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Plant-Based Vaginal Suppository for Vulvovaginal Candidiasis: A Natural Remedy Revisited – Formulation, Optimization, and Antifungal Efficacy

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Abstract

Recent advancements in the development of plant-based vaginal suppositories highlight their growing potential as effective and well-tolerated alternatives to conventional antifungal therapies. Various formulations incorporating standardized herbal extracts—such as Nigella sativa, Clove, Lawsonia inermis, and Glycyrrhiza glabra—have demonstrated promising antifungal efficacy, physicochemical stability, and patient acceptability. Optimization techniques, including base selection, displacement value calculation, and compatibility analysis, have further enhanced formulation quality. In vitro and in vivo evaluations consistently reveal therapeutic outcomes comparable to standard treatments like clotrimazole. This review aims to critically synthesize current evidence on the formulation, optimization, and antifungal efficacy of plant-based vaginal suppositories.

Keywords: Plant-based vaginal suppositories, herbal extracts, antifungal efficacy, formulation optimization, vulvovaginal candidiasis,

1. Introduction

Vulvovaginal candidiasis (VVC) is a prevalent mucosal infection that ranks second only to bacterial vaginosis in terms of frequency, accounting for nearly 50–72% of vaginal infection cases. Predominantly caused by Candida albicans, the condition manifests with symptoms such as pruritus, swelling, erythema, and a characteristic curd-like vaginal discharge. These symptoms can significantly impair a woman's physical and psychological well-being. Globally, the burden of VVC is substantial, with projections estimating over 158 million affected individuals by the 2030s. While most cases are manageable with antifungal therapy, recurrence is common, especially in the context of growing resistance to conventional treatments, notably azole antifungals (Dalabehera et al., 2024; Chew & Than, 2016).

The pathogenicity of C. albicans is enhanced by its ability to form biofilms, adhere to epithelial surfaces, and undergo phenotypic switching, all of which contribute to treatment resistance and chronic infection. Moreover, factors such as immunosuppression, hormonal imbalances, pregnancy, and prior antibiotic use

can predispose individuals to recurrent episodes. These complexities underscore the urgent need for novel therapeutic approaches that are not only effective but also safe and well-tolerated over extended periods (Faustino et al., 2025).

In light of these challenges, increasing attention has been directed towards alternative therapies, particularly those derived from medicinal plants. Phytotherapy offers a promising route due to the broad-spectrum antimicrobial, antifungal, and anti-inflammatory properties of various plant species. Notably, plant-based treatments have been shown to exert antifungal effects against Candida species while minimizing the adverse effects often associated with synthetic antifungal agents. For instance, botanical extracts such as Thymus vulgaris, Nigella sativa, Zataria multiflora, and Melaleuca alternifolia have demonstrated remarkable efficacy in reducing the clinical symptoms of vaginal infections, including discharge, irritation, and inflammation (Kamali et al., 2024).

Moreover, the integration of herbal medicine into conventional gynecological care is supported by evidence highlighting the therapeutic potential of phytochemicals. Palmeira-de-Oliveira et al. (2013) emphasize that over 40% of new pharmacological agents introduced between 1981 and 2006 were derived from natural sources, reinforcing the role of natural products in drug discovery. Given the escalating issue of antifungal resistance, the development of plant-based vaginal formulations—such as suppositories, creams, and gels—has gained momentum. These delivery systems ensure localized, sustained release of bioactive compounds directly at the site of infection, enhancing efficacy while reducing systemic exposure and side effects.

Therefore, the resurgence of interest in natural remedies for VVC is timely and warranted. This review explores the formulation, optimization, and antifungal efficacy of plant-based vaginal suppositories as a viable therapeutic alternative.

2. Role of Medicinal Plants in Treating VVC

Recent studies highlight the promising role of medicinal plants in managing vulvovaginal candidiasis (VVC), particularly in the context of rising antifungal resistance. Ostróżka-Cieślik et al. (2025) emphasized the potential of plant-based hydrogels in treating vaginal and vulvar infections, noting their advantages such as enhanced bioavailability, targeted delivery, and the ability to incorporate various antimicrobial phytochemicals. These novel formulations offer a modern approach to combat vaginal pathogens and may improve therapeutic outcomes compared to conventional treatments. Complementing this, Ray et al. (2007) demonstrated that boric acid vaginal suppositories achieved a significantly higher mycological cure rate (63.6%) compared to oral fluconazole (28.6%) in diabetic women with Candida glabrata infections, suggesting the utility of alternative therapies when standard antifungals are less effective.

