotics supplemented groups demonstrated a significantly (P < 0.05) lower sensitivity to mechanical stimulation compared to their corresponding control. The results of this study suggest a protective effect of probiotics on nociception circuits, which propose a direct result of the weight reduction or an indirect result of anti-inflammatory properties of the probiotics. Deciphering the exact underlying mechanism of the weight loss and lowering nociception effect of the probiotic applied in this study require further investigation.

STUDY 47

47. Larsson P.-G., Brandsborg E, Forsum U, Pendharkar S, Andersen KK, Nasic S, Hammarström L, Marcotte L.; Extended antimicrobial treatment of bacterial vaginosis combined with human lactobacilli to find the best treatment and minimize the risk of relapses.; https://www.ncbi.nlm.nih.gov/pubmed/21854593

Abstract

BACKGROUND:

The primary objective of this study was to investigate if extended antibiotic treatment against bacterial vaginosis (BV) together with adjuvant lactobacilli treatment could cure BV and, furthermore, to investigate factors that could cause relapse.

METHODS:

In all, 63 consecutive women with bacterial vaginosis diagnosed by Amsel criteria were offered a much more aggressive treatment of BV than used in normal clinical practice with repeated antibiotic treatment with clindamycin and metronidazole together with vaginal gelatine capsules containing different strains of lactobacilli both newly characterised and a commercial one (109 freeze-dried bacteria per capsule). Oral clindamycin treatment was also given to the patient's sexual partner.

RESULTS:

The cure rate was 74.6% after 6 months. The patients were then followed as long as possible or until a relapse. The cure rate was 65.1% at 12 months and 55.6% after 24 months. There was no significant difference in cure rate depending on which Lactobacillus strains were given to the women or if the women were colonised by lactobacilli. The most striking factor was a new sex partner during the follow up period where the Odds Ratio of having a relapse was 9.3 (2.8-31.2) if the patients had a new sex partner during the observation period.

CONCLUSIONS:

The study shows that aggressive treatment of the patient with antibiotics combined with specific Lactobacillus strain administration and partner treatment can provide long lasting cure. A striking result of our study is that change of partner is strongly associated with relapse of BV.

STUDY 48

48. Keller MK, Brandsborg E, Holmstrøm K, Twetman S.; Effect of tablets containing probiotic candidate strains on gingival inflammation and composition of the salivary microbiome: a randomised controlled trial; https://www.ncbi.nlm.nih.gov/pubmed/29264967

Abstract

The aim of the study was to investigate clinical and microbial effects of probiotic candidate strains in patients with moderate gingivitis. The null hypothesis was that the clinical measurements with treatment would not differ from placebo. 47 adult patients were enrolled in a randomised placebo-controlled trial with a 4-week intervention of tablets containing a mix of Lactobacillus rhamnosus PB01, DSM 14869 and Lactobacillus curvatus EB10, DSM 32307 or placebo. Clinical examinations and samplings were done at baseline and after 2, 4 and 6 weeks. The clinical endpoints were general bleeding on probing (BOP), general plaque index (PI) and flow of gingival crevicular fluid (GCF). In addition, the concentration of selected cytokines (interleukin (IL)-1ß, IL-6, IL-8, IL-10, tumour necrosis factor alpha (TNF-α)) in GCF was determined with multiplex immunoassays. The profiles of the salivary microbiome were analysed with Next Generation Sequencing (NGS) and qPCR. In contrast to the placebo group, there was a significant reduction in BOP and amount of GCF ($P<0.05$) after 4 weeks in the probiotic test group when compared with baseline. The general PI was less affected although there was a tendency of decreased plaque levels in the probiotic group ($P=0.05$-0.09). The cytokines were unaffected by the intervention as well as the salivary microbiome. The Shannon index showed no significant differences between the groups or alterations over time. The occurrence of both probiotic strains increased in saliva of the test subjects during the intervention but returned to baseline levels within 2 weeks. Although a marked improvement in gingival health was recorded in the probiotic group, the null hypothesis could not be rejected.

STUDY 49

49. Dardmeh F, Alipour H, Gazerani P, van der Horst G, Brandsborg E, Nielsen HI.; Lactobacillus rhamnosus PB01 (DSM 14870) supplementation affects markers of sperm kinematic parameters in a diet-induced obesity mice model.; https://www.ncbi.nlm.nih.gov/pubmed/29016685

Abstract

Probiotics have been proposed as alternatives to pharmacological products in several medical conditions including the modulation of obesity, which is frequently associated with poor semen quality. However, effects of probiotics on male fertility have been less investigated. This study assessed the effect of Lactobacillus rhamnosus PB01 (DSM-14870) on sperm kinematic parameters in Normal-weight (NW) and diet-induced obese (DIO) models. NW and DIO C57BL/6NTac mice were divided into two subgroups with or without a single daily dose (1x109CFU) of L. rhamnosus for four weeks. Sperm motility and kinematics together with blood lipid profiles and reproductive hormone levels were assessed using the sperm class analyzer system. Probiotic supplementation increased serum testosterone, LH and FSH levels in both NW and DIO groups resulting in significantly ($P<0.05$) higher velocity (VSL, VCL and VAP) and percentages of progressively motile sperm and significantly lower percentages of immotile sperm. Other kinematic parameters (Lin, STR, ALH and BCF)

were also increased in both probiotic supplemented DIO and NW groups at the 10% level of significance. Probiotic supplemented DIO mice demonstrated significantly higher percentages of progressively motile sperm versus DIO controls. This study demonstrated the potential of L. rhamnosus PB01 as a regulatory agent with positive effects on weight loss and reproductive-hormones, significantly improving sperm motility and kinematic parameters in male DIO models.

STUDY 50

50. Ceapa C, Lambert J, van Limpt K, Wels M, Smokvina T, Knol J, Kleerebezem M.; Correlation of Lactobacillus rhamnosus genotypes and carbohydrate utilization signatures determined by phenotype profiling; https://www.ncbi.nlm.nih.gov/pubmed/26048937

