

Science Review: Lactobacilli strains and their effect on women's urogenital health

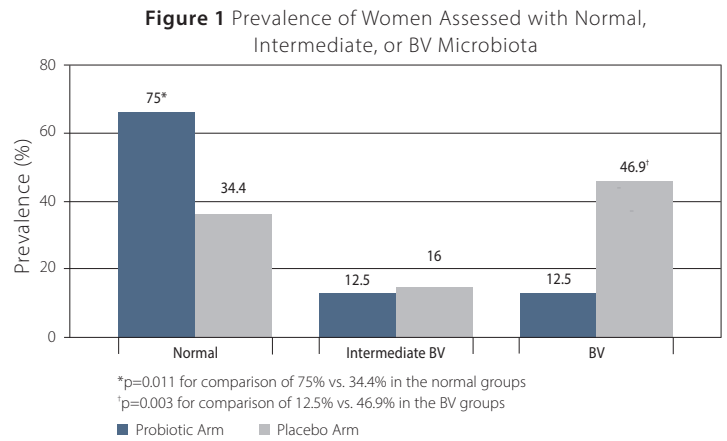
Lactobacillus rhamnosus GR-1® and *Lactobacillus reuteri* RC-14® are probiotic strains with clinically demonstrated effects on women's urogenital health. The combination has shown positive benefits in women with bacterial vaginosis (BV), urinary tract infections (UTI), and vulvovaginal candidiasis (yeast).¹

Research Highlights

- ✓ In a study of 64 women ages 16-51 years diagnosed with BV, a 75% resolution rate was seen in the probiotic group with antibiotic vs. 50% in the antibiotic group with placebo.²
- ✓ During a six-week study of 544 adult women ages 18-58 with BV, a restitution of balanced vaginal microbiota was seen in 61.5% of the probiotic arm, compared with 26.9% in the placebo arm.³
- ✓ In a study of 252 postmenopausal women with recurrent UTIs, it was determined that development of antibiotic resistance is considerably lower with the use of lactobacilli and that it may be an acceptable alternative for prevention of UTIs, especially in women who dislike taking antibiotics.⁴
- ✓ The same study concluded that the potential exists for *L. rhamnosus* GR-1 and *L. reuteri* RC-14 to restore a normal urogenital microbiota and thereby reduce the risk of UTI, bacterial vaginosis, and yeast vaginitis.⁴
- ✓ A randomized study of 55 women ages 16-46 years demonstrated significantly lower presence of *Candida* (10.3%) compared with the placebo group (38.5%).⁵

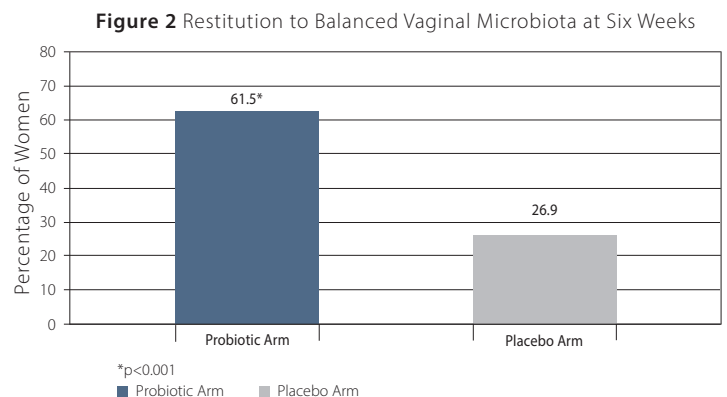
L. rhamnosus GR-1 and *L. reuteri* RC-14 with Tinidazole in women diagnosed with BV

In a randomized study of 64 women ages 16 to 51 years diagnosed with BV (confirmed by the Amsel criteria and the Nugent scoring), the participants were administered a single 2 g dose of Tinidazole and GR-1/RC-14 (1 billion CFU each), or placebo (two capsules) from day one to 28. At the study endpoint, a significantly lower prevalence of BV (12.5%) was seen in the probiotic group, compared with the placebo group (46.9%). Additionally, a 75% resolution rate was seen in the probiotic group compared with 34.4% in the placebo group.² (Figure 1)