Expanding on this, essential oils such as Eugenia caryophyllata and Piper nigrum showed potent fungicidal activity, with MFC/MIC ratios ≤4. Their efficacy is attributed to bioactive compounds like eugenol and alpha-pinene, reinforcing the therapeutic relevance of traditional plant-based remedies (Ates & Kanbar, 2023). Further supporting these findings, a polyherbal vaginal tablet comprising Rosa damascena, Punica granatum, Quercus infectoria, Myrtus communis, and Nardostachys jatamansi demonstrated significant clinical efficacy. Following seven days of use, 63% of the treatment group tested negative for fungal growth, compared to only 13% in the placebo group, with marked improvements in symptoms such as

itching and discharge (Khalilzadeh et al., 2020). The extract, prepared via hydroalcoholic maceration and standardized for phenolic content, showed minimal side effects, highlighting its safety and potential as a plant-based alternative for VVC treatment.

3. Formulation of Plant-Based Vaginal Suppositories

Several recent efforts have been made to formulate vaginal suppositories incorporating medicinal plant extracts for the treatment of vulvovaginal infections. Đurić et al. (2021) developed three types of herbal suppositories using oleous extracts of Calendula officinalis, Capsella bursa-pastoris, Matricaria chamomilla, Hypericum perforatum, and Achillea millefolium. The extracts were obtained through a five-day olive oil maceration process and used in formulations labeled Vagitories A (a blend of all five extracts at 5.5% w/w), Vagitories B (containing 200 mg of tea tree oil), and Vagitories C (comprising 32% w/w Hypericum perforatum extract). Each formulation maintained physical stability and uniformity, ensuring suitability for clinical application.

In another formulation approach, Mustapha et al. (2021) successfully prepared vaginal suppositories containing 20% Nigella sativa extract using cocoa and shea butter bases. The cocoa butter-based suppositories exhibited greater stability, improved disintegration, and more favorable drug release profiles, confirming their potential as localized antifungal delivery systems. Similarly, Olayemi et al. (2022) incorporated 40% w/w clove ethanol extract into a macrogol-based suppository. The final product exhibited acceptable pH (4.78 ± 0.09), melting point (35.5 ± 0.5 °C), and visual uniformity, indicating its practicality for vaginal use.

Further supporting the feasibility of plant-based formulations, Saghafi et al. (2018) developed dill seed extract suppositories using Soxhlet extraction and Witepsol as the base. Each 2 g suppository contained 2% w/w of dried extract and provided consistent dosing with minimal reported side effects, such as mild burning and itching. Likewise, Sirilun et al. (2018) prepared Glycyrrhiza glabra (licorice) extract suppositories using a PEG matrix. The formulation was thermally stable and retained antifungal activity over three months, attributed to its high phenolic and flavonoid content, particularly glabridin.

Standardization also played a key role in the formulation of QIFH suppositories, where Simbar et al. (2025) used an ethanolic extract rich in tannins, primarily pyrogallol (5.6–8.4 mg per unit). The extract was prepared through 48-hour percolation in 60% ethanol, and the final product met all quality control parameters without causing irritation or allergic reactions upon mucosal testing.

Askari et al. (2013) introduced MOGS suppositories formulated with freeze-dried aqueous extracts of myrtle and oak gall, standardized to contain 276.81 ± 4.89 µg of gallic acid per unit as quantified by HPLC. The extracts were embedded in a PEG 600/3350 base, with the formulation adapted from Persian traditional medicine and optimized for modern pharmaceutical use. Similarly, Rahman et al. (2023) prepared Lawsonia inermis suppositories using the pour molding (hot fusion) technique. The plant extract was incorporated into a PEG-Tween-Span base, molded, and stored in airtight conditions. Several formulations were tested to ensure optimal stability, efficacy, and patient compliance.

