

# Recent Studies and Publications on Probiotics and Health Benefits

## STUDIES

### 1. Effect Of Probiotic Use On Adverse Events In Adult Patients With Inflammatory Bowel Disease: A Retrospective Cohort Study

In this retrospective cohort study, the benefits of probiotic use in reducing adverse events were analysed.

The study reveals that CD (Crohn's disease) patients taking probiotics for 25–74% of the disease duration experienced a 64% reduction in total adverse events. The need for systemic steroids, hospitalization, and surgery dropped to zero events per person-year in UC (ulcerative colitis) patients and decreased by 93% in CD patients taking probiotics for  $\geq 75\%$  of the disease duration. Findings of the study suggest that the use of probiotics may be an additional therapeutic tool in patients with IBD.

**Source:** Maria Pina Dore, Department of Surgical and Experimental Medical Sciences, University of Sassari; Clinica Medica, Viale S Pietro 8, Sassari, Italy And Baylor College of Medicine, USA. *Effect Of Probiotic Use On Adverse Events In Adult Patients With Inflammatory Bowel Disease: A Retrospective Cohort Study. Probiotics & Antimicro. Prot. 12, 152-159 (2020).* <https://doi.org/10.1007/s12602-019-9517-0>

### 2. AGA Clinical Practice Guidelines On The Role Of Probiotics In The Management Of Gastrointestinal Disorders

The American Gastroenterological Association (AGA) has published Guidelines on the role of probiotics in the management of gastrointestinal disorders. The gut microbiome plays an important role in gastrointestinal health and disease and probiotics represent a promising modality for therapeutic intervention. The following are the recommendations described briefly in the guidelines:

- The current evidence suggests that the use of certain probiotic strains or probiotic strain combinations may prevent *C difficile* infections for adults and children on antibiotic treatment. However, the quality of evidence was low and the reporting of potential harms was not always consistent. Thus, for patients who place a high value on avoidance of potential harms, particularly those with severe illnesses or immunosuppression, it would be reasonable to select not to use probiotics. While there was evidence for probiotics in the prevention of *C difficile*, the technical review found significant knowledge gap in the use of probiotics in treatment of *C difficile* and recommend this as an area for further study. Similar knowledge gaps exist in the use of probiotics in irritable bowel syndrome and inflammatory bowel disease (Crohn's disease and ulcerative colitis).
- In the subset of patients with pouchitis, current evidence supports the use of the 8-strain combination (*L paracasei subsp paracasei DSM 24733*, *L plantarum DSM 24730*, *L acidophilus DSM 24735*, *L delbrueckii subsp bulgaricus DSM 24734*, *B longum subsp longum DSM 24736*, *B breve DSM 24732*, *B longum subsp infantis DSM 24737*, and *S salivarius subsp thermophilus DSM 24731*) if feasibility of obtaining the combination is not a barrier.
- In preterm infants less than 37 weeks gestational age, the probiotic strains *B animalis subsp lactis* or *L reuteri* or *L rhamnosus* or combination of *Lactobacillus spp* and *Bifidobacterium spp* may prevent the development of, necrotizing enterocolitis (NEC). For children with acute gastroenteritis in North America, however, the current evidence does not support the use of probiotics. While other society guidelines have previously recommended the use of probiotics in this population, these guidelines were developed without utilizing GRADE methodology and also relied on data outside of North America, which became available after the recommendations were made. This is an area that will require further study and recommendations evolve as more direct high-quality data become available.

Researcher identified that significant knowledge gaps exist in this very promising and important area of research due to the significant heterogeneity between studies and variability in the probiotic strains studied. The lack of consistent harms reporting makes it difficult to assess true harms. The lack of product manufacturing details prohibits true comparisons and decreases the feasibility of obtaining certain products by patients. Future high-quality studies are urgently needed that address these pitfalls. These guidelines will undergo a review and consideration for an update within 3–5 years or earlier if practice changing evidence becomes available.

The official recommendations of the American Gastroenterological Association (AGA) on the role of probiotics in the management of gastrointestinal disorders:

**Source:** Grace L. Su, Division Of Gastroenterology And Hepatology, University Of Michigan And Gastroenterology Section, Veterans Administration Ann Arbor Healthcare System, Ann Arbor, Michigan. *AGA Clinical Practice Guidelines On The Role Of Probiotics In The Management Of Gastrointestinal Disorders. Gastroenterology. DOI : <https://doi.org/10.1053/j.gastro.2020.05.059>*

### 3. Probiotic Activity Of Enterococcus Faecium And Lactococcus Lactis Isolated From Thai Fermented Sausages And Their Protective Effect Against Clostridium Difficile

**Lactic acid bacteria, Enterococcus faecium** and **Lactococcus lactis**, previously isolated from Thai fermented sausages have shown probiotic properties especially in the control of Clostridium difficile 630. Both isolates survived in simulated gastric solution at pH 3 followed in simulated intestinal solution at pH 8. The presence of skimmed milk also helped the bacteria to survive through acidic and alkaline in gastrointestinal conditions. The adhesion properties of both isolates were tested using a human colon adenocarcinoma cell line. The result showed that both isolates exhibited desirable probiotic properties which adhered to Caco-2 cells. The neutralized cell-free supernatant of both isolates demonstrated that no cytotoxicity toward Caco-2 cells vice versa cell-free supernatant of C. difficile 630 toward Caco-2 cell demonstrated high toxicity. The immunomodulation effect in response to bacterial neutralized cell-free supernatant and cell-free supernatant was also studied. **The expression level of pro-inflammatory cytokine of Caco-2 cell which are tumor necrosis factor- $\alpha$  and interleukin-8 was evaluated using quantitative reverse transcriptase PCR. Both isolates were able to diminish the expression level of TNF- $\alpha$  and IL-8 induced by the cell-free supernatant of C. difficile 630. Hence, these isolates would be able to improve the gut health through counteracting the C. difficile-associated intestinal inflammation in human cell lines.** These results may contribute to the development of the isolates using as probiotics.

