

# Exploring the Efficacy of ZB-06 Vaginal Biofilm as a Novel Treatment for Recurrent Bacterial Vaginosis

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**ABSTRACT**

The purpose of this research was to investigate the efficacy of ZB-06 vaginal biofilm as a novel treatment for recurrent bacterial vaginosis (BV). BV is a prevalent vaginal infection that primarily affects women of reproductive age and is linked to adverse health outcomes. Biofilm production allows bacteria to cling to the vaginal epithelium, making antibiotics harder to penetrate and treat the illness efficiently. ZB-06 is a vaginal biofilm inhibitor that may dissolve the biofilm generated by the bacteria causing BV, enhancing antibiotic therapy efficacy and lowering the risk of recurrence. The current literature on BV, biofilm formation, and the possible function of ZB-06 as a therapy option for recurrent BV is reviewed in this article. More research is needed to determine ZB-06's safety and efficacy.

**KEYWORDS:** *Bacterial vaginosis, efficacy, novel treatment, polymicrobial biofilm, recurrent bacterial vaginosis, vaginal biofilm, vaginal microbiome, ZB-06*

**B**acterial vaginosis (BV), also known as BV, is an infection caused by an overgrowth of the vaginal microbiota, which causes an alteration in the vaginal flora that moves away from *Lactobacillus* species and toward more varied species of bacteria, particularly facultative anaerobes. Most *Lactobacillus* species act as important host-defense mechanisms against BV that inhibit the overgrowth of other microorganisms. Imbalances in the vaginal microbiota can cause BV, with symptoms including off-white, grayish vaginal discharge and malodor in over 50% of affected females.<sup>[1]</sup> The BV prevalence rates vary among different races and ethnicities, with higher rates in East and South African women,<sup>[2]</sup> followed by the US<sup>[3]</sup> and Australian women.<sup>[4]</sup> Risk factors for BV include smoking, multiple sex partners, douching, and Africans or Hispanic ethnicity.<sup>[5]</sup>

Recurrent BV is defined as two or more clinically diagnosed episodes in 12 months, with recurrence rates as high as 60%.<sup>[6]</sup> Causes of recurrent infection include residual infection and antimicrobial resistance. A biofilm formed by bacteria causing BV facilitates resistance to antimicrobial agents. Factors contributing to BV recurrence include the inability to recolonize the normal

flora of the vagina with lactobacilli, immune factors/ host genetics, and sexual behaviors.<sup>[7]</sup> BV increases the risk of gynecological and obstetric problems, including intrauterine fetal death, premature birth, perinatal mortality, miscarriages, chorioamnionitis, preterm rupture of the membranes, and postpartum infections postabortion. In nonpregnant women, it causes cervicitis, endometritis, pelvic inflammatory disease, salpingitis, urinary tract infections, tubal infertility, and cervical cancer. BV increases the risk of acquiring HIV, human papillomavirus, and herpes simplex virus.<sup>[7]</sup>

The BV treatment aims to stop the proliferation of bacteria and restore the vaginal flora. The treatment options for BV include antibiotics such as oral metronidazole, clindamycin, nitroimidazoles, and *Lactobacillus* probiotics. The World Health Organization recommends oral metronidazole as the first line of treatment. However, antibiotics can disrupt the normal vaginal flora, and *Lactobacillus* probiotics have been proposed as an alternate therapy for vaginal flora

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stabilization. Women should be urged to abstain from sexual activity or use condoms regularly and properly during the BV treatment regimen to avoid reinfection. It is important to note that there is evidence of a disulfiram-like interaction between alcohol and metronidazole, which could lead to unpleasant side effects. Therefore, women undergoing metronidazole treatment should be advised to refrain from alcohol consumption.<sup>[7]</sup>

BV is a result of the disruption of normal vaginal flora and an overgrowth of harmful bacteria, which can be caused by biofilms formed by bacteria like *Gardnerella vaginalis*, which enable bacteria to attach to the vaginal epithelium, making it difficult for antibiotics to penetrate and effectively treat the infection.<sup>[8]</sup> Vaginally inserted devices, such as tampons and intrauterine devices, despite being cost-effective and safe, have the lowest efficacy rates and have been found to promote the formation of biofilms in the vaginal environment.<sup>[9,10]</sup> Therefore, understanding the role of biofilms in vaginal infections is crucial to develop effective treatment options. One potential treatment being investigated is the use of a vaginal biofilm inhibitor, ZB-06, to disrupt the biofilm formed by the bacteria causing BV. By disrupting the biofilm, ZB-06 may improve the effectiveness of antibiotic treatments and reduce the risk of recurrence.

ZB-06 is a novel vaginal film incorporating an engineered human contraceptive antibody (HC4-N) that is safe and highly effective, with no reported adverse events or colposcopic findings in the study.<sup>[11]</sup> This contrasts with other nonhormonal contraceptives like nonoxynol-9, which have been found to cause inflammation of the vaginal mucosa and alter the vaginal microbiota, increasing the risk of HIV-1 infection.<sup>[11]</sup> The highly effective treatment of BV includes the use of probiotics, indicating that restoring and maintaining healthy vaginal flora are essential for long-term female health. Future trials should explore the microbicidal potential of ZB-06 contraceptive film, including the addition of *Lactobacillus* strains or specific lactic acid isoforms to effectively treat and limit the spread of BV during intercourse, as this antimicrobial compound is the primary defense mechanism of *Lactobacillus* strains against *G. vaginalis* and sexually transmitted infection (STIs).<sup>[12]</sup> If successful, ZB-06 could provide a new and effective treatment option for women with recurrent BV, reducing the associated health risks and improving the quality of life. The incorporation of MB66 film with antiviral activity against HIV-1 and HSV 1 and 2 into ZB-06 film could help protect against HIV with its contraceptive capability.<sup>[8]</sup> Future studies and

trials should explore this possibility to help reduce the susceptibility to HIV infection associated with vaginal dysbiosis in BV.

In conclusion, the development of ZB-06, a novel on-demand, nonsurfactant, nonhormonal contraceptive film, is safe and highly effective, with no adverse events compared to other on-demand, nonhormonal contraceptives. Furthermore, the use of IUDs has been linked to an increased risk of BV, highlighting the need for safe and effective noninvasive contraceptive options. Long-term studies on diverse populations with extended follow-ups are required to gauge the effectiveness of this contraceptive film and explore its broader potential, including the potential for BV treatment. The addition of *Lactobacillus* strains and specific lactic acid isoforms to the contraceptive film could be explored to effectively treat and limit the spread of BV during intercourse. In addition, the incorporation of antiviral activity against HIV-1 and HSV 1 and 2 into ZB-06 film could provide an added layer of protection against STIs. Overall, the development of ZB-06 has the potential to offer a safe and reliable contraceptive option for women while also addressing important issues related to vaginal health.

#### Ethical approval

This article did not involve patients; therefore, no ethical approval was required.

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#### Conflicts of interest

There are no conflicts of interest.

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