These studies collectively demonstrate the potential of various plant-based vaginal suppository formulations. By ensuring standardization, stability, and bioactivity, they present promising alternatives or adjuncts to conventional antifungal therapies in managing vulvovaginal infections.

4. Optimization Techniques

The formulation of plant-based vaginal suppositories requires targeted optimization to enhance therapeutic efficacy, stability, and user acceptability. Đurić et al. (2021) optimized their formulations by individually macerating herbal extracts in olive oil, promoting efficient extraction of lipophilic compounds. Three distinct formulations were developed: Vagitories A (5.5% w/w of five plant extracts) aimed at synergistic action; Vagitories B (200 mg of tea tree oil with ≥30% terpinen-4-ol) for antimicrobial effect; and Vagitories C (32% w/w Hypericum perforatum) for anti-inflammatory and tissue-regenerative benefits. Base selection played a critical role in other formulations. Mustapha et al. (2021) compared cocoa butter and shea butter for Nigella sativa suppositories, finding cocoa butter superior in stability and extract release (56.95 ± 1.37 minutes). Conversely, Olayemi et al. (2022) found cocoa butter unsuitable due to structural instability. They achieved optimization using hydrophilic PEG 1000 and 4000, calculating displacement values for uniformity. FTIR analysis confirmed no incompatibility between clove extract and PEG, validating the formulation's chemical stability.

Sirilun et al. (2018) evaluated seven formulations (F1–F7) with various combinations of PEG6000, PEG400, water, glycerin, and propylene glycol. Formulation F6 showed optimal hardness and disintegration time (~20 minutes), while others with unbalanced hydrophilic components had suboptimal mechanical properties, emphasizing the importance of excipient balance. Askari et al. (2013) used Design-Expert software to conduct 16 design runs varying PEG 600/3350 ratios and extract concentrations for MOGS suppositories. Probe sonication of extract with PEG 600, followed by blending with PEG 3350, yielded a formulation with favorable disintegration time, mechanical strength, and particle size. Rahman et al. (2023) applied a two-stage optimization for Lawsonia inermis suppositories. Eleven batches were initially screened for visual and physical traits. Three (F3, F8, F11) underwent further testing for disintegration, mucoadhesiveness, and melting point, with batch F8 outperforming the rest.

Together, these findings highlight that precise optimization—through appropriate base selection, standardization of active compounds, and rigorous evaluation of physicochemical parameters—is essential for developing safe, effective, and acceptable plant-based vaginal suppositories.

5. In Vitro and In Vivo Antifungal Efficacy

The antifungal efficacy of plant-based vaginal suppositories has been validated through a combination of in vitro assessments and in vivo clinical trials, demonstrating their potential as alternatives or adjuncts to conventional antifungal therapies. Đurić et al. (2021) reported significant clinical improvements in both reproductive-aged and postmenopausal women following treatment with tea tree oil-based suppositories. Redness and discharge, common symptoms of vulvovaginal candidiasis, were notably reduced from 93.9% and 95.9% to 4.3% and 6.4%, respectively, in the reproductive group, while symptoms were completely resolved in the postmenopausal group. Although in vitro analyses were not provided, the clinical data alone suggest robust therapeutic effects.

These clinical findings are supported by extensive in vitro evaluations of plant extracts and oils. Ates and Kanbur (2023) screened 100 plant-based products and identified 20 essential and fixed oils with significant anticandidal activity. Oils such as Piper nigrum, pine turpentine, pine tar, and clove oil exhibited MICs ranging from 0.125 to 2 µL/mL and inhibition zones ≥20 mm, values comparable to fluconazole and amphotericin B. The presence of potent antifungal compounds, including eugenol, α-pinene, and

limonene, was confirmed by GC-MS analysis, further validating their efficacy. Consistent with these findings, Mustapha et al. (2021) demonstrated that both methanolic extracts and commercial Nigella sativa oil were effective against Candida albicans, producing inhibition zones up to 32.33 ± 3.21 mm. When formulated into vaginal suppositories, these extracts retained activity with inhibition zones between 10.00 ± 1.00 mm and 23.67 ± 2.08 mm, confirming the suitability of such formulations for local delivery.