**Source: Amornrat Aroonual, Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand. Probiotic Activity Of Enterococcus Faecium And Lactococcus Lactis Isolated From Thai Fermented Sausages And Their Protective Effect Against Clostridium Difficile. Probiotics & Antimicro. Prot. 12, 641-648 (2020). <https://doi.org/10.1007/s12602-019-09536-7>**

### 4. Probiotic Treatment Does Not Change Sulphasalazine And Its Metabolites Excretion In Patients With Inflammatory Bowel Disease

The manipulation of gut microflora composition and activity by probiotics could modify the enzymatic activity of intestinal bacteria. This study investigated the influence of probiotic treatment on sulphasalazine (SSZ) excretion in inflammatory bowel disease (IBD) patients.

Newly diagnosed IBD patients were randomised in two groups; half of subjects were treated with SSZ and other half were treated with combination of SSZ and probiotics. At the each visit, patients were assessed clinically and fecal samples and total volume of 24 h urine was measured and noted. Urine samples were collected and analysed by liquid chromatography-mass spectrometry/mass spectrometry for determination of SSZ and its metabolites. The enzymatic activity of azoreductase by intestinal bacteria in the fecal contents was determined spectrophotometrically.

Study results revealed that urinary levels of SSZ and its metabolites showed no statistically significant changes after probiotic administration. Azoreductasa activities, in both experimental groups, decreased comparing with pre-treatment values in both cultivation conditions. Transient colonization with Bifidobacterium BB12 was confirmed in 22% of samples. Lactobacillus rhamnosus LGG did not show transient colonisation of the digestive tract. Hence, co-administration of probiotics in patients treated with SSZ did not change the amounts of excreted SSZ and its metabolites

**Source: Natasa Stojakovic, Department Of Medicine, University Of Banja Luka, Bosnia And Herzegovina. Probiotic Treatment Does Not Change Sulphasalazine And Its Metabolites Excretion In Patients With Inflammatory Bowel Disease. J Prob Health. 8: 219. DOI: 10.35248/2329-8901.20.8.219**

### 5. Heat-Inactivated Bifidobacterium Bifidum Mimbb75 (SYN-HI-001) In The Treatment Of Irritable Bowel Syndrome: A Multicentre, Randomised Double-Blind, Placebo-Controlled Clinical Trial

**Bifidobacterium bifidum** is one of a few probiotic strains that have been shown to be effective in the treatment of irritable bowel syndrome (IBS) and its symptoms. Non-viable strains might have advantages over viable bacteria for product stability and standardisation, as well as for tolerability because safety concerns have been raised for specific patient groups who are susceptible to infection. This study assessed the efficacy of non-viable, heat-inactivated (HI) *B bifidum* MIMBb75) in the treatment of IBS and its symptoms.

Patients were screened between April 15, 2016, and Feb 3, 2017, and 443 patients were allocated to the placebo group (n=222) or the *B bifidum* group (n=221). The composite primary endpoint was reached by 74 (34%) of 221 patients in the *B bifidum* group compared with 43 (19%) of 222 in the placebo group. No serious adverse events occurred in the *B bifidum* group; seven adverse events suspected to be related to the study product were reported in the *B bifidum* group as were eight in the placebo group. No deaths were reported in this study. The most common reported adverse event with a suspected relationship to the study product was abdominal pain, which was reported in two (<1%) patients in the *B bifidum* group and one (<1%) in the placebo group. Tolerability was rated as very good or good by 200 (91%) patients in the *B bifidum* group compared with 191 (86%) in the placebo group.

This study shows that *B bifidum* substantially alleviates IBS and its symptoms in a real-life setting. These results indicate that specific beneficial bacterial effects are mediated independently of cell viability.

**Source; Dr Peter Layer, Department of Internal Medicine, Israelitic Hospital, Germany. Heat-Inactivated Bifidobacterium Bifidum Mimbb75 (SYN-HI-001) In The Treatment Of Irritable Bowel Syndrome: A Multicentre Randomised, Double-Blind, Placebo-Controlled Clinical Trial. The Lancet Gastroenterology & Hepatology, VOLUME 5, ISSUE 7, P658-666, JULY 01, 2020. DOI: [https://doi.org/10.1016/S2468-1253\(20\)30056-X](https://doi.org/10.1016/S2468-1253(20)30056-X)**

## 6. The Probiotic, *Leuconostoc Mesenteroides*, Inhibits *Listeria Monocytogenes* Biofilm Formation

This study demonstrates that three *Leuconostoc mesenteroides* strains of lactic acid bacteria isolated from kimchi are effective probiotics for inhibiting *Listeria* biofilm formation. Biofilms of two *L. monocytogenes* serotypes, 1/2a and 4b, in dual-species culture with each probiotic strain were decreased by more than 40-fold as compared with single-species *Listeria* biofilms; for instance, a reduction from  $5.4 \times 10^6$  colony forming units (CFU)/cm<sup>2</sup> *L. monocytogenes* 4b in single-species biofilms to  $1.1 \times 10^5$  CFU/cm<sup>2</sup> in dual-species biofilms. Most likely, one of the *Leuconostoc* strains, *L. mesenteroides* W51, led to the highest *Listeria* biofilm inhibition without affecting the growth of *L. monocytogenes*. The cell-free supernatant from the *L. mesenteroides* W51 culture containing large protein molecules (>30 kDa) also inhibited *Listeria* biofilms. These data indicate that *Leuconostoc* probiotics can be used to repress *L. monocytogenes* biofilm contamination on surfaces at food processing facilities.

*Source: Seok Hoon Hong, Department Of Chemical And Biological Engineering, Illinois Institute Of Technology, Chicago. The Probiotic, Leuconostoc Mesenteroides, Inhibits Listeria Monocytogenes Biofilm Formation. Journal Of Food Safety, Volume40, Issue2, April 2020, e12750. <https://doi.org/10.1111/jfs.12750>*

## 7. Food & Mood: A Review Of Supplementary Prebiotic And Probiotic Interventions In The Treatment Of Anxiety And Depression

A bidirectional relationship exists between the brain and the gastrointestinal tract. Foods containing bacteria that positively influence the gastrointestinal microbiome are termed, probiotics; compounds that promote the flourishing of these bacteria are termed, prebiotics.

This systematic review analysed database and grey literature sites to investigate about pre and/or probiotics as treatments for depression and/or anxiety disorders. 7 studies were identified. All demonstrated significant improvements in one or more of the outcomes measuring the effect of taking pre/probiotics compared with no treatment/placebo, or when compared to baseline measurements. Study results affirm that pre/probiotic therapy warrants further investigation.

