Real-World Evidence on the Safe and Effective Use of a Medical Device Based on Substances for the Treatment of Vulvovaginitis (VVC) and Vaginosis (BV)

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Medical device: Dermoxen Bactor vaginal ovules

Abstract

Background/Objectives: Vulvovaginal infections, particularly Candida vulvovaginitis (VVC) and bacterial vaginosis (BV), most commonly associated with Gardnerella vaginalis, are highly prevalent gynecological conditions that significantly affect women's quality of life. Symptoms such as pruritus, burning, abnormal discharge, unpleasant odor, and discomfort often lead to recurrent medical consultations and repeated treatments. Both conditions are characterized by an imbalance of the vaginal microbiota: VVC results from the overgrowth of Candida species, while BV is associated with a reduction in protective lactobacilli and the proliferation of anaerobic bacteria, including Gardnerella vaginalis. The multifactorial pathogenesis and high recurrence rates represent a clinical challenge, particularly in women with recurrent or mixed infections.

Aim: This cross-sectional research collected real-world data (RWD) on the effectiveness, safety, and usage patterns of a vaginal medical device indicated for the management of vulvovaginal infections, including VVC and BV.

Methods: The device, based on non-pharmacological active substances with barrier-forming, pH-modulating, and mucosa-supporting properties, is designed to help restore the physiological vaginal microenvironment and relieve local symptoms. Surveys were conducted in different countries with 53 participants, including 35 patients, 2 pharmacists, and 16 physicians using a questionnaire that allows voluntary participants to share their experiences with the device. The validated platform was designed to comply with post-market surveillance requirements of EU Regulation 2017/745. Statistical analyses included descriptive evaluations of responses to gauge overall effectiveness and safety of the device.

Results: These findings are consistent with the results obtained from the additional post-market surveys, in which more than 85% of patients reported positive outcomes regarding efficacy, symptom improvement, quality of life, and safety following the use of Dermoxen Bactor vaginal ovules. Furthermore, healthcare professionals confirmed high effectiveness across the main etiological causes of vaginal infections, with successful treatment rates ranging from approximately 84% for *Gardnerella vaginalis* infections to 98% for *Candida* infections. Overall, the available evidence supports a favorable benefit–risk profile for the medical device, characterized by high user satisfaction, clinically relevant symptom improvement, and an excellent safety profile, with no adverse events reported during the surveys.

Conclusions: The results provide real-world evidence supporting the role of such medical devices as a safe and well-tolerated complementary option in the integrated management of Candida vulvovaginitis and Gardnerella-related bacterial vaginosis. Continuous RWD collection is essential, as it offers insights into real-world practice and ensures ongoing confirmation of the product's safety and effectiveness. Ultimately, this will advance vaginal infections patient care by integrating real-world evidence into clinical management.

1. Introduction

Vaginal infections are among the most common gynecological conditions in women of reproductive age and represent a significant cause of medical consultations worldwide [1,2]. In particular, vulvovaginal candidiasis (VVC) and bacterial vaginosis (BV), most frequently associated with *Candida* spp. and *Gardnerella vaginalis*, respectively, account for the majority of symptomatic vaginal disorders [1–3]. These conditions are characterized by alterations of the vaginal microenvironment and present symptoms such as abnormal discharge, itching, burning, irritation, unpleasant odor, and discomfort during urination or sexual intercourse [2,4].

Vulvovaginal candidiasis is primarily caused by the overgrowth of *Candida albicans*, although non-*albicans* species are increasingly reported [3,5]. It is estimated that up to 75% of women experience at least one episode of VVC during their lifetime, with 5–8% developing recurrent forms [3,6]. Bacterial vaginosis, on the other hand, results from dysbiosis characterized by a reduction in protective lactobacilli and an overgrowth of anaerobic bacteria, including *Gardnerella vaginalis* [2,7]. BV is the most prevalent cause of vaginal discharge in women of childbearing age and is associated with an increased risk of pelvic inflammatory disease, sexually transmitted infections, and adverse obstetric outcomes [2,7,8].

Although not typically life-threatening, these infections exert a considerable burden on affected individuals. Recurrent or persistent symptoms can significantly impair daily activities, intimate relationships, and emotional well-being [9,10]. Women frequently report embarrassment, reduced self-esteem, sexual dysfunction, and anxiety related to odor or discharge [9]. Chronic or recurrent vulvovaginal conditions are also associated with decreased work productivity and increased healthcare utilization [10]. Overall, the impact on quality of life can be substantial, particularly in women experiencing repeated episodes or inadequate symptom control [9,10].

