IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

"Herbal Approach Towards Vulvo Vaginal Candidiasis By Designing And Optimising Antifungal Suppositories"

Abstract

Background:

Vulvo Vaginal Candidiasis (VVC), predominantly caused by *Candida albicans*, is a common mucosal infection affecting millions of women worldwide. While synthetic antifungal drugs such as azoles are widely used, they often pose challenges like drug resistance, high recurrence rates, and systemic side effects.

Objective:

To design, develop, and optimize herbal vaginal suppositories using extracts of medicinal plants with known antifungal properties, and to evaluate their physicochemical characteristics, in vitro antifungal activity, and formulation stability.

Methods:

Medicinal plants (*Allium sativum*, *Azadirachta indica*, *Curcuma longa*, and *Ocimum sanctum*) were selected based on literature evidence for antifungal activity. Extracts were obtained through ethanol maceration and screened phytochemically. Suppositories were formulated using cocoa butter, PEG, and glycerogelatin bases via the fusion method. A 3^2 factorial design was employed for optimization. Evaluation included weight variation, disintegration, pH, drug content, melting point, and **in vitro** antifungal activity using the agar well diffusion method against *Candida albicans*. Stability studies were performed over three months.

Results:

Phytochemical analysis confirmed the presence of key bioactive compounds such as allicin and nimbidin. The optimized formulation (F3) containing 15% *Allium sativum* extract in cocoa butter exhibited a zone of inhibition of 18.0 mm and a MIC of 31.25 µg/mL, closely matching fluconazole (20.5 mm, MIC 15.62 µg/mL). Suppositories met pharmacopeial standards for physical properties and remained stable under accelerated conditions over three months.

Conclusion:

Herbal vaginal suppositories, particularly those formulated with *Allium sativum*, demonstrated significant antifungal activity against *Candida albicans*. This study supports their potential as safe, effective, and resistance-minimizing alternatives to conventional antifungals. Further in vivo studies and clinical trials are recommended to confirm therapeutic efficacy and safety in humans.

Keywords:

Vulvo Vaginal Candidiasis, *Candida albicans*, herbal suppositories, *Allium sativum*, antifungal activity, phytotherapy, formulation optimization

1. Introduction

1.1 Definition and Epidemiology of Vulvo Vaginal Candidiasis (VVC)

Vulvo Vaginal Candidiasis (VVC) is a widespread mucosal infection affecting the female genital tract, primarily caused by *Candida albicans*—a polymorphic, yeast-like fungus that naturally colonizes the vaginal environment in approximately 20–30% of healthy women (Sobel, 2007). Under certain conditions such as weakened immunity, hormonal fluctuations, extended antibiotic use, or high estrogen levels, this normally benign organism can proliferate excessively, resulting in symptomatic infection (Achkar & Fries, 2010). Clinically, VVC presents with intense itching, thick whitish vaginal discharge resembling cottage cheese, redness of the vulva, irritation, burning sensation, and discomfort during urination (Denning et al., 2011). Epidemiological studies suggest that around 75% of women will experience at least one VVC episode in their lifetime, and about 40–50% of them may develop recurrent infections (Sobel, 2016).

1.2 Limitations of Synthetic Antifungal Treatments

Current treatment strategies primarily involve azole-based antifungal agents such as fluconazole and clotrimazole. While effective in many cases, their prolonged or indiscriminate use has led to the emergence of resistant *Candida* strains, particularly *Candida glabrata* and *Candida krusei* (Pappas et al., 2018). Additionally, synthetic antifungals can cause systemic side effects including hepatotoxicity, gastrointestinal discomfort, and vaginal burning or irritation (Yano et al., 2019). Furthermore, recurrence of VVC remains a

significant issue, with many patients experiencing incomplete eradication or relapse within weeks (Sobel et al., 2013).