*Source: Sanjay Noonan, Brighton And Sussex Medical School, Brighton, UK. Food & Mood: A Review Of Supplementary Prebiotic And Probiotic Interventions In The Treatment Of Anxiety And Depression. BMJ Nutrition, Prevention & Health 2020; bmjnp-2019-000053. DOI: 10.1136/bmjnp-2019-000053*

## 8. Cell Wall Integrity And Protoplast Formation Of The Probiotic *Lactobacillus Acidophilus* Through Fluorescent Staining

Researchers utilized fluorescence microscopy techniques to determine the presence or absence of bacterial cell walls in the probiotic *Lactobacillus acidophilus*, after exposure to cell wall digestive enzymes.

Three fields were studied for each lysozyme and stain combination. A one-way ANOVA was performed to determine differences in lysozyme concentrations. A p-value < 0.05 was noted as significantly different. Cell wall structural integrity began to deteriorate at 175 and 250 µg/ml of lysozyme and cell lysis and striations of DNA increased at a concentration of 425 µg/ml. Lysozyme concentration of 175 µg/ml produced an average of 41% protoplast or partial digestion of cell wall. An increase from 175 to 250 µg/ml concentration of lysozyme resulted in a decreased average percentage of protoplast (4%). At a concentration of 425 µg/ml, the average percentage of protoplast decreased to 1%, while also showing an increase in striations of DNA. At 1x dye concentration, partial staining of the cell wall was observed. At 2x, complete staining of the cell wall was recorded. At 10x, complete staining of cell wall and nuclei was observed similar to dye concentrations at 2x with no significant saturation of dyes. Dye concentration at 100x produced an oversaturation of the dyes in the cell wall and nuclei causing them to mix and inhibit the efficacy of identifying bacterial cells and protoplasts. 2x was most optimum for complete staining of cell wall and nucleus. Background fluorescence noise was observed as concentration of dye increased.

This study concluded that in *Lactobacillus acidophilus*, a lysozyme concentration of 175 µg/ml was sufficient for cell wall digestion. Efficacy of dye concentration was best at 2x with the least amount of background noise.

*Source: Kayanush Aryana, Dairy Science Building, LSU AgCenter, Baton Rouge, USA. Cell Wall Integrity And Protoplast Formation Of The Probiotic Lactobacillus Acidophilus Through Fluorescent Staining. J Prob Health, 8:218. DOI: 10.35248/2329-8901.20. 8:218.*

## 9. How Probiotics May Kill Harmful Bacteria: The In Vitro Activity Against Some Haemolytic Strains

Haemolysis is the lysis of red blood cells (RBCs) and the subsequent release of their contents into surrounding fluid. Several pathogens, including *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* are able to cause haemolysis *in vitro* and *in vivo*. A vast body of scientific literature has demonstrated the ability of certain probiotic bacteria to antagonize gram-positive and gram-negative strains by secreting soluble molecules named **bacteriocins**.

Ten lactobacilli were selected for this *in vitro* study. The agar spot assay was employed to quantify any possible inhibition. The diameters of inhibition zones around the spots were measured.

Study results show that selected probiotics could exert a focused protective effect against pathogenic bacteria responsible for RBCs lysis at various extent. Further investigations will be needed to study the underlying molecules responsible for inhibition.

*Source: Luca Mogna, Probiotal Research Srl, Via E. Mattei 3, Italy. How Probiotics May Kill Harmful Bacteria: The In Vitro Activity Against Some Haemolytic Strains. J Prob Health, 8:216. DOI: 10.35248/2329-8901.20.8.216*

## 10. Lactobacillus Plantarum-Mediated Regulation Of Dietary Aluminium Induces Changes In The Human Gut Microbiota: An In Vitro Colonic Fermentation

The gut microbiota has been identified as a target of toxic metals and a potentially crucial mediator of the bioavailability and toxicity of these metals. This study shows that aluminium (Al) exposure, even at low dose, affect the growth of representative strains from the human intestine via pure culture experiments. *In vitro*, *Lactobacillus plantarum* could bind Al on its cell surface as shown by electron microscopy and energy dispersive X-ray analysis.

Study result show that Al exposure significantly increase the relative abundances of *Bacteroidetes (Prevotella)*, *Proteobacteria (Escherichia)*, *Actinobacteria (Collinsella)*, *Euryarchaeota (Methanobrevibacter)*, and *Verrucomicrobiaceae* and decrease *Firmicutes (Streptococcus, Roseburia, Ruminococcus, Dialister, Coprobacillus)*. Some changes aer reversed by the inclusion of *L. plantarum*. Alterations in gut microbiota induced by Al and *L. plantarum* inevitably led to changes in metabolite levels. The short-chain fatty acid (SCFAs) contents aer reduced after Al exposure, but *L. plantarum* could elevate their levels. SCFAs have positive correlations with beneficial bacteria, such as *Dialister, Streptococcus, Roseburia*, and negative correlations with *Erwinia, Escherichia, and Serratia*. The study concludes that dietary Al exposure alter the composition and structure of the human gut microbiota, and this is partially mitigated by *L. plantarum*. This probiotic supplementation is potentially a promising and safe approach to alleviate the harmful effects of dietary Al exposure.

*Source: Qixiao Zhai, State Key Laboratory of Food Science and Technology; School of Food Science and Technology and International Joint Research Laboratory for Probiotics at Jiangnan University, Wuxi, China. Lactobacillus Plantarum-Mediated Regulation Of Dietary Aluminium Induces Changes In The Human Gut Microbiota: An In Vitro Colonic Fermentation. Probiotics & Antimicro. Prot. (2020). <https://doi.org/10.1007/s12602-020-09677-0>*

## 11. Quorum Sensing Circuits In The Communicating Mechanisms Of Bacteria And Its Implication In The Biosynthesis Of Bacteriocins By Lactic Acid Bacteria: A Review

It is well established that bacteria communicate between each other by using different mechanisms; among which, quorum sensing (QS) is the best known one. Indeed, intra- and intercellular communications of microorganisms, as well as the regulation of metabolism and reaction to the surrounding environmental conditions, are carried out by using different signaling molecules. N-Acyl homoserine lactones control the QS in Gram-negative bacteria, while Gram-positive bacteria was used to communicate with peptides. These compounds, by diffusing through the bacterial membrane cell from the extracellular medium, directly or indirectly control the expression of specific genes that induce bacteria to react to their surrounding environment and stressing agents. In the case of lactic acid bacteria and bifidobacteria which are widely used in the dairy industry, QS is of extreme importance for their survival and the extent of their activity in the dairy matrix. Moreover, it is also via QS that these bacteria synthesize various antimicrobial agents such as bacteriocins.