Abstract

Lactobacillus rhamnosus is a bacterial species commonly colonizing the gastrointestinal (GI) tract of humans and also frequently used in food products. While some strains have been studied extensively, physiological variability among isolates of the species found in healthy humans or their diet is largely unexplored. The aim of this study was to characterize the diversity of carbohydrate utilization capabilities of human isolates and food-derived strains of L. rhamnosus in relation to their niche of isolation and genotype. We investigated the genotypic and phenotypic diversity of 25 out of 65 L. rhamnosus strains from various niches, mainly human feces and fermented dairy products. Genetic fingerprinting of the strains by amplified fragment length polymorphism (AFLP) identified 11 distinct subgroups at 70% similarity and suggested niche enrichment within particular genetic clades. High-resolution carbohydrate utilization profiling (OmniLog) identified 14 carbon sources that could be used by all of the strains tested for growth, while the utilization of 58 carbon sources differed significantly between strains, enabling the stratification of L. rhamnosus strains into three metabolic clusters that partially correlate with the genotypic clades but appear uncorrelated with the strain's origin of isolation. Draft genome sequences of 8 strains were generated and employed in a gene-trait matching (GTM) analysis together with the publicly available genomes of L. rhamnosus GG (ATCC 53103) and HN001 for several carbohydrates that were distinct for the different metabolic clusters: l-rhamnose, cellobiose, l-sorbose, and α-methyl-d-glucoside. From the analysis, candidate genes were identified that correlate with l-sorbose and α-methyl-d-glucoside utilization, and the proposed function of these genes could be confirmed by heterologous expression in a strain lacking the genes. This study expands our insight into the phenotypic and genotypic diversity of the species L. rhamnosus and explores the relationships between specific carbohydrate utilization capacities and genotype and/or niche adaptation of this species.

STUDY 51

51. Farrow, J.A.E. & Collins, M.D. (1984); DNA base composition, DNA-DNA homology and long-chain fatty acid studies on Streptococcus thermophilus and Streptococcus salivarius.; https://www.ncbi.nlm.nih.gov/pubmed/6726177

Abstract

DNA base composition, DNA-DNA homology and long-chain fatty acid studies were performed on Streptococcus thermophilus and Streptococcus salivarius. These species possess similar mol % G + C values (about 37 to 41), long-chain fatty acid profiles and belong to a single DNA homology group. On the basis of the present and earlier studies it is proposed that Streptococcus thermophilus (Orla-Jensen) be reclassified as Streptococcus salivarius subsp. thermophilus comb. nov.

52. Schleifer, K.H., Ehrman, M., Krusch, U. & Neve, H. (1991). Revival of the species Streptococcus thermophilus (ex Orla-Jensen, 1919) nom. rev. Appl. Microbiol. 14:386-388.

53. Aguirre, M. & Collins, M.D. (1993). Lactic acid bacteria and human clinical infections. J. Appl. Bact. 75:95-107.

54. Gueimonde, M., Ouwehand, A.C. & Salminen, S. (2004). Safety of probiotics. Scandandinavian Journal of Nutrition. 48:42-48

55. Mogensen, G., Salminen, S., O'Brien, J., Ouwehand, A.C., Holzapfel, W., Shortt, C., Fonden, R., Miller, G.D., Donohue, D., Playne, M., Crittenden, R., Salvadori, B. & Zink, R. (2002). Inventory of microorganisms with a documented history of safe use in food. Bulletin of the International Dairy Federation. 377:10-19.

56. Lammers, K.M., Brigidi, P., Vitali, B., Gionchetti, P., Rizello, F., Caramelli, E., Matteuzzi, D. & Campieri, M. (2003).; Immunomodulatory effects of probiotic bacteria DNA: IL-1 and IL-10 response in human peripheral blood mononuclear cells.; https://www.ncbi.nlm.nih.gov/pubmed/13129651

Abstract

A new therapeutic approach for inflammatory bowel diseases is based on the administration of probiotic bacteria. Prokaryotic DNA contains unmethylated CpG motifs which can activate immune responses, but it is unknown whether bacterial DNA is involved in the beneficial effects obtained by probiotic treatment. Peripheral blood mononuclear cells (PBMC) from healthy donors were incubated with pure DNA of eight probiotic strains and with total bacterial DNA from human feces collected before and after probiotic ingestion. Cytokine production was analyzed in culture supernatants. Modification of human microflora after probiotic administration was proven by polymerase chain reaction analysis. Here we show that Bifidobacterium genomic DNA induced secretion of the antiinflammatory interleukin-10 by PBMC. Total bacterial DNA from feces collected after probiotic administration modulated the immune response by a decrease of interleukin-1 beta and an increase of interleukin-10.

57. Haarman, M. & Knol, J. (2006).; Quantitative Real-Time PCR Analysis of Fecal Lactobacillus Species in Infants Receiving a Prebiotic Infant Formula; https://www.ncbi.nlm.nih.gov/pubmed/16597930

The developing intestinal microbiota of breast-fed infants is considered to play an important role in the priming of the infants' mucosal and systemic immunity. Generally, Bifidobacterium and Lactobacillus predominate the microbiota of breast-fed infants. In intervention trials it has been shown that lactobacilli can exert beneficial effects on, for example, diarrhea and atopy. However, the Lactobacillus species distribution in breast-fed or formula-fed infants has not yet been determined in great detail. For accurate enumeration of different lactobacilli, duplex 5' nuclease assays, targeted on rRNA intergenic spacer regions, were developed for Lactobacillus acidophilus, Lactobacillus casei, Lactobacillus delbrueckii, Lactobacillus fermentum, Lactobacillus paracasei, Lactobacillus plantarum, Lactobacillus reuteri, and Lactobacillus rhamnosus. The designed and validated assays were used to determine the amounts of different Lactobacillus species in fecal samples of infants receiving a standard formula (SF) or a standard formula supplemented with galacto- and fructo-oligosaccharides in a 9:1 ratio (OSF). A breast-fed group (BF) was studied in parallel as a reference. During the 6-week intervention period a significant increase was shown in total percentage of fecal lactobacilli in the BF

group (0.8% +/- 0.3% versus 4.1% +/- 1.5%) and the OSF group (0.8% +/- 0.3% versus 4.4% +/- 1.4%). The Lactobacillus species distribution in the OSF group was comparable to breast-fed infants, with relatively high levels of L. acidophilus, L. paracasei, and L. casei. The SF-fed infants, on the other hand, contained more L. delbrueckii and less L. paracasei compared to breast-fed infants and OSF-fed infants. An infant milk formula containing a specific mixture of prebiotics is able to induce a microbiota that closely resembles the microbiota of BF infants.