Current treatment strategies for VVC and BV mainly rely on antifungal and antibiotic agents, administered either topically or systemically [2,3,8]. While generally effective in the short term, these pharmacological treatments may be associated with recurrence, antimicrobial resistance, alteration of the microbiota, and local or systemic side effects [3,8,12]. In addition, repeated courses of antimicrobials may further disrupt the vaginal ecosystem, potentially contributing to chronicity or recurrent infections [7,12]. As a result, many women report dissatisfaction with available therapeutic options, highlighting the need for alternative or adjunctive approaches that focus on restoring vaginal homeostasis rather than solely targeting pathogens [9,10].

The pathophysiology of vaginal infections involves complex and interconnected factors, including alterations in vaginal pH, disruption of the epithelial barrier, hormonal fluctuations, antibiotic use, sexual activity, and immune responses [2,4,7]. In healthy conditions, the vaginal ecosystem is dominated by lactobacilli, which maintains an acidic pH and contribute to the integrity of the mucosal barrier [7,11]. When this balance is disrupted, pathogens such as *Candida* spp. or anaerobic bacteria may proliferate, leading to inflammation, mucosal irritation, and symptomatic infection [2,3]. Restoring the physiological vaginal microenvironment and supporting mucosal defense mechanisms are therefore key therapeutic goals [7,11].

In this context, Dermoxen Bactor vaginal ovules, a Class IIa Medical Device, developed in accordance with the Medical Devices Directive (MDD), may represent an innovative non-pharmacological option for the management of vulvovaginal candidiasis and bacterial vaginosis. The device, based on non-pharmacological

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active substances with barrier-forming, pH-modulating, and mucosa-supporting properties, is designed to help restore the physiological vaginal microenvironment and relieve local symptoms. By forming a protective barrier on the vaginal mucosa, the device may help shield the epithelium from irritative stimuli and microbial overgrowth. Its pH-modulating action supports the re-establishment of an acidic environment favorable to lactobacilli, while the mucosa-supporting properties contribute to maintaining epithelial integrity and physiological defense mechanisms [7,11].

Through this multimodal, non-antibiotic approach, the device aims not only to alleviate symptoms such as itching, burning, discharge, and discomfort, but also to promote the restoration of vaginal homeostasis, potentially reducing the risk of recurrence. By addressing key pathophysiological mechanisms underlying vaginal dysbiosis, this strategy may offer a valuable addition to current management options, with a focus on safety, tolerability, and long-term support of vaginal health.

2. Materials and Methods

2.1 Product

Dermoxen Bactor vaginal ovules is a Class IIa Medical Device based on substances, developed in accordance with the Medical Devices Directive (MDD) (Ekuberg Pharma, Carpignano Salentino – Italy). Dermoxen Bactor vaginal ovules contains no antibiotic substances or estrogens. The formulation contains Hyaluronic acid (sodium salt), Vitamin E, Lipophilic extract of Aloe vera, Chlorhexidine dihydrochloride, Lactic acid, Semisynthetic glycerides, Propolis extract. The product is indicated for the prevention and treatment of vaginal infections, including vulvovaginitis (VVC) and bacterial vaginosis (BV), characterized by abnormal discharge, itching, burning, irritation, unpleasant odor, and discomfort during urination or sexual intercourse [2,4]. Patients are advised to take 1 ovule a day for 7 days, preferably in the evening before going to bed.

2.2 Research Design

Observational surveys involving patients, physicians and pharmacists were conducted to evaluate the effectiveness and safety profile of Dermoxen Bactor vaginal ovules.

This evaluation is required by the new EU Medical Device Regulation (EU) 2017/745, which has established updated criteria for the authorization, classification, and ongoing post-market surveillance of medical devices, focusing on their safety and performance. Under this regulation, manufacturers are now obligated to continuously gather clinical data on devices already on the market. This data collection may occur through clinical investigations, the use of questionnaires, or the collection of RWD, which is increasingly recognized as valuable evidence in assessing device effectiveness and safety [13, 14].

Aiming to gather real-world evidence (RWE), clinical data was collected through a questionnaire that enabled voluntary participants (patients, pharmacists and physicians) to share their own experiences regarding the use of the device. Data collection was obtained in the following countries: Italy, Serbia, Poland, Malaysia and Belarus, from February 2026 to March 2026. The digital questionnaires were specifically designed for the surveyed cohorts and encompassed various aspects, including effectiveness, symptoms relief, quality of life, general satisfaction and side effects. Answers regarding QoL and symptoms improvement, safety/tolerability and effectiveness were assessed using a single-item question with a 4-point Likert scale: “**Yes”**, “**No**”, “**Sometimes**”, “**Not assessable”**. The survey collected qualitative data, summarized

as percentage distributions of responses. Patients were requested to provide feedback on their experiences with the device, while physicians and pharmacists were asked about their professional experience with device use. Device use was confirmed by entering the batch number *(L.50421 EXP.2028/07)* and unique code from the device box at the start of the online questionnaire. Pharmacists and physicians were exempt from this step, as they did not need to verify product use. This method enabled the indirect verification of data reported by patients.