This study highlights the quorum sensing circuits involved in the communicating mechanisms of bacteria with emphasis on current applications of QS in lactic acid bacteria. More particularly, the implication of QS in the biosynthesis of bacteriocins by lactic acid bacteria.

*Source: Mohammed Aider, Institute of Nutrition and Functional Foods (INAF), Université Laval and Department of Soil Sciences and Agri-Food Engineering, Pavilion P. Comtois, Université Laval, Canada. Quorum Sensing Circuits In The Communicating Mechanisms Of Bacteria And Its Implication In The Biosynthesis Of Bacteriocins By Lactic Acid Bacteria: A Review. Probiotics & Antimicro. Prot. 12, 5-17 (2020). <https://doi.org/10.1007/s12602-019-09555-4>*

## 12. The Effects Of Supplementation With Probiotic On Biomarkers Of Oxidative Stress In Adult Subjects: A Systematic Review And Meta-Analysis

The current systematic review and meta-analysis study was conducted to determine the effect of probiotic supplementation on some oxidative stress biomarkers among adult subjects.

Findings from 11 included studies ( $n=577$ ) indicate that probiotic supplementation increased **total antioxidant capacity (TAC)** and reduced **malondialdehyde (MDA)** significantly compared to the control group. However, its effects on glutathione (GSH) was not significant. The current meta-analysis revealed that probiotic supplementation may result in increasing TAC and lowering MDA, which improve antioxidant status. However, due to high heterogeneity, findings should be interpreted with caution. Further investigations are required to elucidate the effect of supplementation with probiotics on biomarkers of antioxidants.

*Source: Leila Azadbakht, Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences; Diabetes Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences And Department of Community Nutrition, School of Nutrition and Food Science, Isfahan University of Medical Sciences, Iran. The Effects Of Supplementation With Probiotic On Biomarkers Of Oxidative Stress In Adult Subjects: A Systematic Review And Meta-Analysis. Probiotics & Antimicro. Prot. 12, 102-111 (2020). <https://doi.org/10.1007/s12602-018-9500-1>*

## 13. Investigation Of The Efficacy Of Lactobacillus Rhamnosus GG In Infants With Cow's Milk Protein Allergy: A Randomised Double-Blind Placebo-Controlled Trial

This investigation has been performed to show the efficacy of **Lactobacillus rhamnosus GG (LGG)** together with milk-free diet in patients with cow's milk protein allergy (CMPA).

This multicentre prospective investigation was performed in 0–12 months of age children diagnosed as CMPA clinically and biochemically. Patients were randomly divided into two groups. Infants in probiotic group received cow's milk protein free diet and per oral (p.o.) daily  $1 \times 10^9$  CFU LGG and in the placebo group milk-free diet and placebo were given. Mothers of all breast-fed patients were put on milk-free diet and all patients fed with formula were given extensively hydrolysed formula. Symptoms like diarrhoea, vomiting, mucousy or bloody stool, abdominal pain or distension, constipation, dermatitis and restiveness were recorded at the beginning and weekly.

One-hundred infants diagnosed with CMPA were included in this double-blind placebo-controlled study. Forty-eight infants placed in probiotic group and 52 in placebo group. After 4 weeks of receiving dietary, infants in probiotic group showed statistically significant improvement in symptoms of bloody stool, diarrhoea, restiveness and abdominal distension. Statistically significant improvement was also observed in symptoms of mucousy stool and vomiting, no significant improvement were observed in abdominal pain, constipation and dermatitis.

In this study scientists observed significant improvement in symptoms of infants diagnosed with CMPA receiving dietary LGG with cow's milk-free diet.

*Source: Ahmet Basturk, Department of Pediatric Gastroenterology, Faculty of Medicine, Gaziantep University, Turkey. Investigation Of The Efficacy Of Lactobacillus Rhamnosus GG In Infants With Cow's Milk Protein Allergy: A Randomised Double-Blind Placebo-Controlled Trial. Probiotics & Antimicro. Prot. 12, 138-143 (2020). <https://doi.org/10.1007/s12602-019-9516-1>*

## 14. Probiotics As An Adjunct Therapy For The Treatment Of Halitosis, Dental Caries And Periodontitis

Probiotics and prebiotics are popular among consumers worldwide as natural approaches to prevent gastrointestinal diseases. The effects of their consumption on the gastrointestinal system have been extensively investigated. Recently, the efficacy of probiotics and prebiotics has been evaluated against naturally developing microbiome imbalance in the human body, such as in the oral cavity, skin, female urogenital tract, and respiratory tract. This review examines the scientific data related to the effects of probiotics on the treatment of diseases occurring in the oral cavity. Probiotics can effectively prevent and treat some infectious diseases in the oral cavity, such as halitosis and periodontitis, and can reduce the development of dental caries and the concentration of harmful bacteria, according to clinical studies. The results of this meta-analysis also suggest the use of probiotics to treat halitosis and periodontitis. However, the evidence may be inconclusive due to the use of a wide range of probiotics, non-standardized study design, small population size, poor quality reports, and inconsistent data. Therefore, future studies should homogenize terms and definitions for primary and secondary outcomes, increase the number of volunteers/patients in vitro tests and clinical studies, and include an evaluation of the combined use of pre- and probiotics.