STUDY 58

58. Dicks, L.M.T., D Plessis, E.M., Dellaglio, F. & Lauer, E. (1996).; Reclassification of Lactobacillus casei subsp. casei ATCC 393 and Lactobacillus rhamnosus ATCC 15820 as Lactobacillus zeae nom. rev., designation of ATCC 334 as the neotype of L. casei subsp. casei, and rejection of the name Lactobacillus paracasei.; https://www.ncbi.nlm.nih.gov/pubmed/8573516

Abstract

The type strain of Lactobacillus casei subsp. casei (ATCC 393) exhibits low levels of DNA homology with other strains of L. casei subsp. casei (8 to 46%) and strains of Lactobacillus paracasei (30 to 50%), but exhibits a level of DNA similarity of 80% with Lactobacillus rhamnosus ATCC 15820, the original type strain of "Lactobacterium zeae" Kuznetsov 1959. Strains ATCC 393T (T = type strain) and ATCC 15820T are members of one protein profile cluster that is separate from the other Lactobacillus spp. The randomly amplified polymorphic DNA PCR profile of strain ATCC 393T is also different from the profiles obtained for the other species. L. casei ATCC 334T is genetically closely related to L. casei subsp. casei strains (71 to 97%) and L. paracasei strains (71 to 91%), is a member of the same protein profile cluster as these organisms, and shares several DNA amplicons with L. paracasei strains. On the basis of these results, we propose that L. casei subsp. casei ATCC 393T and L. rhamnosus ATCC 15820 should be reclassified as members of Lactobacillus zeae nom. rev. (type strain, ATCC 15820), that strain ATCC 334 should be designated the neotype strain of L. casei subsp. casei, and that the name L. paracasei should be rejected.

STUDIES 59, 60

59. Dellaglio, F., Dicks, L.M.T., Du Toit, M. & Torriani, S. (1991). Designation of ATCC 334 in place of ATCC 393 (NCDO 161) as the neotype strain of Lactobacillus casei subsp. casei and rejection of the name Lactobacillus paracasei (Collins et al., 1989). Request for an opinion. Int. J. Syst. Bacteriol. 41: 340-342.

60. Dobson, C.M., Chaban,B., Deneer, H. & Ziola, B. (2004).; Lactobacillus casei, Lactobacillus rhamnosus, and Lactobacillus zeae isolates identified by sequence signature and immunoblot phenotype; https://www.ncbi.nlm.nih.gov/pubmed/15381972

Abstract

Species taxonomy within the Lactobacillus casei group of bacteria has been unsettled. With the goal of helping clarify the taxonomy of these bacteria, we investigated the first 3 variable regions of the 16S rRNA gene, the 16S-23S rRNA interspacer region, and one third of the chaperonin 60 gene for Lactobacillus isolates originally designated as L. casei, L. paracasei, L. rhamnosus, and L. zeae. For each genetic region, a phylogenetic tree was created and signature sequence analysis was done. As well, phenotypic analysis of the various strains was

performed by immunoblotting. Both sequence signature analysis and immunoblotting gave immediate identification of L. casei, L. rhamnosus, and L. zeae isolates. These results corroborate and extend previous findings concerning these lactobacilli; therefore, we strongly endorse recent proposals for revised nomenclature. Specifically, isolate ATCC 393 is appropriately rejected as the L. casei type strain because of grouping with isolates identified as L. zeae. As well, because all other L. casei isolates, including the proposed neotype isolate ATCC 334, grouped together with isolates designated L. paracasei, we support the use of the single species L. casei and rejection of the name L. paracasei.

STUDIES 61, 62

61. Kandler, O. & Weiss, N. (1986). Genus Lactobacillus, p. 1209-1234. In Sneath, P.H.A., Mair, N.S., Sharpe, M.E. & Holt, J.G. (ed.). Bergey's manual of systematic bacteriology, vol. 2. Williams and Wilkins, Baltimore, Maryland. 2. Mitsuoka, T. (1996). Intestinal flora and human health. Asia Pacific J. Clin. Nutr. 5:2-9.

62. Reuter, G. (2001).; The Lactobacillus and Bifidobacterium microflora of the human intestine: composition and succession.; https://www.ncbi.nlm.nih.gov/pubmed/11721280

Abstract

Lactobacillus and bifidobacterial cultures are increasingly used as probiotics in pharmaceuticals and in foods. The selection of strains is performed often for technological rather than for microecological reasons. Detailed reports about species and strains composition of these microorganisms in the intestinal microflora of man are rare. Our investigations were performed with samples originating from infants and adults, taken from faeces and from upper sections of the intestinal tract including mouth and stomach, and from caecum and colon. Post mortem cases as well as test subjects under physiological conditions were analyzed using an automatic capsule system sampling at defined times in different parts of the intestinal tract. The fate of selected strains after oral intake was studied, too. Furthermore, influences of the microflora originating from food were considered. The identification of autochthonous (indigenous) and allochthonous (transient) species could be achieved with descriptions of new species in the genera Lactobacillus and Bifidobacterium. L. gasseri and L. reuteri proved to be predominant autochthonous Lactobacillus species in infants as well as in adults. Both species were occasionally present even in the stomach. This was also the case with an anaerobic lactic acid bacterium, previously named Catenabacterium catenaforme, later classified as L. ruminis, a non-motile variant of this species. The bifidobacterial microflora differed in composition between infants and adults and in different stages of the host's life. Up to 5 species or special strains of bifidobacteria could be present in different, individually fixed, combinations. Species typical for infants were B. bifidum, B. infantis, B. breve, and B. parvulorum. Typical for adults were 4 different variants of B. adolescentis. B. bifidum and B. longum could often be found in both groups, but in lower numbers. B. longum showed some oxygen tolerance whereas B. bifidum and B. adolescentis required strict anaerobic and fastidious conditions for cultivation. The autochthonous Lactobacillus and Bifidobacterium microflora in man will remain stable life-long. With lactobacilli, however, some successions may be caused by transient species derived from food or from the oral cavity, thus giving the impression of an altered microflora. Nevertheless L. gasseri, L. reuteri, L. ruminis, and to some degree, L. salivarius, may be present as autochthonous species all of the time. With bifidobacteria, a decreasing tendency in counts and in multiple composition in elderly people exists. Furthermore, this microflora is also influenced by consumption habits, which are probably caused by geographical circumstances.

63. Rogosa, M., Wiemann, R.F., Mitchell, J.A., Disraely, M.N. & Beaman, A.J. (1953). Species differentiation of oral lactobacilli from man including description of Lactobacillus salivarius nov spec and Lactobacillus cellobiosus nov spec. Journal of Bacteriology. 65(6):681-99.

64. Yin Li, Raftis, E., Canchaya, C., Fitzgerald, G. F., Van Sinderen, D. & O'Toole, P. W. (2006). Polyphasic analysis indicates that Lactobacillus salivarius subsp. salivarius and Lactobacillus salivarius subsp. salicinius do not merit separate subspecies status. International Journal of Systematic and Evolutionary Microbiology. 56 (10), 2397-2403.

65. Yuan, J.; Zhu, L.; Liu, X.; Li, T.; Zhang, Y.; Ying, T.; Wang, B.; Wang, J.; Dong, H.; Feng, E.; Li, Q.; Wang, J.; Wang, H.; Wei, K.; Zhang, X.; Huang, C.; Huang, P.; Huang, L.; Zeng, M.; Wang, H. (2006). "A Proteome Reference Map and Proteomic Analysis of Bifidobacterium longum NCC2705". Molecular & Cellular Proteomics. 5 (6): 1105–1118. doi:10.1074/mcp.M500410-MCP200. PMID 16549425.