2.3 Statistical Analysis

A descriptive analysis was conducted for each question, and the findings were reported as percentages. For both single-answer and multiple-answer questions, percentages and absolute numbers indicate the proportion of respondents who chose each answer option, unless specified otherwise. Data was collected and analyzed by Ekuberg Pharma employees.

2.4 Institutional Review Board Statement

In accordance with the relevant regulations, ethical approval was not sought since the data were retrieved from voluntary online surveys. Nevertheless, ethical considerations were made in alignment with the principles for research on human subjects, as outlined in the Declaration of Helsinki.

3. Results

The following questionnaires were collected for the study (*Figure 1*).

Fig.1 *Description of the number and category of the participants at the study.*

3.1 Patients

We analyzed a total of **35** questionnaires collected from patients that use Dermoxen Bactor vaginal ovules.

The study population, consisting of women with vaginal infections, had a broad age distribution. The most represented age group was between 14 and 30, which accounted for 40% of the total sample. This was followed by the 31–40 age group, accounting for 28.6% of participants. Women between the ages of 41 and 50 represented 17.1% of the sample, while lower percentages were observed in the 51–60 age groups (8.6%) and those over 61 (5.7%). Overall, over two-thirds of participants (68.6%) were under 40, highlighting a greater representation of younger age groups in the study population (*Figure 1*).

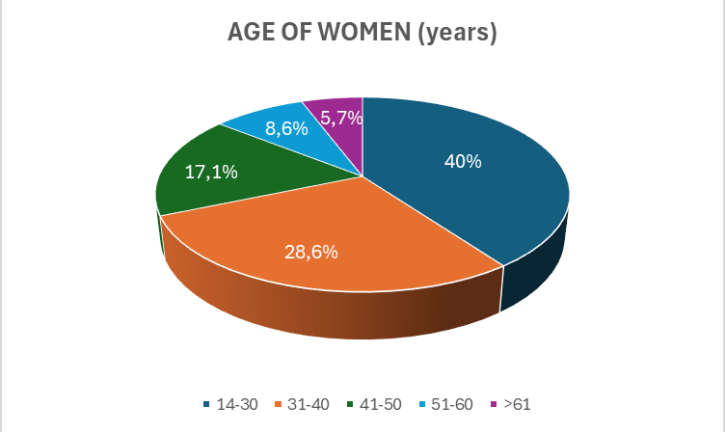

Figure 1. Descriptive analysis of the age of women suffering from vaginal infections enrolled in the study.

Regarding the diagnosis method for vaginal infection, 57.1% of participants reported self-diagnosis, while 42.9% underwent a medical evaluation with a diagnosis made by a physician. This data highlights how over half of the women included in the study self-identified the condition, suggesting a high level of awareness and recognition of symptoms, but also underscoring the importance of an adequate clinical assessment to confirm the diagnosis and correctly direct treatment.

Among the clinical conditions and predisposing factors potentially associated with the development of vaginal infections, 5.7% of participants reported having diabetes mellitus. Furthermore, 48.6% of women reported experiencing stress, while 3.8% reported having undergone previous genitourinary tract surgery. Overall, these conditions are factors known in the literature to potentially alter the balance of the vaginal microbiota and increase susceptibility to vaginal infections.

Analysis of responses regarding perceived efficacy, symptom improvement, quality of life, and treatment safety revealed a high percentage of positive assessments. In particular, 88.6% of participants reported a positive assessment ("Yes") in terms of treatment efficacy, while 5.7% responded "Sometimes" and 5.7% responded "No." Regarding symptom improvement, 91.4% of women reported an improvement ("Yes"), 5.7% indicated occasional improvement ("Sometimes"), and 2.9% experienced no benefit ("No"). Regarding quality of life, 85.7% of participants reported an improvement, 11.4% reported occasional improvement, and 2.9% observed no change. Finally, in terms of safety, 88.6% of women rated the treatment positively, 8.6% indicated an occasional perception of safety, and 2.9% expressed no positive assessment. Overall, the results show high participant satisfaction, with positive response rates exceeding 85% across all parameters analyzed (Figure 2).