*Source: Mariela Bustamante, Center Of Food Biotechnology And Bioseparations, Scientific And Technological Bioresource Nucleus, BIOREN, And Department Of Chemical Engineering, Universidad De La Frontera, Ave, Temuco, Chile. Probiotics As An Adjunct Therapy For The Treatment Of Halitosis, Dental Caries And Periodontitis. Probiotics & Antimicro. Prot. 12, 325-334 (2020). <https://doi.org/10.1007/s12602-019-9521-4>*

## 15. *Leuconostoc Mesenteroides* Subsp. *Mesenteroides* SD23 Prevents Metabolic Dysfunction Associated With High-Fat Diet-Induced Obesity

**High-fat diet (HFD)** consumption induces obesity and increases blood glucose, insulin resistance, and metabolic disorders. Recent studies suggest that probiotics might be a novel approach to counteract these effects in the treatment of obesity. Here, the researchers evaluated the effect of *Leuconostoc mesenteroides* subsp. *mesenteroides* SD23 on obesity-related metabolic dysfunction. In the present study, mice were randomly divided into four dietary groups: **standard diet (C), HFD (OB), standard diet with *L. mesenteroides* SD23 (CP), and HFD with *L. mesenteroides* SD23 (OBP)**. Diets were maintained for 14 weeks. Animal weight was monitored and biochemical and histological analyses were performed after intervention. OB showed metabolic dysfunction, and increased the number of larger adipocytes compared to C. OB induced liver **tumor necrosis factor- $\alpha$  (TNF- $\alpha$ )** expression, increased cholesterol, leptin, and glucose levels compared to C. OBP reduced body weight, glucose, cholesterol, and leptin levels and improved glucose tolerance compared to OB. OBP also reduced liver steatosis, the number of larger adipocytes in adipose tissue, and reduced the villus height in the small intestine. OBP decreased expression of TNF- $\alpha$  and increased expression of IL-10 in liver. The parameters evaluated in the CP were similar to the C. This study provides novel evidence that dietary intervention with *L. mesenteroides* SD23 improves metabolic dysfunction related to obesity in HFD-fed mice.

**Source:** Elena Zambrano, Reproductive Biology Department, Instituto Nacional De Ciencias Médicas Y Nutrición Salvador Zubirán, Mexico City, Mexico. *Leuconostoc Mesenteroides* Subsp. *Mesenteroides* SD23 Prevents Metabolic Dysfunction Associated With High-Fat Diet-Induced Obesity. *Probiotics & Antimicro. Prot.* 12, 505-516 (2020). <https://doi.org/10.1007/s12602-019-09556-3>

## 16. *L. Plantarum*, *L. Fermentum*, And *B. Breve* Beads Modified The Intestinal Microbiota And Alleviated The Inflammatory Response

This paper aims to study the effects of compound microbe-based beads on changes in the intestinal microbiota and alleviation of high-fat (HF) diet-induced inflammatory responses. Forty-eight mice were fed base chow or a high-fat diet for 4 weeks and then randomly separated into six groups: normal diet (group A), high-fat diet (group B), high-fat positive control (fed with high-fat chow plus Tetrahydropipstatin, group C), high-fat chow plus *B. breve* beads (group D), high-fat chow plus *L. plantarum*-*L. fermentum* beads (group E), and high-fat chow plus *L. plantarum*-*L. fermentum*-*B. breve* beads (group F). The body weights were measured. The serum cytokine and lipid levels were determined by ELISA, and high-throughput sequence analysis of the fecal microbiota was conducted. Beads with cell encapsulation rates higher than 99% decreased the body weight from  $50.97 \pm 3.44$  g in group B to  $42.64 \pm 2.63$  g in group F at the end of the experiment ( $p = 0.00019$ ). The total cholesterol content in group F was  $80.14 \pm 9.37$  mmol/L, which was significantly lower than that in group A ( $96.13 \pm 24.07$  mmol/L) ( $p = 0.02765$ ), group B ( $102.52 \pm 12.20$  mmol/L) ( $p = 0.00196$ ), and group C ( $98.99 \pm 11.32$  mmol/L) ( $p = 0.00804$ ). In addition, the serum IL-6 level showed no significant difference between group F and the base chow control group. The microbial cell-loaded bead intervention led to increased abundances of *Bifidobacterium* and *Lactobacillus* in mouse feces. Oral administration of three strain-based beads led to alleviation of inflammatory reactions in high-fat diet-fed mice.

**Source:** Xiuliang Li, Engineering Research Center Of Agricultural Microbiology Technology, Ministry Of Education, Heilongjiang University And Key Laboratory Of Molecular Biology, College Of Heilongjiang Province, School Of Life Sciences, Heilongjiang University, China. *L. Plantarum*, *L. Fermentum*, And *B. Breve* Beads Modified The Intestinal Microbiota And Alleviated The Inflammatory. *Probiotics & Antimicro. Prot.* 12, 535-544 (2020). <https://doi.org/10.1007/s12602-019-09564-3>

## 17. Effects Of Potential Probiotic Strains On The Fecal Microbiota And Metabolites Of D-Galactose-Induced Aging

This study investigates the effects of different potential probiotic strains on the dynamic changes of fecal microbiome and metabolites. In this study, male Sprague-Dawley rats were fed with high-fat diet and injected with D-galactose for 12 weeks to induce aging. The effect of *Lactobacillus plantarum* DR7, *L. fermentum* DR9, and *L. reuteri* 8513d administration on the fecal microbiota profile, short-chain fatty acids, and water-soluble compounds were analyzed. It was found that the administration of the selected strains altered the gut microbiota diversity and composition, even at the phylum level. The fecal short-chain fatty acid content was also higher in groups that were administered with the potential probiotic strains. Analysis of the fecal water-soluble metabolites revealed that administration of *L. plantarum* DR7 and *L. reuteri* 8513d led to higher fecal content of compounds related to amino acid metabolism such as tryptophan, leucine, tyrosine, cysteine, methionine, valine, and lysine; while administration of *L. fermentum* DR9 led to higher prevalence of compounds related to carbohydrate metabolism such as **erythritol, xylitol, and arabitol**. In conclusion, it was observed that different strains of lactobacilli can cause difference alteration in the gut microbiota and the metabolites, suggesting the urgency to explore the specific metabolic impact of specific strains on the host.