66. Ghouri, Yezaz A; Richards, David M; Rahimi, Erik F; Krill, Joseph T; Jelinek, Katherine A; DuPont, Andrew W (9 December 2014).; "Systematic review of randomized controlled trials of probiotics, prebiotics, and synbiotics in inflammatory bowel disease".; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4266241/

Abstract

Background

Probiotics are microorganisms that are ingested either in combination or as a single organism in an effort to normalize intestinal microbiota and potentially improve intestinal barrier function. Recent evidence has suggested that inflammatory bowel disease (IBD) may result from an inappropriate immunologic response to intestinal bacteria and a disruption in the balance of the gastrointestinal microbiota in genetically susceptible individuals. Prebiotics, synbiotics, and probiotics have all been studied with growing interest as adjuncts to standard therapies for IBD. In general, probiotics have been shown to be well-tolerated with few side effects, making them a potential attractive treatment option in the management of IBD.

Aim

To perform a systematic review of randomized controlled trials on the use of probiotics, prebiotics, and synbiotics in IBD.

Results

In our systematic review we found 14 studies in patients with Crohn's disease (CD), 21 studies in patients with ulcerative colitis (UC), and five studies in patients with pouchitis. These were randomized controlled trials using probiotics, prebiotics, and/or synbiotics. In patients with CD, multiple studies comparing probiotics and placebo showed no significant difference in clinical outcomes. Adding a probiotic to conventional treatment improved the overall induction of remission rates among patients with UC. There was also a similar benefit in maintaining remission in UC. Probiotics have also shown some efficacy in the treatment of pouchitis after antibiotic-induced remission.

Conclusions

To date, there is insufficient data to recommend probiotics for use in CD. There is evidence to support the use of probiotics for induction and maintenance of remission in UC and pouchitis. Future quality studies are needed to confirm whether probiotics, prebiotics, and synbiotics have a definite role in induction or maintenance of remission in CD, UC, and pouchitis. Similar to probiotics, fecal microbiota transplantation provides an alternate modality of therapy to treat IBD by influencing the intestinal flora.

67. De Vrese, M.; Winkler, P.; Rautenberg, P.; Harder, T.; Noah, C.; Laue, C.; Ott, S.; Hampe, J.; Schreiber, S.; Heller, K.; Schrezenmeir, J. R. (2005). "Effect of Lactobacillus gasseri PA 16/8, Bifidobacterium longum SP 07/3, B. Bifidum MF 20/5 on common cold episodes: A double blind, randomized, controlled trial". Clinical Nutrition. 24 (4): 481–491.

68. Odamaki T1, Xiao JZ, Iwabuchi N, Sakamoto M, Takahashi N, Kondo S, Miyaji K, Iwatsuki K, Togashi H, Enomoto T, Benno Y.; Influence of Bifidobacterium longum BB536 intake on faecal microbiota in individuals with Japanese cedar pollinosis during the pollen season; J Med Microbiol. 2007 Oct;56(Pt 10):1301-8.

Abstract

It has been reported that intake of yogurt or powder supplemented with the Bifidobacterium longum BB536 probiotic strain alleviated subjective symptoms and affected blood markers of allergy in individuals with Japanese cedar pollinosis (JCPsis) during the pollen seasons of 2004 and 2005, based on randomized, double-blind, placebo-controlled trials. Furthermore, the 2004 study found that intestinal bacteria such as the Bacteroides fragilis group significantly fluctuated during the pollen season in JCPsis individuals and intake of BB536 yogurt tended to suppress these fluctuations. The present study investigated faecal microbiota to examine whether any changes occurred during the pollen season and whether any influence was exerted by intake of BB536 powder in the 2005 pollen season, which happened to be a heavy season, to confirm the 2004 findings and to evaluate the relationship of microbiota with symptom development. In a randomized, double-blind, placebo-controlled trial, 44 JCPsis subjects received BB536 or a placebo for 13 weeks during the pollen season. Another 14 Japanese cedar pollen (JCP)-specific IgE negative healthy subjects received placebo for the same period. Faecal samples were collected before (week 0), during (weeks 4, 8 and 13) and after (week 17) intervention, and out of JCP season (week 28). Faecal microbiota were analysed using terminal-RFLP (T-RFLP) and real-time PCR methods. Principal component analysis based on T-RFLP indicated distinct patterns of microbiota between healthy subjects and JCPsis subjects in the placebo group, but an intermediate pattern in the BB536 group at week 13, the last stage of the pollen season. The coordinate of principal component 1 at week 13 correlated with composite scores of JCPsis symptoms recorded during the pollen season. Faecalibacterium prausnitzii and the Bacteroides fragilis group were identified as the main contributors to microbiotal fluctuations. Real-time PCR indicated that BB536 intake suppressed increases in the Bacteroides fragilis group compared with the placebo group ($P < 0.05$). These results suggest that faecal microbiota in JCPsis subjects, but not healthy subjects, fluctuate at the end of the pollen season and that BB536 intake plays a role in maintaining normal microbiota.

69. H.Wang, C.Braun, E.F.Murphy, P.Enck: Bifidobacterium longum 1714 Strain Modulates Brain Activity of Healthy Volunteers During Social Stress; American Journal of Gastroenterology 2019; doi: 10.14309/

Abstract

OBJECTIVES:

Accumulating evidence indicates that the gut microbiota communicates with the central nervous system, possibly through neural, endocrine, and immune pathways, and influences brain function. B. longum 1714™ has previously been shown to attenuate cortisol output and stress responses in healthy subjects exposed to an acute stressor. However, the ability of B. longum 1714™ to modulate brain function in humans is unclear.

METHODS:

In a randomized, double-blinded, placebo-controlled trial, the effects of B. longum 1714™ on neural responses to social stress, induced by the "Cyberball game," a standardized social stress paradigm, were studied. Forty healthy volunteers received either B. longum 1714™ or placebo for 4 weeks at a dose of 1 × 109 cfu/d. Brain activity was measured using magnetoencephalography and health status using the 36-item short-form health survey.

RESULTS:

B. longum 1714™ altered resting-state neural oscillations, with an increase in theta band power in the frontal and cingulate cortex ($P < 0.05$) and a decrease in beta-3 band in the hippocampus, fusiform, and temporal cortex ($P < 0.05$), both of which were associated with subjective vitality changes. All groups showed increased social stress after a 4-week intervention without an effect at behavioral level due to small sample numbers. However, only B. longum 1714™ altered neural oscillation after social stress, with increased theta and alpha band power in the frontal and cingulate cortex ($P < 0.05$) and supramarginal gyrus ($P < 0.05$).