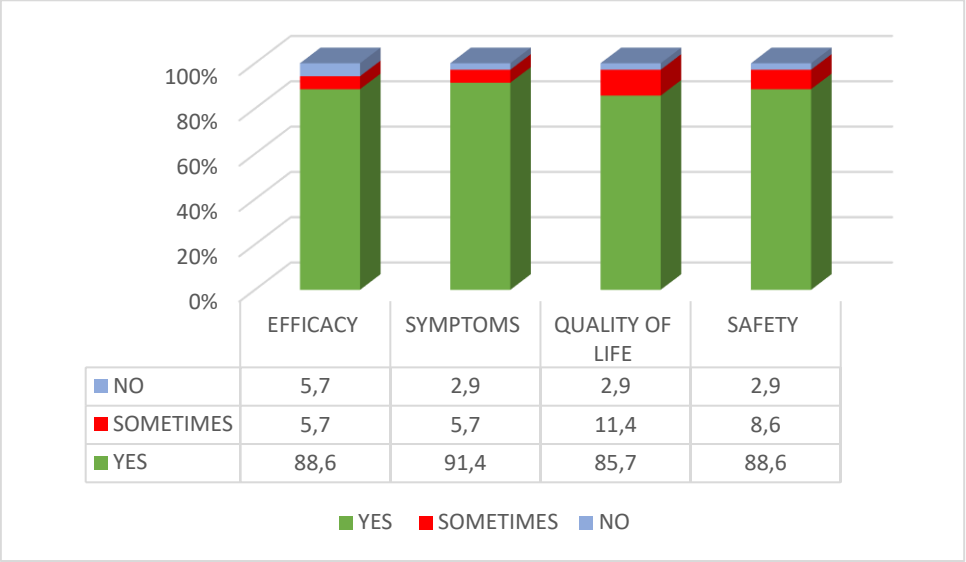

Figure 2. Descriptive analysis of the outcome of the study from patients: efficacy, symptoms, quality of life and safety, after the use of Dermoxen Bactor vaginal ovules.

Analysis of treated symptoms showed a high percentage of improvement for all clinical manifestations considered. In particular, itching was the symptom with the highest percentage of positive responses, with improvement reported by 88.6% of participants. Burning followed, with 85.7% of women reporting a benefit. Leukorrhea improved in 80.0% of cases, while bad odor was reduced in 77.1% of participants. Overall, the data indicate a clinically relevant improvement in the main symptoms associated with vaginal infections in the majority of patients included in the study.

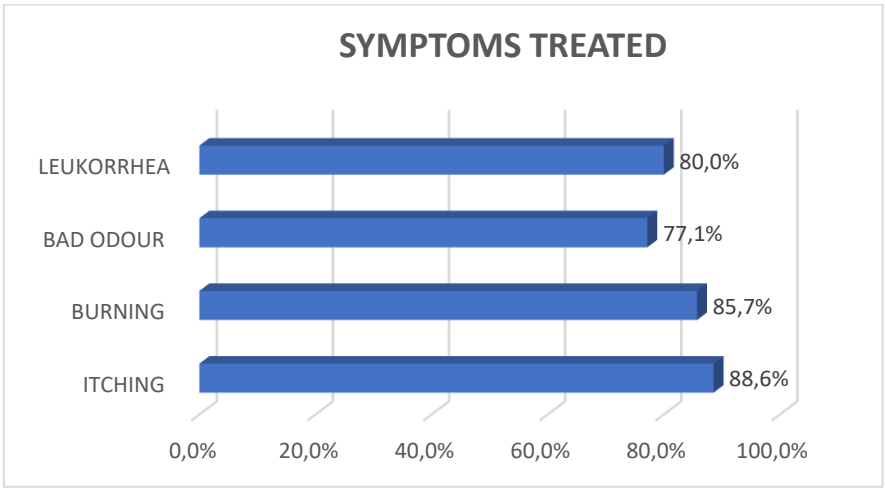

Figure 3. Descriptive analysis of the symptoms treated with Dermoxen Bactor vaginal ovules in the study: itching, burning, bad odour and leukorrhea.

3.2 Pharmacists and Physicians

A total of 2 pharmacists and 16 physicians (especially gynaecologists) participated in the survey, providing insights into their customers' experiences with the Dermoxen Bactor vaginal ovules.

Analysis of treated vaginal infections showed a high percentage of positive outcomes across all infection categories considered. In particular, infections associated with *Candida albicans* or other *Candida* species showed the highest rate of successful treatment, with effectiveness reported in approximately 98% of cases. Aerobic vaginitis, including infections caused by *E. coli, Staphylococcus aureus, Streptococcus agalactiae,* and *Enterococcus faecalis*, was effectively treated in about 92% of cases. Similarly, infections associated with *Gardnerella vaginalis* showed a high treatment success rate, with effectiveness reported in approximately 84% of women. Overall, these findings indicate that the medical device demonstrated a high level of effectiveness across the main etiological causes of vaginal infections included in the study (Figure 4).