Efficacy of oral *L. rhamnosus* GR-1 and *L. reuteri* RC-14 in otherwise healthy women diagnosed with BV

During a multi-center, six-week study of 544 adult women, ages 18 to 58 with vaginal infection, participants received 1 billion CFU each GR-1/RC-14 or two placebo capsules daily. At the study conclusion, 61.5% in the probiotic arm experienced restitution of balanced vaginal microbiota, compared with 26.9% in the placebo arm.³ Additionally, at six weeks post-trial, normal vaginal microbiota were still present in 51.1% in the probiotic arm, but only 20.8% in the placebo arm.² (Figure 2)



L. rhamnosus GR-1® and *L. reuteri* RC-14® vs. Trimethoprim-sulfamethoxazole for prevention of UTI

GR-1/RC-14 and Trimethoprim-sulfamethoxazole (TMP-SMX) were administered in a double-blind, double-dummy, non-inferiority study of 252 postmenopausal women with recurrent UTIs. The women were randomized to one capsule containing 1 billion CFU GR-1/RC-14 twice daily, plus one placebo tablet at night, or one placebo capsule twice daily, plus one tablet containing 480 mg TMP-SMX at night. While a large reduction of UTIs was seen in both groups after a 12-month duration with three months followup (Figure 3), the group receiving GR-1/RC-14 treatment had a lower prevalence of *E. coli* harboring antibiotic-resistant genes compared to the antibiotic group.⁴ (Figure 4)

Figure 3 *E. coli* Resistance to TMP-SMX in Urine From Women with Asymptomatic Bacteriuria

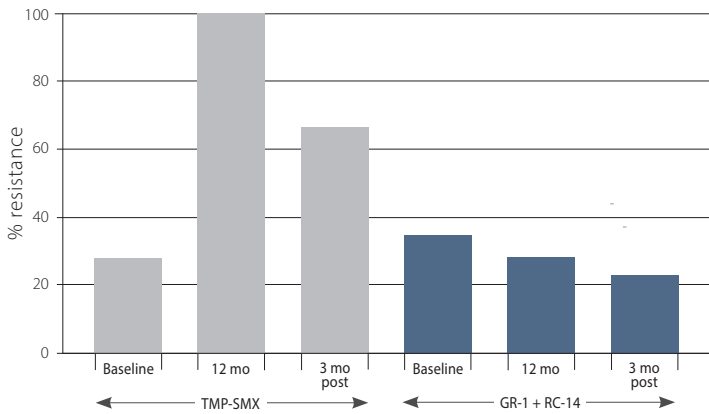
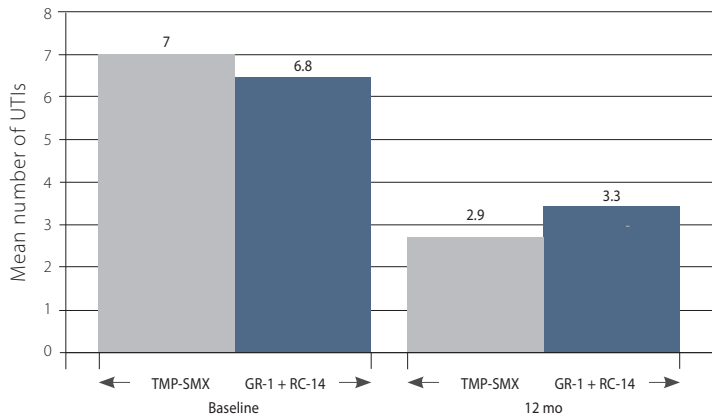