DISCUSSION:

B. longum 1714™ modulated resting neural activity that correlated with enhanced vitality and reduced mental fatigue. Furthermore, B. longum 1714™ modulated neural responses during social stress, which may be involved in the activation of brain coping centers to counter-regulate negative emotions.

STUDY 70

70. Song AA, In LLA, Lim SHE, Rahim RA., A review on Lactococcus lactis: from food to factory, Microb Cell Fact. 2017 Apr 4;16(1):55. doi: 10.1186/s12934-017-0669-x; https://www.ncbi.nlm.nih.gov/pubmed/28376880

Abstract

Lactococcus lactis has progressed a long way since its discovery and initial use in dairy product fermentation, to its present biotechnological applications in genetic engineering for the production of various recombinant proteins and metabolites that transcends the heterologous species barrier. Key desirable features of this gram-positive lactic acid non-colonizing gut bacteria include its generally recognized as safe (GRAS) status, probiotic properties, the absence of inclusion bodies and endotoxins, surface display and extracellular secretion technology, and a diverse selection of cloning and inducible expression vectors. This have made L. lactis a desirable and promising host on par with other well established model bacterial or yeast systems such as Escherichia coli, Saccharomyces [corrected] cerevisiae and Bacillus subtilis. In this article, we review recent technological advancements, challenges, future prospects and current diversified examples on the use of L. lactis as a microbial cell factory. Additionally, we will also highlight latest medical-based applications involving whole-cell L. lactis as a live delivery vector for the administration of therapeutics against both communicable and non-communicable diseases.

STUDY 71

71. Mercier-Bonin M, Chapot-Chartier MP., Surface Proteins of Lactococcus lactis: Bacterial Resources for Muco-adhesion in the Gastrointestinal Tract., Front Microbiol. 2017 Nov 23;8:2247. doi: 10.3389/fmicb.2017.02247. eCollection 2017.; https://www.ncbi.nlm.nih.gov/pubmed/29218032

Abstract

Food and probiotic bacteria, in particular lactic acid bacteria, are ingested in large amounts by humans and are part of the transient microbiota which is increasingly considered to be able to impact the resident microbiota and thus possibly the host health. The lactic acid bacterium Lactococcus lactis is extensively used in starter cultures to produce dairy fermented food. Also because of a generally recognized as safe status, L. lactis has been considered as a possible vehicle to deliver in vivo therapeutic molecules with anti-inflammatory properties in the gastrointestinal tract. One of the key factors that may favor health effects of beneficial bacteria to the host is their capacity to colonize transiently the gut, notably through close interactions with mucus, which covers and protects the intestinal epithelium. Several L. lactis strains have been shown to exhibit mucus-binding properties and bacterial surface proteins have been identified as key determinants of such capacity. In this review, we describe the different types of surface proteins found in L. lactis, with a special focus on mucus-binding proteins and pili. We also review the different approaches used to investigate the adhesion of L. lactis to mucus, and particularly to mucins, one of its major components, and we present how these approaches allowed revealing the role of surface proteins in muco-adhesion.

STUDY 72

72. Selle K, Klaenhammer TR (2013). "Genomic and phenotypic evidence for probiotic influences of Lactobacillus gasseri on human health". FEMS Microbiol Rev (Review). 37 (6): 915–35. doi:10.1111/1574-6976.12021. PMID 23488471.; https://www.ncbi.nlm.nih.gov/pubmed/23488471

Abstract

Certain lactic acid bacteria (LAB) have the capacity to occupy mucosal niches of humans, including the oral cavity, gastrointestinal tract, and vagina. Among commensal, LAB are species of the acidophilus complex, which have proven to be a substantial reservoir for microorganisms with probiotic attributes. Specifically, Lactobacillus gasseri is an autochthonous microorganism which has been evaluated for probiotic activity based on the availability of genome sequence and species-specific adaptation to the human mucosa. Niche-related characteristics of L. gasseri contributing to indigenous colonization include tolerance of low pH environments, resistance to bile salts, and adhesion to the host epithelium. In humans, L. gasseri elicits various health benefits through its antimicrobial activity, bacteriocin production, and immunomodulation of the innate and adaptive systems. The genomic and empirical evidence supporting use of L. gasseri in probiotic applications is substantiated by clinical trial data displaying maintenance of vaginal homeostasis, mitigation of Helicobacter pylori infection, and amelioration of diarrhea.

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74. Chouraqui et al. 2004; Saavedra et al. 1994, Acidified milk formula supplemented with bifidobacterium lactis: impact on infant diarrhea in residential care settings.; Journal of Pediatric Gastroenterology and Nutrition 38(3):288-92

Abstract

Probiotics may be useful in preventing acute infectious diarrhea. Bifidobacteria are particularly attractive as probiotics agent because they constitute the predominant colonic flora of breastfed infants and are thought to play a role in the decreased incidence of diarrhea in breastfed infants. This was a multicenter, double-blind, controlled study to evaluate the efficacy of a milk formula supplemented with viable Bifidobacterium lactis strain Bb 12 (BbF) in the prevention of acute diarrhea in infants younger than 8 months living in residential nurseries or foster care centers. Ninety healthy children received either the BbF or a conventional formula (CF) daily. The mean duration of the stay in the residential center was similar (137 v 148 days). At enrollment, there were no differences between the two groups with respect to age (3.7 +/- 2.1 months), gender, anthropometric data, history of allergy or gastrointestinal disease, frequency of breast-feeding in the neonatal period or timing of introduction of solid food. Altogether, 28.3% of the BbF infants had diarrhea during the study compared with 38.7% of controls (NS). There was a statistically insignificant trend for shorter episodes of diarrhea in the BbF group (5.1 +/- 3.3 days v 7 +/- 5.5 days, NS). The number of days with diarrhea was 1.15 +/- 2.5 in the BbF group with a daily probability of diarrhea of 0.84 versus 2.3 +/- 4.5 days and 1.55, respectively, in the CF group (P = 0.0002 and 0.0014). Feeding infants with the BbF reduced their risk of getting diarrhea by a factor of 1.9 (range, 1.33-2.6). Analysis of the cumulative incidence of diarrheal episodes showed a trend that the first onset of diarrhea occurred later in the BbF group. These results provide some evidence that viable Bifidobacterium lactis strain Bb 12, added to an acidified infant formula, has some protective effect against acute diarrhea in healthy children.