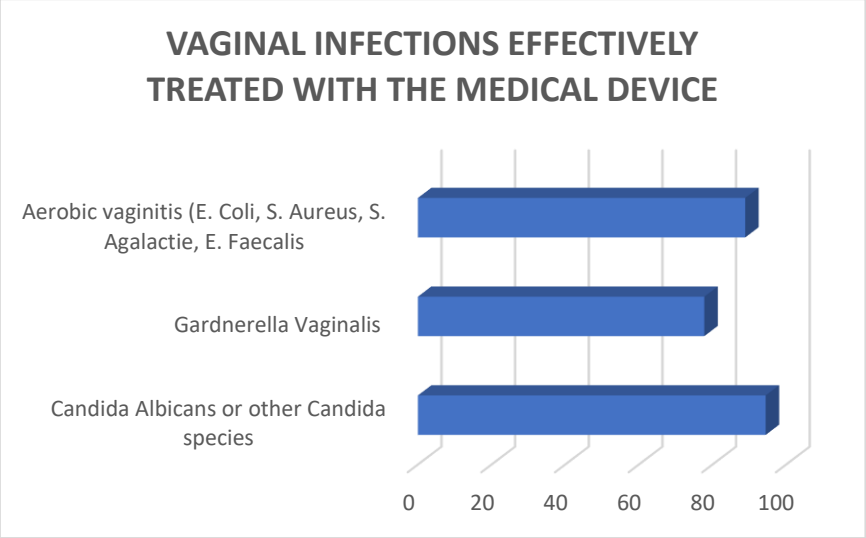

Figure 4. Descriptive analysis of vaginal infections effectively treated with the medical device, according to the etiological agent involved.

Analysis of patient-reported outcomes revealed very high levels of satisfaction following the use of the medical device. Regarding treatment efficacy, 85.9% of participants provided a positive assessment ("Yes"), while 12.8% reported occasional efficacy ("Sometimes") and only 1.3% reported no perceived efficacy ("No"). General satisfaction was particularly high, with 100% of participants expressing a positive evaluation. Similarly, quality of life improved in 94.4% of women, whereas 5.6% reported only occasional improvement and no participants reported a negative outcome. Safety was rated positively by all participants (100%), with no reports of occasional or negative assessments. Overall, the results demonstrate a very high degree of patient satisfaction, with positive response rates ranging from 85.9% to 100% across all evaluated parameters (Figure 5).

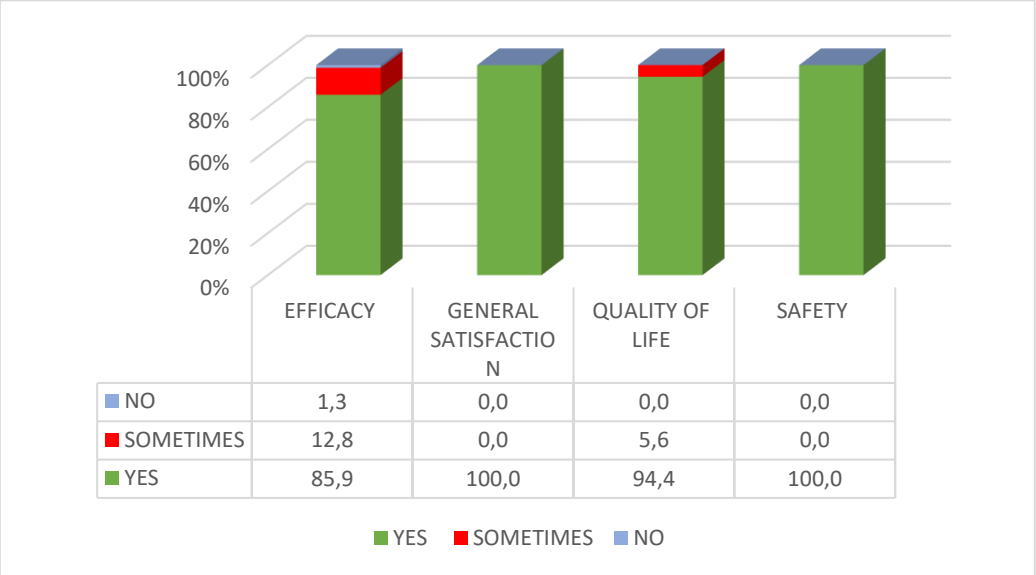

Figure 5. Descriptive analysis of the outcome of the study from physicians: efficacy, symptoms, quality of life and safety, after the use of Dermoxen Bactor vaginal ovules.

