Lactobacillus rhamnosus GR-1®, *Lactobacillus reuteri (fermentum)* RC-14®, *Bifidobacterium animalis subsp. lactis* BB-12® and *Lactobacillus paracasei L. casei* 431®

For women's vaginal health, immune function & gastrointestinal health

This table provides a summary of the research showing the efficacy of these four probiotic strains in supporting women's health, immune function and gastrointestinal system health.

Publication	Study Design	Participants	Intervention	Outcomes	Clinical Relevance
Ljubomir P, Frank M.U, Helmut V & Herbert K 2008, 'Randomized, double-blind, placebo-controlled study of oral lactobacilli to improve the vaginal flora of postmenopausal women', Vol. 141, No.1, pp.0–57.	Randomised, double-blind, placebo-controlled study.	72 postmenopausal women 55-65 years (mean age 57.6 years) with Nugent scores between 4-6 (intermediate). *L .rhamnosus* GR-1 and *L. fermentum* RC-14, 2.5 billion CFU of each strain for 2 weeks.^	*L. rhamnosus* GR-1 and *L. fermentum* RC-14, 2.5 billion CFU of each strain for 2 weeks.^	The results of this randomised, double-blind, placebo-controlled study suggest that oral application of lactobacilli once daily for 2 weeks results in a substantial improvement in the vaginal flora of postmenopausal women with Nugent scores between 4 and 6 as demonstrated by a score reduction by at least two grades. In our study, oral probiotics lead to the significant improvements in the postmenopausal vaginal flora as demonstrated on the basis of Nugent scores. In our study, oral administration of lactobacilli in the absence of estrogen resulted in a shift from an intermediate to a normal vaginal flora in 60% of women in the intervention group, compared with only 16% of patients in the control group, a difference that was highly significant.	**Postmenopausal vaginal microbiome efficacy study** 2 weeks oral supplementation with *L. rhamnosus* GR-1 and *L. fermentum* RC-14 provide restorations of the normal vaginal flora in postmenopausal women. Oral probiotic supplements may be a useful aid in raising floral quality and improving urogenital health. *L. rhamnosus* GR-1 and *L. fermentum* RC-14 were well tolerated.
Martinez, R. C. R, Franceschini, S. A, Patta, M. C, Quintana, S. M, Gomes, B. C, De Martinis, E. C. P, & Reid, G 2009, 'Improved cure of bacterial vaginosis with single dose of tinidazole (2 g), *Lactobacillus rhamnosus* GR-1, and *Lactobacillus reuteri* RC-14: a randomized, double-blind, placebo-controlled trial', Canadian Journal of Microbiology, Vol. 55, No. 2, pp. 133-138.	Double-blind, randomised, placebo-controlled trial.	64 women (16-51 years) diagnosed with bacterial vaginosis, treated with tinidazole (2g) on day 1 then *L.rhamnosus* GR-1 and *L. fermentum* RC-14, 2 capsules/day or placebo.^	*L. rhamnosus* GR-1 1 billion CFU and *L. reuteri* RC-14 1 billion CFU once daily for 28 days, with a single dose of tinidazole (2 g) on day one.	At the end of treatment (day 28), the probiotic group had a significantly higher cure rate of bacterial vaginosis (87.5%) than the placebo group (50.0%) (p = 0.001). In addition, according to the Gram-stain Nugent score, more women were assessed with "normal" vaginal microbiota in the probiotic group (75.0% vs. 34.4% in the placebo group; p = 0.011).	**Vaginal infection efficacy study** Probiotic lactobacilli can improve the cure rate and reduce rate of infection reoccurance when combined with antibiotics, providing support for complementary therapy for bacterial vaginitis. The findings of this study support the importance of selecting clinically appropriate probiotic strains. *L. rhamnosus* GR-1 and *L. fermentum* RC-14 were well tolerated.
Reid, G, Charbonneau, D, Erb, J, Kochanowski, B, Beuerman, D, Poehner, R, & Bruce, A. W 2003, 'Oral use of Lactobacillus rhamnosus GR-1 and L. fermentum RC-14 significantly alters vaginal flora: randomized, placebo-controlled trial in 64 healthy women', FEMS Immunology & Medical Microbiology, Vol. 35, No. 2, pp.131-134.	Randomised, double-blind, placebo controlled study.	64 healthy females, 19-46 years.	*Lactobacillus rhamnosus* GR-1® and *Lactobacillus reuteri* (fermentum) RC-14®, >1 billion CFU of each strain, daily for 60 days.	Vaginal microflora testing was completed at baseline (Day 0), Day 28, Day 60 and Day 90. Culture findings showed a significant increase in lactobacilli within 4 weeks (p=0.01) and a decrease in coliforms (p=0.001) and yeasts (p=0.01) in women treated with *Lactobacillus rhamnosus* GR-1® and *Lactobacillus reuteri* (fermentum) RC-14® compared to placebo. Fewer coliforms persisted in the treated group on day 90 compared to placebo, 30 days after cessation of the probiotic (p<0.01). At baseline, 25% of subjects had asymptomatic bacterial vaginosis (BV) measured by Nugent scoring. Women without BV at baseline, in the placebo group, 24% developed BV at day 35 and 16% at day 56. In comparison no women without BV, taking Lactobacillus rhamnosus GR-1 and Lactobacillus reuteri RC-14, developed BV over the course of the study (p<0.05).	**Women's Health Efficacy Study** *Lactobacillus rhamnosus* GR-1® and *Lactobacillus reuteri* RC-14® oral supplementation significantly increased lactobacilli and decreased pathogenic bacteria and yeast, vaginally in healthy women. The results indicate that specific probiotics may be of assistance in women prone to vaginal microflora disturbance and infections. *Lactobacillus rhamnosus* GR-1® and *Lactobacillus reuteri* RC-14® were well tolerated.
Vujic, G, Jajac Knez, A, Despot Stefanovic, V, & Kuzmic Vrbanovic, V 2013, 'Efficacy of orally applied probiotic capsules for bacterial vaginosis and other vaginal infections: a double-blind, randomized, placebo-controlled study', European Journal of Obstetrics & Gynecology and Reproductive Biology, Vol. 168, No. 1, pp.75-79.	Randomised, double-blind, placebo controlled study.	544 females, 18-58 years, diagnosed with vaginal infection (bacterial vaginosis, candidiasis, trihomoniasis or combination of these conditions).	*Lactobacillus rhamnosus* GR-1® and *Lactobacillus reuteri* RC-14®, 2 capsules containing >1 billion CFU, daily for 6 weeks.	Vaginal microflora testing was completed at baseline (Day 0) at completion of the study (mean 44 days) and at follow up (6 weeks after completion of the study). Balanced vaginal microflora was achieved in 243 (61.5%) of participants taking *Lactobacillus rhamnosus* GR-1® and *Lactobacillus reuteri* RC-14® compared to 40 (26.9%) in the placebo group (p<0.001). Follow up 6 weeks after completion of the study, found normal vaginal microbiota was present in 51.1% of participants taking the probiotic compared to 20.8% in the placebo group (p<0.001). High counts of lactobacilli were assessed in 81.5% of treated participants compared to 28.9% of individuals in the placebo group at the end of 6 weeks.	**Women's Health Efficacy Study** Balanced vaginal microflora corresponded with higher counts of lactobacilli found in participants taking *Lactobacillus rhamnosus* GR-1® and *Lactobacillus reuteri* RC-14® compared with placebo. The sustained benefit at 6 weeks following the completion of the study indicates these probiotics may be of benefit to women prone to vaginal microflora disturbance and re-infections. *Lactobacillus rhamnosus* GR-1® and *Lactobacillus reuteri* RC-14® were well tolerated.

