

Flora SAP

Science-based suppository probiotic for vaginal health

Genitourinary infections affect more than 1 billion women worldwide every year, and are the most common reason a woman will see a gynecologist.^[1] These infections can be bacterial in nature (bacterial vaginosis) or fungal in nature (vulvovaginal candidiasis). The types of bacteria in the vaginal canal will fluctuate based on a variety of factors, including hormone levels, diet, sexual contact, and douching; however, the basic composition is *Lactobacilli*-dominant in healthy females.^[1] It is the depletion of these healthy organisms that can leave a woman prone to urinary and vaginal infections.^[1] There are probiotic bacteria that can help in modulating the immune system and displacing pathogens that can cause these infections.^[2] A healthy vaginal canal should be colonized by *Lactobacilli* as the dominant bacterial species. *Lactobacilli* produce H₂O₂, which helps maintain a vaginal pH close to 4.0, which is essential for vaginal health.^[3] Maintenance of a vaginal pH around 4.0 decreases a woman's risk of developing vaginosis.^[3]

ACTIVE INGREDIENTS

Each vaginal capsule contains:

<i>Lacticaseibacillus rhamnosus</i> HA-111	1 billion CFU
<i>Limosilactobacillus fermentum</i> HA-179	1 billion CFU
<i>Limosilactobacillus reuteri</i> HA-188	0.5 billion CFU

Other ingredients: Magnesium stearate, silicon dioxide, lactose, skim milk powder, sucrose, and ascorbic acid in a capsule composed of vegetable carbohydrate gum and purified water.

This product is non-GMO and vegetarian friendly.

Contains no: Gluten, wheat, eggs, yeast, citrus, preservatives, artificial flavour or colour, or starch.

Contains 10 capsules per bottle, plus an applicator.

Keep refrigerated.

DIRECTIONS FOR USE

Adult women: Use 1 capsule per day. Insert one capsule intravaginally daily before bed for 10 days or as directed by your healthcare practitioner. If you are using vaginally inserted antibiotics, use this product at least 2–3 hours before or after taking them.

INDICATIONS

Flora SAP may help prevent:

- And treat recurrent vulvovaginal candidiasis and bacterial vaginosis.
- Growth of Group-B streptococci (GBS) during pregnancy.
- Spontaneous preterm delivery associated with intrauterine infection.
- Recurrent urinary tract infections.

SAFETY

Lactobacilli are considered to be safe because they are components of the commensal human flora and due to the fact that they have been used for a long time in food industry and in douches, even by pregnant women, without harmful effects.^[3] Can be taken by women who are allergic to lactose, as the capsule does not enter the gastrointestinal tract.

PURITY, CLEANLINESS, AND STABILITY

All ingredients listed for all **Flora SAP** lot numbers have been tested by a third-party laboratory for identity, potency, and purity.



Scientific Advisory Panel (SAP):
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Vaginal infections — including bacterial vaginosis and vulvovaginal candidiasis — can cause symptoms including vaginal itching, discharge and discomfort. In recent years, there has been more research looking at the strains of bacteria that commonly colonize the vaginal canal and their ability to help prevent and eliminate other harmful bacteria or yeast from the region. The types of microbes in the vaginal canal will fluctuate but the basic composition is that *Lactobacilli* are the dominant species in healthy females.[1] *Lactobacillus rhamnosus* was proven to be effective at helping to restore and maintain a healthy vaginal canal.[1] In addition to *L. rhamnosus*, a selective review of probiotic applications in urogenital treatment have found *L. fermentum* to be useful as a biosurfactant, which prevents the adhesion of various uropathogens such as *Klebsiella pneumoniae*, and *Enterococcus faecalis*, as well as genital pathogens such as *Candida albicans* [2]. The mechanism by which the bacteria work is not completely understood, but the possibilities include a reduction in pathogen ascension from the anus, modulation of host immunity, as well as being able to interfere with the colonization of pathogens [1].

URINARY TRACT INFECTIONS

Urinary tract infections (UTIs) are extremely common in women and depletion of vaginal *Lactobacilli* is associated with an increased risk of UTI [3]. In a double-blind, placebo-controlled study, researchers randomized 100 women with a history of recurrent UTI who had received antimicrobials into either the treatment or control group [3]. Women in the treatment group used a vaginal suppository probiotic daily for 5 days then once weekly for 10 weeks. 15% of women in the treatment group had a recurrence of their UTI compared to 27% of women in the control group [3]. Researchers concluded that using a vaginal suppository probiotic after treatment for cystitis is associated with a reduced risk for a recurrent UTI [3].