4. Discussion

Here, we performed a large survey on 53 participants, including patients, physicians, and pharmacists. The primary objective of this survey was to gather real-world insights into the perceived effectiveness, safety, tolerability, and usage patterns of Dermoxen Bactor vaginal ovules, medical device for treating vaginal infections, including VCC and BV and commonly related symptoms.

Questionnaires were specifically designed for patients to report their personal experience with the product use, while pharmacists and physicians evaluated its performance based on patient-reported outcomes or direct observations of symptom improvement.

As a result, the overall assessment of the Dermoxen Bactor vaginal ovules performance in terms of effectiveness and symptom improvement was highly positive among patients and similarly praised by healthcare professionals. Such benefits were further highlighted by the remarkable improvement in patients' quality of life, consistently reported by all three cohorts.

In particular, the results showed consistently high positive ratings across all evaluated outcomes, including efficacy, general satisfaction, quality of life, and safety. Notably, no adverse events were reported, supporting the favorable safety and tolerability profile of the medical device.

These preclinical results are consistent with the concept that Dermoxen Bactor vaginal ovules act through barrier-forming, pH-modulating, and mucosa-supporting properties in the presence of vaginal infections. Thanks to the moisturising action of functional components such as hyaluronic acid and Aloe vera, the product provides relief in case of irritation of the vaginal mucosa and exerts a lubricating effect. Hyaluronic acid is known for its hygroscopic and film-forming properties, promoting tissue hydration, epithelial repair, and protection of damaged mucosa [15]. Aloe vera has demonstrated soothing, moisturizing, and anti-

inflammatory properties on epithelial tissues, supporting mucosal healing processes [16]. These ingredients also exert a protective barrier effect on the vaginal mucosa. By adhering to the epithelial surface and retaining physiologically present water, hyaluronic acid forms a protective film that soothes, lubricates, and protects the vaginal mucosa from potential irritants and mechanical stress [15,17]. The formation of a mucoadhesive protective layer is consistent with the known biological behavior of high-molecular-weight hyaluronic acid on mucosal tissues [15]. Lactic acid rebalances the intravaginal pH, promoting the maintenance of an acidic environment and thus supporting the physiological well-being of the vaginal ecosystem. The dominance of lactobacilli in healthy vaginal microbiota is associated with lactic acid production, which maintains vaginal pH between 3.5 and 4.5 and inhibits pathogen overgrowth [18, 19]. Lactic acid, a physiological component of the vaginal environment, promotes rapid pH correction and facilitates the natural restoration of the delicate vulvovaginal ecosystem [18-20]. In the presence of vaginal infections such as vulvovaginal candidiasis or bacterial vaginosis, the immune system activates a defensive inflammatory response that is associated with increased oxidative stress in vaginal epithelial cells [21,22]. Elevated levels of reactive oxygen species (ROS) and lipid peroxidation markers have been documented in women with vaginal infections, suggesting a role for oxidative imbalance in mucosal damage and symptom persistence [21]. Thanks to the presence of Propolis extract and Tocopheryl acetate (vitamin E acetate), the device contributes to reducing free radicals through a non-pharmacological, non-FIM mechanism. Propolis has well-documented antioxidant and free radical scavenging properties, attributed mainly to its flavonoid and phenolic compound content [22,23]. Tocopheryl acetate, a stable form of vitamin E, acts as a lipid-soluble antioxidant, protecting cellular membranes from oxidative damage and reducing ROS-mediated injury [24-26]. Overall, the combined barrier-forming, pH-modulating, moisturizing, and antioxidant activities are consistent with a mechanism of action aimed at restoring the physiological vaginal microenvironment, protecting the mucosa, and relieving local symptoms associated with vaginal infections.

Significantly, beyond its favorable safety profile, the introduction of Dermoxen Bactor vaginal ovules as a non-pharmacological, barrier-based medical device may contribute to a more prudent use of antimicrobial therapies in the management of vaginal infections. Current standard treatments for bacterial vaginosis rely primarily on antibiotics such as metronidazole and clindamycin, while vulvovaginal candidiasis is commonly treated with azole antifungals administered topically or systemically [27,28]. Although these therapies are generally effective in the short term, recurrence rates remain high, particularly in bacterial vaginosis, where relapse within 3–12 months is frequently reported [29]. Repeated or inappropriate exposure to antimicrobial agents may contribute to the development of resistance phenomena. Reduced susceptibility of Candida species to azole antifungals has been increasingly documented, especially in recurrent vulvovaginal candidiasis and in non-albicans species [28,30]. Similarly, antimicrobial resistance and biofilm-associated persistence have been described in bacterial vaginosis-related pathogens, potentially contributing to therapeutic failure and recurrence [29,31]. For these reasons, international health authorities emphasize the importance of antimicrobial stewardship and the need to limit unnecessary or repeated antibiotic use [32].