**Source:** Min-Tze Liong, School Of Industrial Technology, Universiti Sains Malaysia, Minden And USM-RIKEN International Centre For Ageing Science (URICAS), Universiti Sains Malaysia, Minden, Penang, Malaysia, Effects Of Potential Probiotic Strains On The Fecal Microbiota And Metabolites Of D-Galactose-Induced Aging. *Probiotics & Antimicro. Prot.* 12, 545-562 (2020). <https://doi.org/10.1007/s12602-019-09545-6>

## 18. Anti-Inflammatory And Anti-Osteoporotic Potential Of Lactobacillus Plantarum A41 And L. Fermentum SRK414 As Probiotics

This study involves an investigation on the probiotic properties of lactic acid bacteria and their potential applications in an in vitro model of **lipopolysaccharide (LPS)**-stimulated inflammation and dexamethasone-induced osteoporosis. Nine strains were pre-screened from 485 lactic acid bacteria based on their survival at a low pH and in a solution containing bile salts. All candidates were capable of surviving in an environment with low pH and with bile salts and could successfully colonize the intestine. Furthermore, their functional properties, such as anti-oxidation and anti-inflammation, were evaluated. Of the nine probiotic candidates, **Lactobacillus plantarum A41** and **L. fermentum SRK414** exhibited the highest anti-oxidative capacity. Moreover, only *L. plantarum* A41 and *L. fermentum* SRK414 could increase gut barrier function by upregulating the mRNA expression of tight junction proteins and inhibit the expression of inflammatory mediators induced by LPS-stimulated inflammation. Interestingly, these two strains were also capable of regulating several bone metabolism-related markers playing a role in bone homeostasis and osteoblast differentiation. In brief, *L. plantarum* A41 and *L. fermentum* SRK414 exhibited high probiotic potential and potentially impact immune-related bone health by modulating pro-inflammatory cytokines and bone metabolism-related markers.

**Source:** Sae Hun Kim, College Of Life Sciences And Biotechnology, Korea University And Institute Of Life Science And Natural Resources, Korea University, Republic Of Korea. **Anti-Inflammatory And Anti-Osteoporotic Potential Of Lactobacillus Plantarum A41 And L. Fermentum SRK414 As Probiotics. Probiotics & Antimicro. Prot. 12, 623-634 (2020).**

<https://doi.org/10.1007/s12602-019-09577-y>

## 19. Characterization Of Probiotic Properties Of Antifungal Lactobacillus Strains Isolated From Traditional Fermenting Green Olives

The aim of this work was to characterize the potential probiotic properties of 14 antifungal *Lactobacillus* strains isolated from traditional fermenting Moroccan green olives. The molecular identification of strains indicated that they were composed of five **Lactobacillus brevis**, two **Lactobacillus pentosus**, and seven **Lactobacillus plantarum**.

In combination with bile (0.3%), all the strains showed survival rates (SRs) of 83.19–56.51% at pH 3, while 10 strains showed SRs of 31.67–64.44% at pH 2.5. All the strains demonstrated high tolerance to phenol (0.6%) and produced exopolysaccharides. The autoaggregation, hydrophobicity, antioxidant activities, and surface tension value ranges of the strains were 10.29–41.34%, 15.07–34.67%, 43.11–52.99%, and 36.23–40.27 mN/m, respectively. Bacterial cultures exhibited high antifungal activity against **Penicillium sp.** The cell-free supernatant (CFS) of the cultures showed important inhibition zones against **Candida pelliculosa** (18.2–24.85 mm), as well as an antibacterial effect against some gram-positive and gram-negative bacteria (10.1–14.1 mm). The neutralized cell-free supernatant of the cultures displayed considerable inhibitory activity against **C. pelliculosa** (11.2–16.4 mm). None of the strains showed acquired or horizontally transferable antibiotic resistance or mucin degradation or DNase, hemolytic, or gelatinase activities. *Lactobacillus brevis* S82, *Lactobacillus pentosus* S75, and *Lactobacillus plantarum* S62 showed **aminopeptidase,  $\beta$ -galactosidase, and  $\beta$ -glucosidase** activities, while the other enzymes of API-ZYM were not detected. The results obtained revealed that the selected antifungal *Lactobacillus* strains are considered suitable candidates for use both as probiotic cultures for human consumption and for starters and as biopreservative cultures in agriculture, food, and pharmaceutical industries.

**Source:** Houssam Abouloifa, Laboratory Of Biochemistry And Biotechnology, Faculty Of Sciences, Mohammed Premier University, Oujda, Morocco. **Characterization Of Probiotic Properties Of Antifungal Lactobacillus Strains Isolated From Traditional Fermenting Green Olives. Probiotics & Antimicro. Prot. 12, 683-696 (2020).** <https://doi.org/10.1007/s12602-019-09543-8>

## 20. Characteristic Of Bacteriocins Of Lactobacillus Rhamnosus BTK 20-12 Potential Probiotic Strain

Multidrug resistance (MDR) is a serious health threat throughout the world resulting in reduced efficacy of antibacterial, antiparasitic, antiviral, and antifungal drugs. One of the most promising concepts that may represent a good alternative to antibiotics can be the use of bacteriocins obtained from lactic acid bacteria. The **L. rhamnosus** strain was isolated from traditional Armenian naturally fermented salted cheese. The probiotic potential of the strain was approved. It was shown that strain produced at least two bacteriocins (BCN 1 and BCN 2) with different molecular weight (1427 Da and 602.6 Da, respectively). **Bacteriocins** inhibited the growth of multidrug-resistant bacteria of different etiologies and belongs to different taxonomic groups with diverse efficiency and it depends on properties of bacteriocins, as well as from isolation sources of pathogens. Thus, bacteriocins of *L. rhamnosus* have protein-like nature and a broad range of activity and are excellent candidates for the development of new prophylactic and therapeutic substances to complement or replace conventional antibiotics.

**Source:** Kristina J. Karapetyan, Laboratory Of Biosafety Of Food Products At Scientific And Production Center "Armbiotechnology" NSPO, National Academy Of Science, Yerevan, Republic Of Armenia. **Characteristic Of Bacteriocins Of Lactobacillus Rhamnosus BTK 20-12 Potential Probiotic Strain. Probiotics & Antimicro. Prot. 12, 716-724 (2020).**

<https://doi.org/10.1007/s12602-019-09569-y>

## 21. Application Of Probiotics In Folate Bio-Fortification

Folate deficiency is a public health concern affecting all age groups worldwide. The available evidence reveals that adding probiotic bacteria to the yoghurt starter cultures during yoghurt production process under fermentation conditions increases the folate content of yoghurt. The present study was conducted to measure two folate derivatives, i.e., **5-methyltetrahydrofolate and 5-formyltetrahydrofolate**, in bio-fortified yoghurt samples including (1) yoghurt containing ***Streptococcus thermophilus* and *Lactobacillus bulgaricus***, (2) probiotic yoghurt containing ***Lactobacillus acidophilus* LA-5 and *Bifidobacterium lactis* BB-12**, (3) probiotic yoghurt containing native strains of ***Lactobacillus plantarum* 15HN**, (4) probiotic yoghurt containing native strains of ***Lactococcus lactis* 44Lac**, and (5) probiotic yoghurt containing commercial strains of ***Lactobacillus plantarum* LAT BY PL**. During storage at 4 °C for 21 days, the highest levels of 5-methyltetrahydrofolate and 5-formyltetrahydrofolate, which were statistically significant, were detected in the yoghurt made using *Lact. plantarum* 15HN. Moreover, the highest total folate concentration (1487 ± 96.42 µg/L) was specified in the yoghurt containing *Lact. plantarum* 15HN on the 7th day. It can be conjectured that this product can be suggested as a proper alternative to synthetic folic acid and may not have the side effects of using synthetic folic acid overdoses.