BACTERIAL VAGINOSIS

The link between probiotic supplementation as an effective treatment for bacterial vaginosis has been well established. A meta-analysis of 1304 patients from 12 clinical trials showed that probiotic supplementation significantly improved the number of patients cured of bacterial vaginosis [4]. A study looking at the effect of *L. rhamnosus* and *L. reuteri* on patients with bacterial vaginosis compared the treatment with vaginal application of 0.75% metronidazole gel (n=40). Administration of two capsules containing 1x10⁹ CFU of each bacterial strain for 5 days showed improved symptoms of bacterial vaginosis compared to metronidazole treatment in subsequent follow ups [5]. These results were confirmed by the same study group where treatment with *L. rhamnosus* and *L. reuteri* 1x10⁹CFU each for 30 days along with oral metronidazole regimen showed higher rate of recovery compared to treatment with metronidazole alone [6]. The therapeutic potential of *L. reuteri* has been examined in another clinical study where administration of 2.5x10⁹ CFU each of *L. rhamnosus* and *L. reuteri* for 14 days showed an improvement in vaginal flora (n=72) [7]. In another study, researchers looked at the use of long-term vaginal administration of *L. rhamnosus* for the prevention of recurrence of bacterial vaginosis after treatment with metronidazole [8]. 49 women were randomized into 2 groups; both were treated with metronidazole for 1 week, but group 2 followed up the treatment with a weekly vaginal application of 40 mg of *L. rhamnosus* for 6 months. At the 6month follow-up, 96% of women in group 2 had a balanced vaginal ecosystem; follow-up testing at 12 months revealed no statistically significant difference in the vaginal ecosystem in this group from the 6month follow-up [8]. Group 1, however, did have a significant number of women with abnormal flora over time [8]. The study concluded that vaginal administration of *L. rhamnosus* reduces recurrence of bacterial vaginosis and stabilizes the vaginal ecosystem [8]. These results have been further substantiated by a meta-analysis evaluating the effect of probiotics on bacterial vaginosis. The analysis showed that administration of as little as 10 CFU per day for 2 months of *L. rhamnosus* and *L. fermentum* replaces unhealthy vaginal microbiota, lowers pH and promotes production of antimicrobial substances like hydrogen peroxide in the vaginal tract, thereby showing better efficacy compared to oral probiotic administration [9]. Vaginal administration of probiotics has in some cases proven to be more effective than administration of metronidazole in controlling bacterial vaginosis. However, administration of strains such as *L. rhamnosus* following metronidazole therapy may in fact enhance the therapeutic efficacy of metronidazole and avoid the recurrence of bacterial vaginosis. This was demonstrated in a study where *L. rhamnosus* was administered following 500mg twice daily of week-long metronidazole therapy for 2 months, in 84 patients. A follow up study confirmed the findings and hence administration of *L. rhamnosus* appears to reduce recurrence of bacterial vaginosis [10, 11].

VAGINAL CANDIDIASIS

Vaginal candidiasis is most frequently caused by the species *Candida albicans*. In a study looking at *L. rhamnosus*, researchers found that it has the ability to prevent adherence of *Candida albicans* and decrease the pathogen cell division rate [12]. In a separate review article, researchers found studies to support the use of *L. rhamnosus* and *L. fermentum* for the prevention of colonization and infection of the vagina by *Candida albicans*. [13] *L. reuteri* alone or in combination with *L. rhamnosus* has proven to be efficacious in suppressing *Candida albicans* growth on the vaginal cells [14]. In a trial conducted with 55 women who tested positive for vaginal candidiasis, administration of *L. rhamnosus* and *L. reuteri* for 4 weeks in conjunction with fluconazole treatment showed lower vaginal discharge and presence of yeast compared with fluconazole treatment without probiotic [15].

INTRAUTERINE INFECTIONS

In a study by Krauss-Silva et al. (2010), researchers found that in a vaginal canal that is colonized by *Lactobacilli*, a higher amount of H₂O₂ is produced. The quantity of lactic acid and H₂O₂ assists in maintaining a pH close to 4.0 and is therefore protective against pathogenic bacteria and yeast [16]. Intrauterine inflammation appears to be the stimuli that may contribute to the onset of preterm labor [17]. To examine the cause of inflammation, researchers analyzed dried blood spots from 527 newborns delivered via caesarean section in 23–27 weeks gestation [17]. It was found that bacterial vaginosis organisms were associated with the proinflammatory pattern, whereas *Lactobacillus* was associated with a low inflammatory response [17]. This study indicated that the microorganisms that colonize the placenta can provoke a distinctive inflammatory response and that *Lactobacillus* may suppress this response [17].

GROUP-B STREPTOCOCCI IN PREGNANCY

Another study examined the effect of 10 clinical isolates of *Lactobacilli* on the growth of GBS [18]. They found seven of the isolates that had inhibitory effects on the growth of GBS were *L. rhamnosus* [18]. Researchers postulated that the administration of *Lactobacilli* strains may be a safe and less expensive alternative for the prevention of neonatal GBS infections [18].

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