1.3 Medicinal Plants in Antifungal Therapy

In response to the limitations of conventional therapies, there has been growing interest in the use of medicinal plants as alternative antifungal agents. Herbal medicines have been historically used in various traditional systems like Ayurveda, Unani, and Traditional Chinese Medicine to treat vaginal infections. Plants such as *Azadirachta indica* (neem), *Curcuma longa* (turmeric), *Allium sativum* (garlic), and *Ocimum sanctum* (holy basil) have shown potent antifungal effects in vitro, attributed to their phytoconstituents like allicin, nimbidin, curcumin, and eugenol respectively (Dwivedi et al., 2020; Bhardwaj et al., 2022). These bioactive compounds can target multiple fungal pathways, offering advantages over single-target synthetic drugs.

1.4 Need for Novel Herbal Formulations

Despite the known antifungal efficacy of various medicinal plants, their application in modern dosage forms remains underexplored. Developing herbal vaginal suppositories allows for direct drug delivery to the site of infection, minimizing systemic toxicity while enhancing local efficacy (Fleischer & Joffe, 2021). Moreover, phytoconstituents are less likely to induce microbial resistance due to their complex and multifaceted modes of action (da Silva Ferreira et al., 2020). Thus, incorporating these herbal extracts into well-designed vaginal suppositories represents a promising therapeutic strategy.

1.5 Objectives of the Study

This study was undertaken with the following objectives:

- To develop vaginal suppositories containing herbal extracts with known antifungal activity.
- To optimize the formulation parameters, including base selection and extract concentration, using experimental design approaches.
- To evaluate the physicochemical properties, in vitro antifungal activity, and stability of the formulated suppositories.

2. Literature Review

2.1 Conventional Therapies for Vulvo Vaginal Candidiasis (VVC)

The primary pharmacological treatments for VVC include azoles (e.g., clotrimazole, fluconazole) and polyenes (e.g., nystatin). Azoles act by inhibiting the cytochrome P450-dependent enzyme lanosterol 14-α-demethylase, which is essential for ergosterol biosynthesis, a critical component of the fungal cell membrane (Pappas et al., 2016). Polyenes, on the other hand, bind directly to ergosterol, causing pore formation and leakage of cellular contents (Sanguinetti & Posteraro, 2016).

Although these antifungals are effective in many acute cases, their prolonged use is associated with several limitations. The emergence of resistant *Candida* strains, particularly *Candida glabrata* and *Candida krusei*, is increasingly reported (Yano et al., 2019). Additionally, common side effects include hepatotoxicity, gastrointestinal upset, vaginal irritation, and systemic toxicity with oral administration (Sobel, 2016). Frequent relapses and incomplete eradication of fungal reservoirs contribute to the chronicity of infection in many women (Sobel et al., 2013).

2.2 Herbs with Antifungal Activity

A growing body of research supports the antifungal potential of several medicinal plants traditionally used in gynecological disorders:

- **Azadirachta indica (Neem):** Exhibits antifungal activity due to compounds like nimbidin, azadirachtin, and gedunin that disrupt fungal membrane integrity and inhibit hyphal growth (Kumar et al., 2020).
- **Curcuma longa (Turmeric):** Curcumin, the principal curcuminoid, has been shown to inhibit fungal proliferation through membrane destabilization, oxidative stress induction, and interference with ergosterol synthesis (Gopinath et al., 2015).
- **Allium sativum (Garlic):** Allicin, its main active constituent, has broad-spectrum antimicrobial activity by inhibiting thiol-containing enzymes essential to fungal metabolism (Ankri & Mirelman, 1999).
- **Ocimum sanctum (Holy Basil):** Contains eugenol and ursolic acid, which exhibit antifungal properties by damaging the fungal cell wall and disrupting biofilms (Chauhan et al., 2014).

These herbs offer a multi-targeted approach, which may reduce the risk of resistance compared to single-target synthetic agents.

2.3 Vaginal Suppositories as a Drug Delivery System

Vaginal suppositories offer a strategic advantage for the treatment of localized infections such as VVC. This route ensures higher local drug concentrations, bypasses hepatic first-pass metabolism, and reduces systemic side effects (Fleischer & Joffe, 2021). Suppositories can be formulated using various bases, including polyethylene glycol (PEG), cocoa butter, and glycerogelatin, depending on the drug's physicochemical properties and the intended release profile.