75. Smith et al. 2013; Taipale et al. 2011; Bifidobacterium animalis subsp. lactis BB-12 in reducing the risk of infections in infancy.; Br J Nutr. 2011 Feb;105(3):409-16. doi: 10.1017/S0007114510003685. Epub 2010 Sep 24. ; https://www.ncbi.nlm.nih.gov/pubmed/20863419

Abstract

The impact of controlled administration of Bifidobacterium animalis subsp. lactis BB-12 (BB-12) on the risk of acute infectious diseases was studied in healthy newborn infants. In this double-blind, placebo-controlled study, 109 newborn 1-month-old infants were assigned randomly to a probiotic group receiving a BB-12-containing tablet (n 55) or to a control group receiving a control tablet (n 54). Test tablets were administered to the infants twice a day (daily dose of BB-12 10 billion colony-forming units) from the age of 1-2 months to 8 months with a novel slow-release pacifier or a spoon. Breastfeeding habits, pacifier use, dietary habits, medications and all signs and symptoms of acute infections were registered. At the age of 8 months, faecal samples were collected for BB-12 determination (quantitative PCR method). The baseline characteristics of the

two groups were similar, as was the duration of exclusive breastfeeding. BB-12 was recovered (detection limit log 5) in the faeces of 62% of the infants receiving the BB-12 tablet. The daily duration of pacifier sucking was not associated with the occurrence of acute otitis media. No significant differences between the groups were observed in reported gastrointestinal symptoms, otitis media or use of antibiotics. However, the infants receiving BB-12 were reported to have experienced fewer respiratory infections (65 v. 94%; risk ratio 0•69; 95% CI 0•53, 0•89; P = 0•014) than the control infants. Controlled administration of BB-12 in early childhood may reduce respiratory infections

STUDY 76

76. Isolauri et al. 2000; Probiotics in the management of atopic eczema; Clin Exp Allergy. 2000 Nov;30(11):1604-10; https://www.ncbi.nlm.nih.gov/pubmed/11069570

Abstract

BACKGROUND:

Over the last two decades the incidence of allergic diseases has increased in industrialized countries, and consequently new approaches have to be explored.

OBJECTIVE:

The potential of probiotics to control allergic inflammation at an early age was assessed in a randomized double-blind placebo-controlled study.

METHODS:

A total of 27 infants, mean age 4.6 months, who manifested atopic eczema during exclusive breast-feeding and who have had no exposure to any infant or substitute formula were weaned to probiotic-supplemented, Bifidobacterium lactis Bb-12 or Lactobacillus strain GG (ATCC 53103), extensively hydrolysed whey formulas or to the same formula without probiotics. The extent and severity of atopic eczema, the growth and nutrition of infants, and concentrations of circulating cytokines/chemokines and soluble cell surface adhesion molecules in serum and methyl-histamine and eosinophilic protein X in urine were determined.

RESULTS:

The SCORAD score reflecting the extent and severity of atopic eczema was 16 (7-25) during breast-feeding, median (interquartile range). After 2 months, a significant improvement in skin condition occurred in patients given probiotic-supplemented formulas, as compared to the unsupplemented group; chi(2) = 12.27, P = 0.002. SCORAD decreased in the Bifidobacterium lactis Bb-12 group to 0 (0-3.8), and in the Lactobacillus GG group to 1 (0.1-8.7), vs unsupplemented 13.4 (4.5-18.2), median (interquartile range), in parallel with a reduction in the concentration of soluble CD4 in serum and eosinophilic protein X in urine.

CONCLUSION:

The results provide the first clinical demonstration of specific probiotic strains modifying the changes related to allergic inflammation. The data further indicate that probiotics may counteract inflammatory responses beyond the intestinal milieu. The combined effects of these probiotic strains will guide infants through the weaning period, when sensitization to newly encountered antigens is initiated. The probiotic approach may thus offer a new direction in the search for future foods for allergy treatment and prevention strategies.

STUDY 77

77. Eskesen D., Jespersen L., Michelsen B., Whorwell PJ., Müller-Lissner S., Morberg CM, Effect of the probiotic strain Bifidobacterium animalis subsp. lactis, BB-12®, on defecation frequency in healthy subjects with low defecation frequency and abdominal discomfort: a randomised, double-blind, placebo-controlled, parallel-group trial., doi: 10.1017/S0007114515003347; https://www.ncbi.nlm.nih.gov/pubmed/26382580

Abstract

The aim of the present study was to investigate the effect of Bifidobacterium animalis subsp. lactis, BB-12®, on two primary end points - defecation frequency and gastrointestinal (GI) well-being - in healthy adults with low defecation frequency and abdominal discomfort. A total of 1248 subjects were included in a randomised, double-blind, placebo-controlled trial. After a 2-week run-in period, subjects were randomised to 1 or 10 billion colony-forming units/d of the probiotic strain BB-12® or a matching placebo capsule once daily for 4 weeks. Subjects completed a diary on bowel habits, relief of abdominal discomfort and symptoms. GI well-being, defined as global relief of abdominal discomfort, did not show significant differences. The OR for having a defecation frequency above baseline for ≥50% of the time was 1•31 (95% CI 0•98, 1•75), P=0•071, for probiotic treatment overall. Tightening the criteria for being a responder to an increase of ≥1 d/week for ≥50 % of the time resulted in an OR of 1•55 (95% CI 1•22, 1•96), P=0•0003, for treatment overall. A treatment effect on average defecation frequency was found (P=0•0065), with the frequency being significantly higher compared with placebo at all weeks for probiotic treatment overall (all P<0•05). Effects on defecation frequency were similar for the two doses tested, suggesting that a ceiling effect was reached with the one billion dose. Overall, 4 weeks' supplementation with the probiotic strain BB-12® resulted in a clinically relevant benefit on defecation frequency. The results suggest that consumption of BB-12® improves the GI health of individuals whose symptoms are not sufficiently severe to consult a doctor (ISRCTN18128385).

STUDY 78

78. Phuapradit P, Varavithya W, Vathanophas K, Sangchai R, Podhipak A, Suthutvoravut U, Nopchinda S, Chantraruksa V, Haschke F., Reduction of rotavirus infection in children receiving bifidobacteria-supplemented formula., J Med Assoc Thai. 1999 Nov;82 Suppl 1:S43-8.; https://www.ncbi.nlm.nih.gov/pubmed/10730517

Abstract

This study was conducted at Pakkred Babies Home, Bangkok, Thailand; with the hypothesis that children receiving probiotic-supplemented milk-based formula may be protected from developing diarrheal diseases. Salivary rotavirus-specific IgA antibody was used as an indicator of rotavirus infection. One hundred and seventy-five children, aged 6-36 months, were enrolled in the study. They were divided into 3 groups according to the type of formula given. There were 81 episodes of diarrhea during an 8-month study period, most of which were caused by bacterial enteropathogens. Ninety-seven pairs of salivary samples were adequate for the analysis of rotavirus antibody. Among 23 children receiving milk-based follow-up formula and serving as control group, 30.4 per cent of them had > or = 4-fold increase in the antibody titre, indicating subclinical rotavirus infection. The majority of children in the other 2 study groups, receiving the same formula supplemented with either Bifidobacterium Bb12 alone or together with Streptococcus thermophilus, had no significant change in the antibody titres between the two time points. The results of this study support our hypothesis that children receiving bifidobacteria-supplemented milk-based formula may be protected against symptomatic rotavirus infection.