The use of traditional medicinal plants in suppository form has also shown promise in direct clinical comparisons with standard antifungals. Saghafi et al. (2018) reported that a 2% Anethum graveolens (dill) vaginal suppository achieved similar efficacy to 100 mg clotrimazole, with post-treatment fungal cultures remaining positive in only 10% and 13.3% of patients, respectively. Similarly, cumin seed extract suppositories produced comparable clinical improvements to clotrimazole over a six-day treatment period (Elmoneen et al., 2020). In addition to antifungal activity, some plant-based suppositories offer stability and antioxidant benefits. Sirilun et al. (2018) observed that Glycyrrhiza glabra extracts retained antifungal efficacy under various storage conditions and exhibited strong antioxidant properties, with MICs ranging from ≥31.25 µg/mL to ≥62.5 µg/mL. This dual functionality adds therapeutic value beyond fungal suppression alone.

Furthermore, innovations in delivery systems have enhanced the clinical relevance of plant-based suppositories. For instance, Olayemi et al. (2022) showed that clove extract in macrogol-based suppositories exhibited in vitro antifungal activity and adhered to excised vaginal mucosa for up to two hours, an important feature for prolonged local action. Similarly, Ellah et al. (2021) formulated essential oil-loaded PEG suppositories (EOCS) that achieved complete drug release within 30 minutes while maintaining anti-Candida activity. Combination herbal formulations have also demonstrated impressive efficacy. The MOGS formulation—comprising myrtle and oak gall—proved superior to placebo and comparable to metronidazole in treating both trichomoniasis and mixed vaginitis (Askari et al., 2020). Additionally, Simbar et al. (2025) reported that Quercus infectoria suppositories significantly reduced pruritus, discharge, and burning, with no statistical difference from clotrimazole in terms of effectiveness, highlighting its potential as a safe alternative.

Mechanistic studies further emphasize the therapeutic promise of these agents. Baofukang suppositories, for instance, inhibited C. albicans hyphal invasion and enhanced host immunity via increased IL-2, IL-6, IL-8, and IL-17 expression in vaginal epithelial cells (Li et al., 2016). Rahman et al. (2023) demonstrated that Lawsonia inermis-based suppositories produced inhibition zones of 19 mm and had an MIC of 45 µg/mL, comparable to standard antifungals. In formulations combining herbal extracts with other natural agents, clinical outcomes remain encouraging. A suppository containing Nigella sativa and honey yielded a 67.5% fungal culture clearance rate, similar to clotrimazole's 74.4%, with substantial reductions in itching and discharge (Norouzi et al., 2022). Likewise, the Forzejeh suppository, composed of Tribulus terrestris, Myrtus communis, Foeniculum vulgare, and Tamarindus indica, demonstrated comparable efficacy to metronidazole in treating bacterial vaginosis and was effective in restoring healthy vaginal flora (Baery et al., 2018).

6. Safety, Efficacy, and Regulatory Aspects

The review of plant-based vaginal suppositories for treating vulvovaginal candidiasis (VVC) highlights their safety, practicality, and regulatory considerations. Recent findings suggest that certain natural

products can effectively eliminate Candida infections and may serve as alternatives to conventional systemic antifungals. The research study aids to examine the development and enhancement of these natural products, as well as their efficacy against fungal infections.Plant-derived vaginal suppositories are typically presented as substitutes for synthetic antifungals, which necessitates careful development of their safety profiles, as some users may experience allergic reactions to specific ingredients. This requires comprehensive screening and testing, particularly if the formulation contains potential irritants, since certain excipients or active pharmaceutical ingredients (APIs) may heighten the irritant potential of the vaginal mucosa. For instance a study by Mustapha et al, 2023 reports that the Clotrimazole possesses broad-spectrum antifungal properties and is well tolerated in suppository form (Mustapha et al, 2023).The effects of plant-based formulations on the vaginal microbiome should be assessed to determine that they will not cause alterations to the flora. There is evidence that natural products have effective inhibitory activity against Candida albicans with some studies reporting similar activity to fluconazole or other synthetic antifungals (Jeanmonod et al., 2024;Van Riel et al., 2023). The overall goal of the natural products was to inhibit VVC and lower the overall recurrence of VVC for patients that relied on conventional therapy as a treatment for VVC, which falls short in addressing the traditional problem of recurrent VVC (Van Riel et al., 2023). This was an exploratory assessment of the formulations and comparison to marketed suppositories, regarding their physicochemical characteristics which included disintegration time and drug release rates. Supplied suppositories with surfactant compounds had similar results in disintegration time which is essential for drug release and any therapeutic effect the formulation may have (Mustapha et al., 2023). There were overall fewer side effects for the participant patients consuming plant-based suppositories than the impact of synthetic antifungals (Mendling et al., 2015). All pharmaceutical products, including vaginal suppositories, must persist with the regulations put in place by the authorities, as part of good manufacturing practices. Product preparations must comply with regulated standards of safety and efficacy as intended for consumers and patients.The evaluation of the physicochemical and mechanical properties in this study brings us closer to meeting these regulatory requirements. However, clinical trials are essential to assess the safety and efficacy of these suppositories in human subjects before they can be authorized for marketing. Such evaluations will provide regulatory bodies with critical information regarding the product's safety and performance, thereby increasing the chances of approval for public use (Mustapha et al., 2023).