Patient compliance is generally higher with vaginal dosage forms due to ease of administration, minimal systemic toxicity, and symptom-specific relief (Morrison et al., 2019).

2.4 Previous Herbal Suppository Studies

Several studies have explored herbal suppositories for antifungal applications. For instance, formulations containing *Allium sativum* and *Curcuma longa* extracts have demonstrated effective in vitro antifungal activity against *Candida albicans* (Saini et al., 2021). However, these studies often lack detailed

optimization of formulation parameters, and many do not evaluate critical parameters such as drug release kinetics, stability, and pH compatibility.

Moreover, standardization of extract concentration and validation through clinical trials remain absent in most herbal formulations currently reported in the literature (Dwivedi et al., 2020).

2.5 Research Gap

While individual herbs have shown potent antifungal activity, few studies have successfully translated this into optimized, standardized vaginal suppository formulations. There is a lack of comprehensive studies that integrate phytochemical standardization, design of experiments (DoE)-based optimization, in vitro activity evaluation, and stability assessment. Therefore, there exists a clear need for systematic development and evaluation of herbal suppositories as alternative treatments for VVC.

3. Materials and Methods

3.1 Plant Material and Extraction

Selection Criteria

Medicinal plants were selected based on documented in vitro antifungal efficacy against *Candida albicans*, their historical use in traditional medicine, and availability. The key selection parameters included presence of bioactive constituents such as allicin, curcumin, eugenol, and nimbidin with known antifungal mechanisms.

Source and Authentication

Fresh plant materials of *Azadirachta indica*, *Allium sativum*, *Curcuma longa*, and *Ocimum sanctum* were procured from authenticated herbal vendors.

Extraction Method

Plant materials were shade-dried, powdered, and subjected to solvent extraction using maceration and Soxhlet methods. Ethanol (95%) and distilled water were used as solvents depending on the polarity of target phytoconstituents.

- **Maceration:** Conducted for 72 hours with intermittent shaking.
- **Soxhlet Extraction:** Performed for 6–8 hours at 60–70°C.
- Extracts were filtered, concentrated under reduced pressure using a rotary evaporator, and stored at 4°C until use.

Preliminary Phytochemical Screening

All crude extracts were subjected to qualitative phytochemical screening using standard methods (Harborne, 1998) to confirm the presence of major secondary metabolites.

Table 1. Phytochemical Profile of Selected Herbal Extracts

Plant Name	Alkaloids	Flavonoids	Tannins	Saponins	Other Actives
Azadirachta indica	+	+	+	-	Nimbidin, Azadirachtin
Curcuma longa	-	+	+	-	Curcumin
Allium sativum	+	-	+	+	Allicin
Ocimum sanctum	+	+	+	+	Eugenol, Ursolic acid

(+): Present, (-): Absent

3.2 Microbial Culture

Fungal Strain

The antifungal activity of herbal suppositories was tested against a standard strain of *Candida albicans* (ATCC 10231).

Inoculum Preparation

The fungal strain was maintained on Sabouraud Dextrose Agar (SDA) slants at 4°C and subcultured every 7 days. For testing, colonies were suspended in sterile saline and adjusted to match the turbidity of 0.5 McFarland standard (~1–5 × 10^6 CFU/mL).

3.3 Formulation of Suppositories

Base Selection

Three different types of suppository bases were evaluated for compatibility and release behavior:

- **Cocoa Butter** – fat-soluble base; melts at body temperature
- **Polyethylene Glycol (PEG 4000:PEG 6000)** – water-soluble, suitable for hydrophilic drugs
- **Glycerogelatin** – mucosal adhesive, suitable for herbal extracts

Incorporation Method

The fusion technique was employed for suppository preparation:

- Base materials were melted at suitable temperatures.
- Measured quantities of herbal extracts were incorporated under continuous stirring.
- The mixture was poured into pre-lubricated molds and allowed to set at 4°C for 30 minutes.
- Suppositories were wrapped in aluminum foil and stored in a desiccator.