Figure 4 Recurrence of UTIs

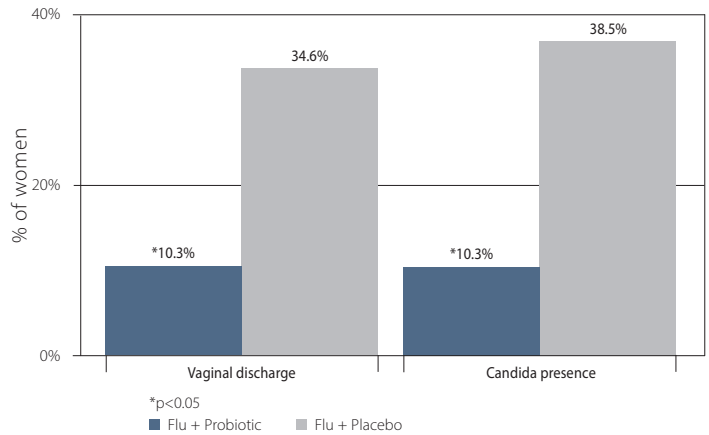


L. rhamnosus GR-1 and *L. reuteri* RC-14 and vulvovaginal candidiasis

In a randomized clinical study of 55 women, ages 16 to 46 with diagnosed vulvovaginal candidiasis (VVC), either a single 150 mg dose of Fluconazole was administered with GR-1/RC-14 (1 billion CFU each), or placebo two capsules daily from day one through 28. At conclusion of the study, the probiotic group showed significantly less vaginal discharge (10.3%)

compared with the placebo group (34.6%). The probiotic group also showed significantly lower presence of *Candida* (10.3%) compared with the placebo group (38.5%).⁵ (Figure 5)

Figure 5 VVC Status of the Women After Treatment



Mechanism of Action (MOA)

In vitro studies demonstrate that *L. rhamnosus* GR-1 and *L. reuteri* RC-14 have an ability to interfere with the growth of bacterial and fungal pathogens, adhesion to uroepithelial cells, and adhesion to surfaces made of the same substrates used to create urinary devices which are known to increase the risk of UTI.⁶ Additionally, studies have shown *L. rhamnosus* GR-1 to reduce colonization of the vagina by Gram-negative pathogens in humans,⁷ while *L. reuteri* RC-14 produces biosurfactants that reduce surface tension and adhesion by pathogenic bacteria and *Candida albicans*.⁸

Conclusion

The probiotic combination of *L. rhamnosus* GR-1 and *L. reuteri* RC-14 is safe and effective to use both on its own and with conventional therapeutic options for urogenital health. This includes demonstrated effectiveness in the maintenance of healthy vaginal microbiota by increasing the number of beneficial lactobacilli, as well as a lowered risk of BV and augmentation of antibiotic treatment efficacy against BV and yeast vaginitis. In addition, long-term use of the probiotic may help reduce the occurrence of antibiotic-resistant *E. coli* in the urine.

References:

- Reid G. The scientific basis for probiotic strains of Lactobacillus. *Appl Environ Microbiol.* 1999;65:3763-766.
- Martinez RC, et al. *Can J Microbiol.* 2009;55(2):133-138.
- Vujan G, et al. *Eur J Obstet Gynecol Reprod Biol.* 2013;168:75-79.
- Beerepoot M, et al. Lactobacilli vs. Antibiotics to Prevent Urinary Tract Infections: A Randomized, Double-Blind, Noninferiority Trial in Postmenopausal Women. *Arch Intern Med.* 2012 May 14;172(9):704-12. doi:10.1001/archinternmed.2012.777.
- Martinez RC, et al. Improved treatment of vulvovaginal candidiasis with fluconazole plus probiotic Lactobacillus rhamnosus GR-1 and Lactobacillus reuteri RC-14. *Lett Appl Microbiol.* 2009 Mar;48(3):269-74. doi: 10.1111/j.1472-765X.2008.02477.x. *Epob* 2009 Feb 2.
- Reid G. The development of probiotics for women's health. *Can J Microbiol.* 63:269-277 (2017).
- Reid G, Bruce A, et al. Persistence of *Lactobacillus fermentum* RC-14 and *Lactobacillus rhamnosus* GR-1 but Not *L. rhamnosus* GG in the Human Vagina as Demonstrated by Randomly Amplified Polymorphic DNA. *Clin Diagn Lab Immunol.* 2002 Jan; 9(1): 92-96.
- Velraeds M, van de Belt-Gritter B, et al. 1998. Interference in initial adhesion of uropathogenic bacteria and yeasts to silicone rubber by a *Lactobacillus acidophilus* biosurfactant. *J. Med. Microbiol.* 47:1081-1085.