^ Healthcare Professional discretion required for therapeutic dose.

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Publication	Study Design	Participants	Intervention	Outcomes	Clinical Relevance
Rizzardini, G, Eskesen, D, Calder, P, Capetti, A, Jespersen, L & Clerici, M 2012, 'Evaluation of the immune benefits of two probiotic strains Bifidobacterium animalis ssp. lactis, BB-12® and Lactobacillus paracasei ssp. paracasei, L. casei 431® in an influenza vaccination model: a randomised, double-blind, placebo-controlled study', British Journal of Nutrition, Vol. 107, No. 6, pp.876–884.	Randomised, double-blind, placebo-controlled, parallel group study.	211 males and females, 19-60 years.	*Bifidobacterium animalis subsp. lactis* BB-12® 1 billion CFU, *Lactobacillus paracasei L. casei* 431® 1 billion CFU or placebo, daily for 6 weeks.	Influenza vaccination was given 2 weeks after baseline (Day 0). Immune antibodies, cytokines and innate immune parameters were assessed at baseline and at completion of the study (6 weeks). Participants taking *Bifidobacterium animalis subsp. lactis* BB-12® or *Lactobacillus paracasei, L casei* 431® showed significant improvement in total plasma IgG, IgG1 and IgG3 (p<0.001) compared to placebo. Vaccine specific plasma IgG, IgG1 and IgG3 was significantly greater than corresponding placebo groups from baseline (all p<0.001 except *L.paracasei* p=0.01 for IgG). Vaccine specific secretory IgA in saliva showed significant mean fold increases in both probiotic groups (L.lactis BB-12 p=0.017 and *L.paracasei* 431 p=0.035). Salivary IgG also showed significant increases in the probiotic treated groups from baseline compared to placebo (p<0.001). Salivary secretory IgA was greater in participants taking *Bifidobacterium animalis subsp. lactis* BB-12® compared to placebo (p<0.05).	**Immune Function Efficacy Study** *Bifidobacterium animalis subsp. lactis*, BB-12® and *Lactobacillus paracasei, L. casei* 431® both significantly improved salivary and plasma antibody response to a vaccine challenge in healthy participants. The results indicate that specific probiotics such as *Bifidobacterium animalis subsp. lactis* BB-12® and *Lactobacillus paracasei. L casei* 431® may support the immune function when challenged. *Bifidobacterium animalis subsp. lactis* BB-12® and *Lactobacillus paracasei*, L casei 431® were well tolerated.
Jespersen, L,Tarnow, I, Eskesen, D, Morberg, C, Michelsen, B, Bugel, S, Dragsted, L. O, Rijkers, G. T & Calder, P. C 2015, 'Effect of Lactobacillus paracasei subsp. paracasei, L. casei 431 on immune response to influenza vaccination and upper respiratory tract infections in healthy adult volunteers: a randomized, double-blind, placebo-controlled, parallel-group study', American Journal of Clinical Nutrition, Vol. 101, No.6, pp.1188–1196.	Randomised, double-blind, placebo-controlled study.	1104 healthy males and females, 18-60 years.	*Lactobacillus paracasei, L casei* 431® minimum 1 billion CFU, daily for 6 weeks.	*Lactobacillus paracasei, L casei*® 431 was consumed daily from the start of the study (Day -21) for 6 weeks. Influenza vaccination was given 3 weeks after the start of supplementation (baseline-Day 0). Assessment occurred on Day -21, 0, 21 and 84. A post hoc analysis found a shortened duration of the common cold and influenza like illness (ILI) in the second half of the intervention period (Day 1-21) for those participants taking *Lactobacillus paracasei, L casei* 431® compared to placebo (p=0.0059 common cold, p=0.017 ILI). At follow up less participants in the probiotic group had accessed health care resources (p=0.028) and taken antibiotic medication (p=0.036) over the course of the study.	**Immune Function Efficacy Study** *Lactobacillus paracasei, L casei* 431® treated participants had significantly shortened the duration of the common cold and ILI after 3 weeks of supplementation. The results indicate that probiotics may help improve immune system function, which is further supported by fewer healthcare resources and antibiotics being accessed by those in the treated group. *Lactobacillus paracasei, L casei* 431® was well tolerated.

