FemFlora Oral

In healthy women of reproductive age, the vaginal microbiome is predominantly composed of Lactobacillus species such as L. crispatus, gasseri, iners, jensenii, reuteri, rhamnosus, and fermentum.^[1] FemFlora Oral includes strains representative of this natural composition. While vaginal suppositories can directly modulate the vaginal microbiota, oral probiotics-particularly lactobacilli-also influence vaginal health via the gut-vaginal axis, reducing rectal-to-vaginal bacterial transfer and supporting immune regulation.^[2] Factors like diet, hormones, stress, and medications can disrupt this balance. FemFlora Oral stands out for its inclusion of L. crispatus, L. gasseri, and L. rhamnosus GG-strains not commonly found in standard multispecies probiotic formulations.

Scientific Rationale

A meta-analysis of 17 randomized controlled trials (RCTs), involving a total of 3,176 participants, found that probiotics alone were significantly more effective than placebo in treating bacterial vaginosis (BV), with a relative risk of 15.20, 95% CI 3.87–59.63).^[3] The analysis also showed that combining probiotics with antibiotic therapy was more effective than using antibiotics alone (relative risk 1.23, 95% CI 1.05–1.43). However, no significant differences in effectiveness were observed between different probiotic strains or between oral and vaginal formulations.^[4]

A meta-analysis reviewed 23 RCTs with a total of 2,212 participants and found that probiotics were effective in preventing recurrent vaginal candidiasis at 6 months, with a pooled relative risk of 0.36 (95% CI 0.21–0.63), indicating that women who used probiotics were 64% less likely to experience a recurrence of vaginal candidiasis compared to those without probiotics.^[5]

In a randomized, double-blind placebo controlled study involving 174 premenopausal women with a history of recurrent urinary tract infections (rUTIs),



participants were randomized to receive one of four interventions over a four-month period: placebo, vaginal probiotic (1 billion CFU), oral probiotic (112 billion CFU), or a combination of oral and vaginal probiotics.^[6] Participants were followed for 12 months to assess the incidence of symptomatic UTIs. At 4 months, both the vaginal- and combination-probiotic groups demonstrated a statistically significant reduction in the mean number of symptomatic UTI recurrences compared to placebo (p < 0.05). These groups also showed a longer time to first recurrence, suggesting sustained benefit beyond the treatment period.^[7]

Probiotic therapy—particularly via the vaginal route or in combination with oral administration—may offer a clinically meaningful strategy for preventing rUTIs in premenopausal women. Proposed mechanisms include:

- inhibition of uropathogen adhesion to uroepithelial cells;
- disruption of biofilm formation;
- suppression of bacterial invasion and proliferation;
- downregulation of virulence factor expression; and
- $\cdot \,$ modulation of host immune responses.

The first company in the industry to have invested in an ISO 17025–accredited laboratory to test for identity, potency, oxidation, disintegration, purity, and more.



Human Clinical Trials Chart

| Gynecological Concern | Probiotic Strains | Studies | Main Results | Ref. |
|--|--|------------------|--|-----------|
| Bacterial Vaginosis | L. crispatus L. jensenii L. gasseri L. rhamnosus High Dose $(\geq 1 \times 10^9 \text{ CFU})$ | 14 RCTs | More effective than placebo RR 15.2 (95% CI 3.87–59.65). More effective with antiobiotics than antiobiotics alone RR 1.23 (95% CI 1.05–1.43). No difference between probiotics alone versus antibiotics alone. | [8] |
| Vaginal candidiasis | L. gasseri L. crispatus | 23 RCTs | Primary outcome: compared to placebo, less recurrence RR 0.36 (95% CI 0.21–0.63) at 6 and 12 months. | [9] |
| Endometriosis | L. gasseri L. acidophilus L. plantarum L. fermentem | 2 RCTs | Between 8 and 12 weeks, compared to placebo, modest decrease in menstrual pain and improved quality of life. | [10],[11] |
| PCOS | L. rhamnosus L. reuteri L. acidophilus L. casei | 17 RCTs | Compared to placebo, decreased fasting plasma glucose (SMD, -1.35; 95% CI -2.22 to -0.49; $p = 0.002$), fasting insulin (SMD, -0.68; 95% CI -1.08 to -0.27; $p = 0.001$), homeostatic model of assessment for IR (SMD, -0.73; 95% CI -1.15 to -0.31; $p = 0.001$), triglycerides (SMD, -0.85; 95% CI -1.59 to -0.11; $p = 0.024$), total cholesterol (SMD, -1.09; 95% CI -1.98 to -0.21; $p = 0.015$), low-density lipoprotein cholesterol (SMD, -0.84; 95% CI -1.64 to -0.03; $p = 0.041$), very-low-density lipoprotein cholesterol (SMD, -0.44; 95% CI -0.70 to -0.18; $p = 0.001$), and increased quantitative insulin sensitivity check index (SMD, 2.00; 95% CI -0.79 to 3.22; $p = 0.001$). | [12] |
| Gestational diabetes | L. gasseri L. crispatus | 11 RCTs | Compared to placebo, significant improvement in FPG (MD = -2.33 , 95% CI -4.27 to -0.40 , $p = 0.02$), FSI (MD = -2.47 , 95% CI -3.82 to -1.12 , $p = 0.0003$), HOMA-IR (MD = -0.40 , 95% CI -0.74 to -0.06 , $p = 0.02$), and TC (MD = -6.59 , 95% CI -12.23 to -0.95 , $p = 0.02$). | [13] |
| Group B streptococcus | L. rhamnosus L. crispatus L. reuteri L. jensenii | 5 RCTs | GBS-positive culture rate was estimated at 31.9% (96 ₃₀₁) in the intervention group compared to 38.6% (109 ₂₈₂) in the control group (OR = 0.62, 95% CI 0.40 to 0.94, I ₂ 4.8%, <i>p</i> = 0.38). Probiotic administration in the third trimester was associated with a reduced GBS rectovaginal colonization at 35–37 weeks and a safe perinatal profile. | [14] |
| Lactational mastitis | L. salivarius L. gasseri | 6 RCTs | Oral probiotics during pregnancy can reduce the incidence of mastitis ($p < 0.0001$). After oral administration of probiotics, the counts of bacteria in the milk of healthy people and mastitis patients were both significantly reduced (in healthy $p < 0.00001$, in mastitis patients $p = 0.0001$). | [15] |
| Cervical intraepithelial neoplasia (CIN)-1 | L. rhamnosus L. reuteri | 1 pilot study | Probiotic users had a twice-as-high chance of clearance of cytological abnormalities (60 v. 31%, $p = 0.05$). HPV was cleared in 19% of control patients versus 29% of probiotic users ($p = 0.41$). | [16] |