STUDY 79

79. Yujin Lee, Zhaoyong Ba, Robert F. Roberts, Connie J. Rogers, Jennifer A. Fleming, Huicui Meng, Emily J. Furumoto, and Penny M. Kris, Effects of Bifidobacterium animalis subsp. lactis BB-12® on the lipid/lipoprotein profile and short chain fatty acids in healthy young adults: a randomized controlled trial, doi: 10.1186/s12937-017-0261-6

Abstract

Background Some probiotics have hypocholesterolemic effects in animal studies, which are mediated, in part, by increases in fecal short chain fatty acids (SCFAs). Clinical trials of probiotics on lipids/lipoproteins are inconsistent. Objective We examined the effects of Bifidobacterium animalis subsp. lactis BB-12® (BB-12®) (3.16×10^9 CFUs/day) on lipids and lipoproteins and fecal excretion of SCFAs in healthy adults. Methods In a randomized, partially blinded, 4-period, crossover study, 30 adults (11 men, 19 women) aged 18–40 years were randomly assigned to: 1) yogurt smoothie with no BB-12® (YS), 2) yogurt smoothie with BB-12® added pre-fermentation (PRE), 3) yogurt smoothie with BB-12® added post-fermentation (POST), 4) BB-12® containing capsule (CAP). We measured serum lipids/lipoproteins, glucose, insulin, C-reactive protein (CRP), and fecal SCFAs at baseline and after each treatment period. Results Total cholesterol (TC), LDL cholesterol (LDL-C), HDL cholesterol (HDL-C), and triglycerides (TGs) did not differ after the PRE, POST, and CAP periods versus the YS or between treatments. Compared to baseline, fecal acetate was significantly increased after the YS (Δ = 211.89 ± 75.87 μg/g, P = 0.007) and PRE (Δ = 204.98 ± 75.70 μg/g, P = 0.009) periods. The percent increase in fecal acetate was significantly greater after the YS versus the POST period (52.2 ± 13.2% vs. 24.5 ± 13.2%, P = 0.023). Fecal total SCFAs, propionate and butyrate did not differ between treatment periods. Fecal total SCFAs were negatively associated with TC (r = -0.22, P = 0.01), LDL-C (r = -0.24, P = 0.004), age (r = -0.33, P < 0.001), and waist circumference (r = -0.25, P = 0.003). Conclusions BB-12® supplementation did not improve lipids, lipoproteins and total and individual fecal SCFAs. Fecal SCFAs were negatively associated with TC, LDL-C, age, and waist circumference

STUDY 80

80. Teemu J. Taipale, Kaisu Pienihäkkinen, Erika Isolauri, Jorma T. Jokela & Eva M. Söderling, Bifidobacterium animalis subsp. lactis BB-12 in reducing the risk of infections in early childhood, Pediatric Research volume 79, pages 65–69 (2016)

Abstract

BACKGROUND:

Specific probiotic bacteria have proven to be effective in the prevention and treatment of infectious diseases in early life in at-risk populations. The impact of administration of Bifidobacterium animalis subsp. lactis BB-12 (BB-12) on the risk of acute infectious diseases was studied in healthy children.

METHODS:

In this double-blind, placebo-controlled study, 109 1-mo-old infants were assigned randomly to a probiotic group receiving a BB-12–containing tablet (n = 55) or a placebo (n = 54). Test tablets were administered to the infants twice a day (daily dose of BB-12 10 billion colony-forming units) until the age of 2 y with a novel slow-release pacifier or a spoon. Breastfeeding habits, pacifier use, dietary habits, medications, and all signs and symptoms of acute infections were registered in diaries by parents and in questionnaires by trained professionals.

RESULTS:

The infants receiving BB-12 were reported to have experienced fewer respiratory tract infections (RTIs; 87 vs. 100%; risk ratio: 0.87; 95% confidence interval: 0.76, 1.00; P = 0.033) than the controls. No significant differences between the groups were observed in reported gastrointestinal symptoms, otitis media, or fever. The baseline characteristics of the two groups were similar, as was the duration of breastfeeding.

CONCLUSION:

Administration of BB-12 in early childhood may reduce RTIs.
were registered in diaries by parents and in questionnaires by trained professionals.

STUDIES 81, 82, 83

81. W. P. Hammes, C. Hertel: The Genera Lactobacillus and Carnobacterium, S. 367

82. Hans G. Schlegel, Christiane Zaborosch: Allgemeine Mikrobiologie. 7. Auflage. Thieme Verlag, Stuttgart/ New York 1992, ISBN 3-13-444607-3, S. 296–299

83. Usui Y, Kimura Y, Satoh T, Takemura N, Ouchi Y, Ohmiya H, Kobayashi K, Suzuki H, Koyama S, Hagiwara S, Tanaka H, Imoto S, Eberl G, Asami Y, Fujimoto K, Uematsu S., Effects of long-term intake of a yogurt fermented with Lactobacillus delbrueckii subsp. bulgaricus 2038 and Streptococcus thermophilus 1131 on mice, Int Immunol. 2018 Jun 26;30(7):319-331. doi: 10.1093/intimm/dxy035.; https://www.ncbi.nlm.nih.gov/-pubmed/29767727

Abstract

The gut is an extremely complicated ecosystem where micro-organisms, nutrients and host cells interact vigorously. Although the function of the intestine and its barrier system weakens with age, some probiotics can potentially prevent age-related intestinal dysfunction. Lactobacillus delbrueckii subsp. bulgaricus 2038 and Streptococcus thermophilus 1131, which are the constituents of LB81 yogurt, are representative probiotics. However, it is unclear whether their long-term intake has a beneficial influence on systemic function. Here, we examined the gut microbiome, fecal metabolites and gene expression profiles of various organs in mice. Although age-related alterations were apparent in them, long-term LB81 yogurt intake led to an increased Bacteroidetes to Firmicutes ratio and elevated abundance of the bacterial family S24-7 (Bacteroidetes), which is known to be associated with butyrate and propanoate production. According to our fecal metabolite analysis to detect enrichment, long-term LB81 yogurt intake altered the intestinal metabolic pathways associated with propanoate and butanoate in the mice. Gene ontology analysis also revealed that long-term LB81 yogurt intake influenced many physiological functions related to the defense response. The profiles of various genes associated with antimicrobial peptides-, tight junctions-, adherens junctions- and mucus-associated intestinal barrier functions were also drastically altered in the LB81 yogurt-fed mice. Thus, long-term intake of LB81 yogurt has the potential to maintain systemic homeostasis, such as the gut barrier function, by controlling the intestinal microbiome and its metabolites.