In this context, a non-antibiotic medical device aimed at restoring the physiological vaginal microenvironment—through barrier-forming, pH-modulating, moisturizing, and antioxidant mechanisms—may represent a valuable adjunctive or supportive option. By helping to re-establish vaginal homeostasis and

relieve local symptoms, such an approach could potentially reduce reliance on repeated pharmacological treatments in selected cases, particularly in mild or recurrent conditions, always under medical supervision. This strategy may be especially relevant in specific populations such as pregnant women. Bacterial vaginosis during pregnancy has been associated with adverse obstetric outcomes, including preterm birth [33]. While certain antibiotics (e.g., metronidazole and clindamycin) can be used during pregnancy when clinically indicated, therapeutic decisions require careful risk–benefit evaluation [26,33]. Moreover, some systemic azoles, such as high-dose fluconazole, have been associated with safety concerns during pregnancy, and their use is generally restricted [27,34]. In such contexts, non-pharmacological approaches with a favorable safety profile may offer supportive management options, provided they are used according to medical advice and regulatory indications. Overall, integrating barrier-based and ecosystem-restoring strategies into the management of vaginal infections aligns with current efforts to promote antimicrobial stewardship, reduce recurrence, and minimize the risk of resistance development, while maintaining attention to patient safety and specific clinical conditions.

A primary limitation is that the quality of life was assessed using a limited set of specific survey items, which may lead to partially inaccurate information. Furthermore, reliance on patient-reported outcome (PRO) measures introduces the potential for recall and reporting bias. Among the strengths of the survey, particular note has to be made of the large population and the high level of coherence among patients, pharmacists, and physicians in their assessments.

5. Conclusion

In summary, the RWD presented herein indicates a strong coherence among patients, pharmacists, and physicians regarding the effectiveness, safety, and tolerability of Dermoxen Bactor vaginal ovules in treating vulvovaginitis and bacterial vaginosis and related symptoms. Given that concerns may arise regarding the effectiveness and safety of available pharmacological treatments for vaginal infections, and that such treatments often address only specific kinds of vaginal infections, there is a clear need for broader therapeutic options with a solid safety profile. Real-world surveys like this one are essential, as they provide insights into patients' actual responses to treatment, especially when data are continuously collected, as in this case. This ongoing monitoring supports the confirmation of the product's clinical performance and contributes to improving patient outcomes.