References

- Wu, L.-Y., T.-H. Yang, Y.-C. Ou, and H. Lin. "The role of probiotics in women's health: An update narrative review." *Taiwanese Journal of Obstetrics and Gynecology*, Vol. 63, No. 1 (2024): 29–36.
- Lehtoranta, L., R. Ala-Jaakkola, A. Laitila, and J. Maukonen. "Healthy vaginal microbiota and influence of probiotics across the female life span." *Frontiers in Microbiology*, Vol. 13 (2022): 819958.
- Chen, R., R. Li, W. Qing, Y. Zhang, Z. Zhou, Y. Hou, Y. Shi, H. Zhou, and M. Chen. "Probiotics are a good choice for the treatment of bacterial vaginosis: A metaanalysis of randomized controlled trial." *Reproductive Health*, Vol. 19, No. 1 (2022): 137.
- 4. Ibid.
- 5. Cooke, G., C. Watson, L. Deckx, M. Pirotta, J. Smith, and M.L. van Driel "Treatment for recurrent vulvovaginal candidiasis (thrush)." *The Cochrane Database of Systematic Reviews*, Vol. 1, No. 1 (2022): CD009151.
- Gupta, V., P. Mastromarino, and R. Garg. "Effectiveness of prophylactic oral and/or vaginal probiotic supplementation in the prevention of recurrent urinary tract infections: a randomized, double-blind, placebo-controlled trial." *Clinical Infectious Diseases*, Vol. 78, No. 5 (2024): 1154–1161.
- 7. Ibid.
- 8. Chen et al, op. cit.
- 9. Cooke et al, op. cit.
- Itoh, M. Uchida, T. Sashihara, Z.S. Ji, J. Li, Q. Tang, S. Ni, L. Song, and S. Kaminogawa. "Lactobacillus gasseri OLL2809 is effective especially on the menstrual pain and dysmenorrhea in endometriosis patients: Randomized, double-blind, placebo-controlled study." Cytotechnology, Vol. 63, No. 2 (2011): 153–161.
- Khodaverdi, S., R. Mohammadbeigi, M. Khaledi, L. Mesdaghinia, F. Sharifzadeh, S. Nasiripour, and M. Gorginzadeh. "Beneficial effects of oral *Lactobacillus* on pain severity in women suffering from endometriosis: A pilot placebo-controlled randomized clinical trial." *International Journal of Fertilily* & Sterility, Vol. 13, No. 3 (2019): 178–183.
- Li, Y., Y. Tan, G. Xia, and J. Shuai. "Effects of probiotics, prebiotics, and synbiotics on polycystic ovary syndrome: A systematic review and metaanalysis." *Critical Reviews in Food Science and Nutrition*, Vol. 63, No. 4 (2023): 522–538.
- J. Mu, X. Guo, Y. Zhou, and G. Cao. "The effects of probiotics/synbiotics on glucose and lipid metabolism in women with gestational diabetes mellitus: A meta-analysis of randomized controlled trials." *Nutrients*, Vol. 15, No. 6 (2023): 1375.
- Menichini, D., G. Chiossi, F. Monari, F. De Seta, and F. Facchinetti. "Supplementation of probiotics in pregnant women targeting group B Streptococcus colonization: A systematic review and meta-analysis." *Nutrients*, Vol. 14, No. 21 (2022): 4520.
- Yu, Q., C. Xu, M. Wang, J. Zhu, L. Yu, Z. Yang, S. Liu, and X. Gao. "The preventive and therapeutic effects of probiotics on mastitis: a systematic review and meta-analysis." *PLoS One*, Vol. 17, No. 9 (2022): e0274467.
- Verhoeven, V., N. Renard, A. Makar, P. Van Royen, J.P. Bogers, F. Lardon, M. Peeters, and M. Baay. "Probiotics enhance the clearance of human papillomavirus-related cervical lesions: A prospective controlled pilot study." *European Journal of Cancer Prevention*, Vol. 22, No. 1 (2013): 46–51.

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| Lactobacillus crispatus UB1947 750 million CFU |
| Lactobacillus gasseri UB9507 750 million CFU |
| Lactobacillus johnsonii UB2214 750 million CFU |
| Lacticaseibacillus paracasei UB8017 600 million CFU |
| Lactobacillus helveticus UB5772 500 million CFU |
| <i>Limosilactobacillus reuteri</i> UB4772 500 million CFU |
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