7. Challenges and Future Directions

Plant-based vaginal suppositories are a viable natural option for the treatment of VVC in the community, but there are some challenges and possibilities related to future research. The main challenges related to plant-based suppositories in treating VVC are related to the formulation process and antifungal efficacy testing. An effective formulation will encompass appropriate formulation properties for the vaginal environment, drug release, and inherent qualities of the plant extracts. Future studies should involve isolating and characterizing plant based components with known antifungal properties that exhibit mixed/combined antifungal effects, developing vaginal targeted delivery systems, and investigating potential drug interactions. As previously mentioned, stability and efficacy present significant challenges for plant-based vaginal suppositories. Furthermore, the use of natural products raises concerns about the potency and stability of plant-extracted substances, which can influence the overall effectiveness of the suppositories, products, or medical conditions. Establishing a standardized method for extracting plant

materials in formulations is essential for achieving consistent therapeutic results, such as drug absorption through the vaginal mucosa. Many traditional formulations struggle with poor solubility and penetration, and the reliability of products regarding the degree of local mucosal absorption remains a largely unexplored issue for vaginal formulations. The effectiveness of a vaginal formulation also depends on how long the drug remains at the surface of the vaginal epithelium.Numerous vaginal formulations lack sufficient mucoadhesive characteristics, which may hinder their retention and clearance duration. Future research on the long-term antifungal efficacy of vaginal suppositories could include clinical trials evaluating the antifungal effectiveness of clinical products or medical conditions over both short and long periods, ideally across diverse populations. Current studies are limited to small scale, thus necessitating larger and randomized controlled trials to confirm the efficacy and safety of the developed formulations. Exploring the combination of various plant extracts and their possible synergistic effects on antifungal activity may result in more potent formulations. By exploring the cutting-edge technologies, such as nanotechnology and hydrogels, can be employed to enhance formulations by improving the solubility and bioavailability of active compounds in plant-based products and additionally by investigating the use of natural polysaccharides to enhance mucoadhesion and facilitate the sustained release of active compounds, along with innovative delivery systems, may yield groundbreaking solutions. Future research should also take into account patient preferences and adherence, potentially incorporating user-friendly self-administration techniques.

8. Conclusion

In conclusion, vaginal suppositories derived from plants exhibit considerable promise as a natural treatment for vulvovaginal candidiasis, especially in boosting antifungal effectiveness. Although initial results suggest positive antifungal characteristics, further optimization, validation, and progression to clinical use are essential. The primary subsequent actions include tackling safety concerns, standardizing the composition of these plant-derived suppositories, and guaranteeing compliance with regulatory standards. Future studies should include extensive clinical trials to assess the safety and efficacy of these formulations in various target populations. Such research will provide substantial evidence to support the clinical use of plant-based therapies. Additionally, improvements in drug delivery technologies could be integrated into these suppositories to boost bioavailability and enhance therapeutic effectiveness. The use of interventions like nanoparticles, hydrogels, or other delivery systems may optimize the therapeutic benefits of plant-based treatments while ensuring they are user-friendly. Advancements in these fields will be crucial for advancing the clinical use of these natural therapies for vulvovaginal candidiasis.

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