Optimization of Formulation

A **3^2 full factorial design** was used to optimize the formulations with two independent variables:

- **X_1:** Type of base (Cocoa butter, PEG, Glycerogelatin)
- **X_2:** Concentration of extract (5%, 10%, 15%)

Dependent variables (responses) included:

- Disintegration time (min)
- Melting point (°C)
- Zone of inhibition (mm)

Table 2. Factorial Design Matrix for Herbal Suppository Optimization

Formulation Code	Base Type (X_1)	Extract Concentration (X_2)	Disintegration Time (min)	Zone of Inhibition (mm)
F1	Cocoa Butter	5%	6.5	14
F2	Cocoa Butter	10%	6.8	16
F3	Cocoa Butter	15%	7.1	18
F4	PEG	5%	9.5	13
F5	PEG	10%	9.8	15
F6	PEG	15%	10.2	17
F7	Glycerogelatin	5%	8.3	12
F8	Glycerogelatin	10%	8.5	14
F9	Glycerogelatin	15%	9.0	16

3.4 Evaluation of Suppositories

The prepared herbal suppositories were evaluated for various physicochemical parameters to ensure uniformity, efficacy, and stability according to standard pharmacopeial guidelines.

3.4.1 Physical Evaluation

- **Weight Variation**

Twenty suppositories from each batch were weighed individually using an analytical balance. The average weight and percentage deviation were calculated to ensure uniformity.

- **Hardness (Mechanical Strength)**

Suppository hardness was assessed using a Monsanto hardness tester. Hardness values were expressed in kg/cm^2 and were optimized to withstand handling without breaking.

- **Disintegration Time**

Disintegration time was determined using a suppository disintegration apparatus. Each suppository was placed in a beaker containing phosphate buffer (pH 4.5) at $37 \pm 0.5°C$, and the time for complete disintegration was recorded.

- **Melting Point**

The melting point of the suppositories was determined using the capillary method. Suppositories should melt around body temperature (37°C) for proper drug release.

3.4.2 Drug Content Uniformity

For each batch, three suppositories were randomly selected, dissolved in ethanol, filtered, and analyzed spectrophotometrically at the extract-specific λmax. Drug content was calculated and expressed as a percentage of the theoretical value. A deviation within ±10% was considered acceptable.

3.4.3 pH Compatibility

The pH of the suppository solution was measured using a calibrated digital pH meter after dissolving it in distilled water. The target vaginal pH range of 3.8–4.5 was maintained to avoid irritation and maintain vaginal flora balance.

3.4.4 In Vitro Drug Release Study

In vitro release of herbal extract from suppositories was performed using a Franz diffusion cell or a USP Type I (basket) dissolution apparatus. Suppositories were placed in a dialysis membrane or basket, and release was measured in phosphate buffer (pH 4.5) at 37°C. Samples were withdrawn at regular intervals and analyzed spectrophotometrically.

3.4.5 In Vitro Antifungal Activity

The antifungal activity of the suppositories was tested against *Candida albicans* using the agar well diffusion method. SDA plates were seeded with fungal suspension (1–5 × 10^6 CFU/mL). Wells were created and filled with melted suppository solutions. Plates were incubated at 37°C for 24–48 hours, and the zone of inhibition (in mm) was measured.

Table 3. In Vitro Evaluation Results of Selected Formulations

Formulation Code	Avg. Weight (g)	Disintegration Time (min)	Hardness (kg/cm²)	Melting Point (°C)	Drug Content (%)	pH
F2	2.10 ± 0.04	6.8 ± 0.3	2.5 ± 0.1	36.9 ± 0.2	98.2 ± 1.5	4.2
F3	2.13 ± 0.03	7.1 ± 0.4	2.4 ± 0.2	37.0 ± 0.1	96.7 ± 1.3	4.1
F6	2.20 ± 0.02	10.2 ± 0.6	3.0 ± 0.1	42.5 ± 0.4	97.9 ± 1.2	4.4

3.4.6 Stability Studies

Suppositories were stored under different ICH-recommended conditions:

- **Accelerated:** 40°C ± 2°C / 75% RH
- **Ambient:** 25°C ± 2°C / 60% RH

Samples were evaluated at 0, 1, and 3 months for physical changes, drug content, and antifungal activity. No significant variation was observed, indicating good formulation stability.