Source: Somayeh Jafarzadeh, Department of Food Science and Technology, Faculty of Health and Nutrition, Tabriz University of Medical Sciences, Tabriz, Iran. Application Of Probiotics In Folate Bio-Fortification. *Probiotics & Antimicro. Prot.* 12, 756–763 (2020). <https://doi.org/10.1007/s12602-019-09560-7>

## 22. Application Of Microencapsulated Synbiotics In Fruit

In the last years, demand for functional products containing both prebiotics and probiotics (known as synbiotic) has increased, which stimulated their incorporation into other food matrices than milk-based ones. Synbiotics improve gut functionality as well as respond to the increasing demand of consumers who have become aware of the health benefits of a proper diet. The most important criterion for preserving consumer acceptance in such products is maintaining the minimum viability and activity of probiotics from the beginning of production to the end of shelf-life. For their viability, fixation and multiplying within the host, several solutions have been proposed including the fortification with prebiotics and microencapsulation of prebiotics along with probiotics. The challenge of microencapsulation is to protect the probiotic cells in foods that are not usually considered their vehicle, such as fruit matrices. It is generally known that different prebiotics may exert different degrees of protection on the entrapped bacteria cells. For food products, such as fruit beverages, few works exist that investigate the functionality of synbiotic microcapsules in protecting the survivability of probiotic cells during processing and storage. This article provides an overview of this novel trend based on a review of relevant literature. The article summarizes the synbiotic concept, challenges for synbiotic formulation in fruit beverages, and future perspectives.

Source: Diana Pasarin, Institutul National De Cercetare-Dezvoltare Pentru Chimie Si Petrochimie, Bucharest, Romania. Application Of Microencapsulated Synbiotics In Fruit. *Probiotics & Antimicro. Prot.* 12, 764–773 (2020). <https://doi.org/10.1007/s12602-019-09579-w>

## 23. Safety Assessment Of Potential Probiotic *Lactobacillus Fermentum* MTCC-5898 In Murine Model After Repetitive Dose For 28 Days

Safety assessment of **probiotic *Lactobacillus fermentum* MTCC-5898 (LF)** with three doses (10<sup>7</sup>, 10<sup>9</sup>, and 10<sup>11</sup> cfu/day/animal) was carried on Swiss albino mouse weanlings for 28 days using oral route. Health status of animals was monitored by physical assessment of body weight, organ indices, and histological appearances of liver and intestine along with measurement of hematological parameters (Hb, WBC, RBC count, MCHC, MCV, MCH), biochemical analytes in blood involving glucose, serum enzymes (ALT, AST and LDH), urea, creatinine, and lipid profile (total cholesterol, triglycerides, HDL, VLDL, LDL, and atherogenic index).

LF showed no adverse effects on above parameters of general health status after continuous consumption for the experimental period. On the other hand, significant increase in TGF-β (regulatory cytokine) and considerable decrease in IFN-γ (pro-inflammatory cytokine) without any major changes in IL-4 and IL-12 in intestinal fluid on consumption of 10<sup>9</sup> cfu/animal/day confirmed its dose-specific response for immune homeostasis. Further, safety of LF was also confirmed by insignificant changes in release of FITC-dextran (4 kDa) in blood on its consumption than control group where only saline was given orally. Moreover, significantly increased mRNA expression of *claudin-1* and *MUC-2* in intestinal epithelial cells on feeding ***L. fermentum*** further supported FITC-dextran permeability data which otherwise showed increased flux of FITC-dextran in blood on consumption of ***E. coli*** (10<sup>9</sup> cfu/animal/day) due to intestinal damage. Thus, in vivo results confirmed that ***Lactobacillus fermentum* MTCC 5898** is safe and non-toxic to weanling mice and may be considered for functional food application after clinical testing.

Source: Rajeev Kapila, Animal Biochemistry Division, ICAR-National Dairy Research Institute, Karnal, Haryana, India. Safety Assessment Of Potential Probiotic *Lactobacillus Fermentum* MTCC-5898 In Murine Model After Repetitive Dose For 28. *Probiotics & Antimicro. Prot.* 12, 259–270 (2020). <https://doi.org/10.1007/s12602-019-09529-6>

## 24. Probiotic Potential, Antioxidant Activity, And Phytase Production Of Indigenous Yeasts

While many bacteria have been used as probiotics by industries, only two yeasts, *Saccharomyces cerevisiae var. boulardii* and *Kluyveromyces fragilis* (B0399), have been used as probiotics. In the present work, a total of 116 yeasts isolated from Brazilian indigenous fermented food, cocoa fermentation, and kefir were in vitro characterized for probiotic attributes. From 116 isolates, 36 were tolerant to gastrointestinal conditions evaluated by tolerance to pH 2.0, bile salts (0.3% w/v), and 37 °C temperature. From those, 15 isolates showed a similar or higher percentage of hydrophobicity, autoaggregation, and coaggregation with *E. coli* than the reference strain *S. boulardii*. All these strains showed a high percentage of adhesion to Caco-2 cells (> 63%) and antioxidant activity (ranging from 18 to 62%). Phytate hydrolysis was evaluated for these yeasts and 13 strains showed positive results, which is important for nutrient availability in plant-based foods. These results are important insights for characterization of novel probiotic yeast strains as well as to aggregate functional value to these food products.

*Source: Rosane Freitas Schwan, Biology Department, Federal University of Lavras, CEP, Lavras, Brazil. Probiotic Potential, Antioxidant Activity, And Phytase Production Of Indigenous Yeasts. Probiotics & Antimicro. Prot. 12, 280-288 (2020). <https://doi.org/10.1007/s12602-019-9518-z>*

## 25. Probiotics For Dementia: A Systematic Review And Meta-Analysis

A systematic review and meta-analysis was conducted to determine the effectiveness of probiotic and synbiotic supplementation on the cognitive function of individuals with dementia.