6. Bibliography

1. Workowski KA, Bachmann LH, Chan PA, Johnston CM, Muzny CA, Park I, et al. Sexually transmitted infections treatment guidelines, 2021. MMWR Recomm Rep. 2021;70(4):1–187.
2. Sobel JD. Vulvovaginal candidosis. Lancet. 2007;369(9577):1961–71.
3. Pappas PG, Kauffman CA, Andes DR, Clancy CJ, Marr KA, Ostrosky-Zeichner L, et al. Clinical practice guideline for the management of candidiasis: 2016 update by the Infectious Diseases Society of America. Clin Infect Dis. 2016;62(4):e1–50.
4. Linhares IM, Summers PR, Larsen B, Giraldo PC, Witkin SS. Contemporary perspectives on vaginal pH and lactobacilli. Am J Obstet Gynecol. 2011;204(2):120.e1–5.
5. Gonçalves B, Ferreira C, Alves CT, Henriques M, Azeredo J, Silva S. Vulvovaginal candidiasis: epidemiology, microbiology and risk factors. Crit Rev Microbiol. 2016;42(6):905–27.
6. Denning DW, Kneale M, Sobel JD, Rautemaa-Richardson R. Global burden of recurrent vulvovaginal candidiasis. Lancet Infect Dis. 2018;18(11):e339–47.
7. Muzny CA, Schwebke JR. Pathogenesis of bacterial vaginosis: discussion of current hypotheses. J Infect Dis. 2016;214(Suppl 1):S1–5.
8. Hillier SL, Nugent RP, Eschenbach DA, Krohn MA, Gibbs RS, Martin DH, et al. Association between bacterial vaginosis and preterm delivery. N Engl J Med. 1995;333(26):1737–42.
9. Bilardi JE, Walker S, Temple-Smith M, McNair R, Mooney-Somers J, Bellhouse C, et al. The burden of bacterial vaginosis: women's experience of the physical, emotional, sexual and social impact. PLoS One. 2013;8(9):e74378.
10. Palma F, Volpe A, Villa P, Cagnacci A; Writing group of AGATA study. Vaginal atrophy of women in postmenopause. Results from a multicentric observational study: the AGATA study. Maturitas. 2016;83:40–4.
11. Petrova MI, Reid G, Vaneechoutte M, Lebeer S. Lactobacillus species as biomarkers and agents that can promote various aspects of vaginal health. Front Physiol. 2017;8:677.
12. Bradshaw CS, Sobel JD. Current treatment of bacterial vaginosis—limitations and need for innovation. J Infect Dis. 2016;214(Suppl 1):S14–20.
13. Dang, A. Real-World Evidence: A Primer. Pharm. Med. 2023, 37, 25‑36. [CrossRef].
14. Cioeta, R.; Cossu, A.; Giovagnoni, E.; Rigoni, M.; Muti, P. A New Platform for Post-Marketing Surveillance and Real-World Evidence Data Collection for Substance-Based Medical Devices. Front. Drug Saf. Regul. 2022, 2, 992359. [CrossRef].
15. Litwiniuk M, Krejner A, Speyrer MS, Gauto AR, Grzela T. Hyaluronic acid in inflammation and tissue regeneration. Wounds. 2016;28(3):78–88.
16. Surjushe A, Vasani R, Saple DG. Aloe vera: a short review. Indian J Dermatol. 2008;53(4):163–6.
17. Casale M, et al. Hyaluronic acid: perspectives in mucosal regeneration. Eur Rev Med Pharmacol Sci. 2016;20(4):620–8.
18. Linhares IM, Summers PR, Larsen B, Giraldo PC, Witkin SS. Contemporary perspectives on vaginal pH and lactobacilli. Am J Obstet Gynecol. 2011;204(2):120.e1–5.
19. O'Hanlon DE, Moench TR, Cone RA. Vaginal pH and microbicidal lactic acid when lactobacilli dominate the microbiota. PLoS One. 2013;8(11):e80074.
20. Petrova MI, Reid G, Vaneechoutte M, Lebeer S. Lactobacillus species as biomarkers and agents that can promote various aspects of vaginal health. Front Physiol. 2017;8:677.
21. Surapaneni KM, Venkataramana G. Status of lipid peroxidation and antioxidant enzymes in patients with bacterial vaginosis. Indian J Med Sci. 2007;61(8):447–52.
22. Ciebiera M, et al. Oxidative stress in gynecological diseases. Int J Mol Sci. 2021;22(6):3086.
23. Wagh VD. Propolis: a wonder bees product and its pharmacological potentials. Adv Pharmacol Sci. 2013;2013:308249.
24. Silva-Carvalho R, Baltazar F, Almeida-Aguiar C. Propolis: a complex natural product with diverse biological activities. Evid Based Complement Alternat Med. 2015;2015:206439.
25. Brigelius-Flohé R, Traber MG. Vitamin E: function and metabolism. FASEB J. 1999;13(10):1145–55.
26. Rizvi S, et al. The role of vitamin E in human health and disease. Sultan Qaboos Univ Med J. 2014;14(2):e157–65
27. Workowski KA, Bachmann LH, Chan PA, Johnston CM, Muzny CA, Park I, et al. Sexually transmitted infections treatment guidelines, 2021. MMWR Recomm Rep. 2021;70(4):1–187.

28. Pappas PG, Kauffman CA, Andes DR, Clancy CJ, Marr KA, Ostrosky-Zeichner L, et al. Clinical practice guideline for the management of candidiasis: 2016 update by the Infectious Diseases Society of America. Clin Infect Dis. 2016;62(4):e1–50.
29. Bradshaw CS, Sobel JD. Current treatment of bacterial vaginosis—limitations and need for innovation. J Infect Dis. 2016;214(Suppl 1):S14–20.
30. Gonçalves B, Ferreira C, Alves CT, Henriques M, Azeredo J, Silva S. Vulvovaginal candidiasis: epidemiology, microbiology and risk factors. Crit Rev Microbiol. 2016;42(6):905–27.
31. Muzny CA, Schwebke JR. Pathogenesis of bacterial vaginosis: discussion of current hypotheses. J Infect Dis. 2016;214(Suppl 1):S1–5.
32. World Health Organization. Antimicrobial resistance: global report on surveillance. Geneva: WHO; 2014.
33. Hillier SL, Nugent RP, Eschenbach DA, Krohn MA, Gibbs RS, Martin DH, et al. Association between bacterial vaginosis and preterm delivery. N Engl J Med. 1995;333(26):1737–42.
34. U.S. Food and Drug Administration (FDA). FDA Drug Safety Communication: FDA evaluates study examining use of oral fluconazole (Diflucan) in pregnancy. 2016.