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89. Bendazzoli, C., Turroni, S., Gotti,R., Olmo, S., Brigidi, P. & Cavrini,V. (2007). Determination of oxalyl-coenzyme A decarboxylase activity in Oxalobacter formigenes and Lactobacillus acidophilus by capillary electrophoresis. Journal of Chromatography B. 854: 350–356.; https://www.ncbi.nlm.nih.gov/pubmed/17499563

Abstract

Oxalyl-coenzyme A decarboxylase (OXC) is a key enzyme in the catabolism of the highly toxic oxalate, catalysing the decarboxylation of oxalyl-coenzyme A (Ox-CoA) to formyl-coenzyme A (For-CoA). In the present study, a capillary electrophoretic (CE) method was proposed for the assessment of the activity of recombinant OXC from two bacteria, namely Oxalobacter formigenes DSM 4420 and Lactobacillus acidophilus LA 14. In particular, the degradation of the substrate Ox-CoA occurring in the enzymatic reaction could be monitored by the off-line CE method. A capillary permanently coated with polyethylenimine (PEI) was used and in the presence of a neutral background electrolyte (50 mM phosphate buffer at pH 7.0), a reversal of the electroosmotic flow was obtained. Under these conditions, the anodic migration of Ox-CoA (substrate) and For-CoA (reaction product) occurred and their separation was accomplished in less than 12 min. The CE method was validated for selectivity, linearity (range of Ox-CoA within 0.005-0.650 mM), sensitivity (LOD of 1.5 microM at the detection wavelength of 254 nm), precision and accuracy. Steady state kinetic constants (V(max), K(m) or k') of OXC were finally estimated for both the bacteria showing that although L. acidophilus LA 14 provided a lower oxalate breakdown than O. formigenes DSM 4420, it could be a potentially useful probiotic in the prevention of diseases related to oxalate.

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Abstract

Oligofructose and inulin are naturally occurring indigestible carbohydrates. In vitro they selectively stimulate the growth of species of Bifidobacterium, a genus of bacteria considered beneficial to health. This study was designed to determine their effects on the large bowel microflora and colonic function in vivo. Eight subjects participated in a 45-day study during which they ate controlled diets. For the middle 15 days, 15 g • day–1 oligofructose was substituted for 15 g • day–1 sucrose. Four of these subjects went on to a further period with 15 g • day–1 inulin. Bowel habit, transit time, stool composition, breath H2 and CH4, and the predominant genera of colonic bacteria were measured. Both oligofructose and inulin significantly increased bifidobacteria from 8.8 to 9.5 log10 g stool–1 and 9.2 to 10.1 log10 g stool–1, respectively, whereas bacteroides, clostridia, and fusobacteria decreased when subjects were fed oligofructose, and gram-positive cocci decreased when subjects were fed inulin. Total bacterial counts were unchanged. Fecal wet and dry matter, nitrogen, and energy excretion increased with both substrates, as did breath H2. Little change in fecal short-chain fatty acids and breath CH4 was observed. A 15-g • day–1 dietary addition of oligofructose or inulin led to Bifidobacterium becoming the numerically predominant genus in feces. Thus, small changes in diet can alter the balance of colonic bacteria towards a potentially healthier microflora.

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93. Vandeputte D, Falony G, Vieira-Silva S, Wang J, Sailer M, Theis S, Verbeke K, Raes J., Prebiotic inulin-type fructans induce specific changes in the human gut microbiota., Gut. 2017 Nov;66(11):1968-1974. doi: 10.1136/-gutjnl-2016-313271. Epub 2017 Feb 17.; https://www.ncbi.nlm.nih.gov/pubmed/28213610

Abstract

OBJECTIVE:

Contrary to the long-standing prerequisite of inducing selective (ie, bifidogenic) effects, recent findings suggest that prebiotic interventions lead to ecosystem-wide microbiota shifts. Yet, a comprehensive characterisation of this process is still lacking. Here, we apply 16S rDNA microbiota profiling and matching (gas chromatography mass spectrometry) metabolomics to assess the consequences of inulin fermentation both on the composition of the colon bacterial ecosystem and faecal metabolites profiles.

DESIGN:

Faecal samples collected during a double-blind, randomised, cross-over intervention study set up to assess the effect of inulin consumption on stool frequency in healthy adults with mild constipation were analysed. Faecal microbiota composition and metabolite profiles were linked to the study's clinical outcome as well as to quality-of-life measurements recorded.

RESULTS:

While faecal metabolite profiles were not significantly altered by inulin consumption, our analyses did detect a modest effect on global microbiota composition and specific inulin-induced changes in relative abundances of Anaerostipes, Bilophila and Bifidobacterium were identified. The observed decrease in Bilophila abundances following inulin consumption was associated with both softer stools and a favourable change in constipation-specific quality-of-life measures.

CONCLUSIONS:

Ecosystem-wide analysis of the effect of a dietary intervention with prebiotic inulin-type fructans on the colon microbiota revealed that this effect is specifically associated with three genera, one of which (Bilophila) representing a promising novel target for mechanistic research.

STUDY 94

94. Helen Steed, George T. Macfarlane, Sandra Macfarlane, Prebiotics, synbiotics and inflammatory bowel disease, https://doi.org/10.1002/mnfr.200700139

Abstract

The normal colonic microflora is intimately involved in the aetiology of inflammatory bowel diseases (IBD) such as ulcerative colitis (UC) and Crohn's disease (CD). These conditions are often refractile to conventional treatments involving the employment of anti-inflammatory and immunosuppressant drugs, and this has led to a search for alternative therapies based on the use of probiotics, prebiotics and synbiotics. The majority of investigations in this area have been done with probiotics, and while there is increasing interest in the abilities of prebiotics and synbiotics to control the symptoms of IBD, very few randomised controlled trials have been reported. Although the results have been variable, human and animal studies have demonstrated that in many circumstances, these functional foods can alter the composition of the colonic microbiota, reduce inflammatory processes in the gut mucosa, and have the potential to induce disease remission. More work is needed to understand the effects of prebiotics and synbiotics on microbial communities in the gut, and their interactions with the host's immune system.