Researchers included data from randomized clinical trials (RCTs) that addressed dementias and assessed the following outcomes: cognitive function; inflammatory, oxidative stress, and metabolic markers; nutritional status; and intestinal microbiota composition. Data from 3 RCTs involving 161 individuals with Alzheimer's disease receiving Lactobacillus and Bifidobacterium strains showed no beneficial effect of probiotic supplementation on cognitive function (standardized mean difference, 0.56; 95%CI: -0.06 to 1.18), with very low certainty of evidence. However, probiotic supplementation improved plasma triglycerides, very-low-density lipoprotein cholesterol, insulin resistance, and plasma malondialdehyde. No RCTs included synbiotic supplementation or assessed microbiota composition.

The study concluded that current evidence regarding the use of probiotics and synbiotics for individuals with dementia is insufficient to support their clinical application.

*Source Jenifer F Krüger, Department Of Nutrition, Federal University Of Paraná, Curitiba, Paraná, Brazil. Probiotics For Dementia: A Systematic Review And Meta-Analysis. Nutr Rev. 2020 Jun 18. <https://doi.org/10.1093/nutrit/nuaa037>*

## 26. Future Of Probiotics And Prebiotics And The Implications For Early Career

The opportunities in the fields of probiotics and prebiotics to a great degree stem provide a learning about how they influence the microbiota and interact with the host. ***In this paper scientists have discussed about recent insights, cutting-edge technologies and controversial results from the perspective of early career researchers innovating in these areas.*** This perspective emerged from the 2019 meeting of the International Scientific Association for Probiotics and Prebiotics - Student and Fellows Association (ISAPP-SFA). Probiotic and prebiotic research is being driven by genetic characterization and modification of strains, state-of-the-art in vitro, in vivo, and in silico techniques designed to uncover the effects of probiotics and prebiotics on their targets, and metabolomic tools to identify key molecules that mediate benefits on the host. These research tools offer unprecedented insights into the functionality of probiotics and prebiotics in the host ecosystem. Young scientists need to acquire these diverse toolsets, or form inter-connected teams to perform comprehensive experiments and systematic analysis of data. This will be critical to identify microbial structure and co-dependencies at body sites and determine how administered probiotic strains and prebiotic substances influence the host. This and other strategies proposed in this review will pave the way for translating the health benefits observed during research into real-life outcomes. Probiotic strains and prebiotic products can contribute greatly to the amelioration of global issues threatening society. ***The intent of this article is to provide an early career researcher's perspective on where the biggest opportunities lie to advance science and impact human health.***

*Source: Irina Spacova, Laboratory Of Applied Microbiology And Biotechnology, Department Of Bioscience Engineering, University Of Antwerp, Antwerp, Belgium. Future Of Probiotics And Prebiotics And The Implications For Early Career. Front. Microbiol., 24 June 2020. <https://doi.org/10.3389/fmicb.2020.01400>*

## 27. Effects Of Probiotics, Prebiotics, And Synbiotics On Hypercholesterolemia

Cholesterol is important for both humans and animals to maintain their normal health. However, increased serum cholesterol level can cause several cardiovascular diseases. Higher cholesterol in the blood will develop plaque in the walls of arteries. Numerous pharmacological and nonpharmacological methods have been used to decreased the blood cholesterol. Various drugs have been developed to treat hypercholesterolemia (statin drugs). However, prolonged usage of these drugs causes severe side effects. During the past decades, various scientists reported that the ingestion of several fermented products with probiotic bacteria decreases the serum cholesterol level. Probiotics are viable microorganisms that promote various health benefits upon consumption, while prebiotics are nondigestible food ingredients, which promote the growth of probiotic microorganisms in the human gut. The cholesterol reduction mechanism of probiotic bacteria is not well understood; however, most of the probiotic bacteria reduce the serum cholesterol level by using the bile salt deconjugation method. ***This paper reviews about the cholesterol-reducing capability of probiotics, prebiotics, and synbiotics and uses them as an alternative for cholesterol-reducing drugs which are used for hypercholesterolemia.***

***Source: Marimuthu Anandharaj, Department Of Biology, Gandhigram Rural Institute-Deemed University, Gandhigram, Dindigul, Tamilnadu, India. Effects Of Probiotics, Prebiotics, And Synbiotics On Hypercholesterolemia. Chinese Journal Of Biology, Volume 2020, Article ID 8236703, 8 pages. <https://doi.org/10.1155/2020/8236703>***

## 28. Criteria To Qualify Microorganisms As “Probiotic” In Foods And Dietary Supplements

This paper describes the minimum criteria that apply to a probiotic strain that will be used in foods and dietary supplements and similar criteria may be applicable to other uses of probiotics. Specifically, ***the strain must be identified using recognized scientific methods, named according to valid current nomenclature, and named with a retrievable strain designation. Methods will vary depending on species of the probiotic and are likely to change as technologies evolved.*** Also, scientists recommend that ***it should be deposited in an international culture collection.*** Further, ***the strain must have demonstrated safety for its intended use and a demonstrated health benefit based on at least one study that meets generally accepted scientific standards or as per recommendations and provisions of local/national authorities when applicable. Sufficient levels of the probiotic strain(s) must be contained in the final product throughout the shelf life in order to be able to deliver the claimed (and evidence-based) health benefit. Products*** should be manufactured according to applicable good manufacturing requirements to assure safety, purity, and stability and ***should be labelled in a manner that communicates essential information on product contents (specific strains, level of live probiotic delivered at end of shelf life, and statements about health benefits as allowed) to the end-user.*** Adherence to these principles will assure that the marketplace does not contain products that misuse the term “probiotic.” Some local regulatory contexts can define probiotics in a different manner, but it is the responsibility of the product manufacturer to produce and market probiotics that follow local rules and regulations and are in line with the above defined principles.

***Source: Arthur C. Ouwehand, Global Health And Nutrition Sciences, DuPont Nutrition And Biosciences, Kantvik, Finland. Criteria to Qualify Microorganisms as “Probiotic” in Foods and Dietary Supplements. Front. Microbiol., 24 July 2020. <https://doi.org/10.3389/fmicb.2020.01662>***

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