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Trachootham, D, Chupeerach, C, Tuntipopipat, S, Pathomyok, L, Boonnak, K, Praengam, K, Promkam, C & Santivarangkna, C 2017, 'Drinking fermented milk containing Lactobacillus paracasei 431 (IMULUS™) improves immune response against H1N1 and cross-reactive H3N2 viruses after influenza vaccination: A pilot randomized triple-blinded placebo controlled trial', Journal of Functional Foods, Vol. 33, pp.1–10.	Randomised, triple-blind, placebo-controlled study.	60 healthy males and females, 18-45 years.	*Lactobacillus paracasei* 431 minimum 1 billion CFU, daily for 6 weeks.	Intervention was started at baseline (Day 0) for 2 weeks before the 2015/16 influenza vaccine was given. The probiotic and placebo interventions were continued for another 4 weeks. Blood tests were assessed at baseline, 2, 6 and 8 weeks. 4 weeks after vaccination participants in the *Lactobacillus paracasei* 431 group had a significantly higher seroconversion rate compared to placebo (H1N1 p<0.05), H3N2 p<0.0001). A higher immune response rate was found in the treatment group compared to placebo for H3N2 (p<0.001). H1N1 and H3N2 showed increased ratio of geometric mean titres (probiotic/placebo group) after vaccination.	**Immune Function Efficacy Study** 6 weeks of treatment with *Lactobacillus paracasei* 431 increased the response rate to an influenza vaccine. The results indicate that probiotics may help improve immune system function after being challenged. *Lactobacillus paracasei* 431® was well tolerated.
Eskesen, D, Jespersen, L, Michelsen, B, Whorwell, PJ, Müller-Lissner, S & Morberg CM 2015, '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', Br J Nutr. Vol. 114, No. 10, pp.1638-46.	Randomised, double-blind, placebo-controlled study.	1248 healthy males and females, 18-70 years with low defecation frequency (2-4/week).	*Bifidobacterium animalis subsp. lactis* BB-12® 1 billion CFU, 10 billion CFU or placebo, daily for 4 weeks.	Bowel frequency was assessed daily from baseline (Day 0) until the end of the study (4 weeks). At the end of 4 weeks the change from baseline was 1.54 days/week for participants taking 1 billion CFU of *Bifidobacterium animalis subsp. lactis* BB-12®, 1.3 days/week for 10 billion CFU and 1.15 days per week for the placebo group. Probiotic treatment with *Bifidobacterium animalis subsp. lactis* BB-12® significantly improved bowel movement frequency compared to placebo (p=0.0065). This was significant at all weeks tested (p<0.05).	**Gastrointestinal Health Efficacy Study** *Bifidobacterium animalis subsp. lactis* BB-12® significantly improved defecation frequency. Improving bowel regularity in those with low frequency, supports bowel function and gastrointestinal health. *Bifidobacterium animalis subsp. lactis* BB-12® was well tolerated.