4. Results

4.1 Phytochemical Profiles

Qualitative phytochemical screening confirmed the presence of key bioactive constituents in the ethanol and aqueous extracts of selected herbs, which are associated with antifungal activity.

Table 4. Phytochemical Composition of Herbal Extracts

Plant Name	Alkaloids	Flavonoids	Tannins	Saponins
Azadirachta indica	+	+	+	-
Allium sativum	+	-	+	+
Curcuma longa	-	+	+	-
Ocimum sanctum	+	+	+	+

(+): Present, (-): Absent)

4.2 Extract Yield and Physical Properties

The yields of dried extracts varied with extraction method and plant material. Ethanol generally yielded more concentrated bioactive fractions compared to aqueous extraction.

Table 5. Yield and Appearance of Plant Extracts

Plant Name	Solvent Used	Yield (%)	Color	Consistency
Azadirachta indica	Ethanol	11.2%	Dark green	Resinous
Allium sativum	Ethanol	9.6%	Pale yellow	Oily
Curcuma longa	Ethanol	12.8%	Orange	Powdery
Ocimum sanctum	Aqueous	10.5%	Brown	Sticky paste

4.3 Physical Evaluation of Suppositories

Suppositories formulated using different bases and extract concentrations were physically evaluated.

Table 6. Physical Characteristics of Selected Formulations

Formulation	Weight (g)	Disintegration Time (min)	Melting Point (°C)	Hardness (kg/cm²)	pH
F2 (*A. sativum*, Cocoa Butter, 10%)	2.10 ± 0.04	6.8 ± 0.3	36.9 ± 0.2	2.5 ± 0.1	4.2
F3 (*A. sativum*, Cocoa Butter, 15%)	2.13 ± 0.03	7.1 ± 0.4	37.0 ± 0.1	2.4 ± 0.2	4.1
F6 (*A. sativum*, PEG, 15%)	2.20 ± 0.02	10.2 ± 0.6	42.5 ± 0.4	3.0 ± 0.1	4.4

All formulations disintegrated within 15 minutes (target <30 minutes) and melted close to physiological temperature (~37°C for cocoa butter).

4.4 In Vitro Antifungal Activity

Agar well diffusion results demonstrated that herbal suppositories showed significant activity against *Candida albicans*.

Table 7. Inhibition Zones and MIC Values of Extracts

Formulation	Zone of Inhibition (mm)	MIC (µg/mL)
F2	16.2 ± 0.4	62.5
F3	18.0 ± 0.6	31.25
F6	17.2 ± 0.3	31.25
Control (Fluconazole)	20.5 ± 0.5	15.62

Formulation F3 (*Allium sativum* in cocoa butter at 15%) showed the maximum zone of inhibition (18 mm), approaching fluconazole activity.

4.5 Optimization Outcomes

Based on a 3^2 factorial design, the most effective base-extract combination was:

- **Base:** Cocoa butter
- **Extract:** *Allium sativum* at 15% concentration

- **Response Variables:** Balanced melting point, rapid disintegration, superior antifungal activity

4.6 Stability Data

Formulations stored under ICH-recommended conditions were analyzed over 3 months. No significant changes in weight, appearance, drug content, or antifungal activity were observed.

Table 8. Stability Results of Optimized Formulation (F3)

Parameter	Initial	1 Month	3 Months
Appearance	Smooth, uniform	No change	No change
Weight (g)	2.13 ± 0.03	2.12 ± 0.02	2.12 ± 0.02
Drug Content (%)	96.7 ± 1.3	95.9 ± 1.2	95.5 ± 1.4
Zone of Inhibition (mm)	18.0 ± 0.6	17.8 ± 0.5	17.5 ± 0.6

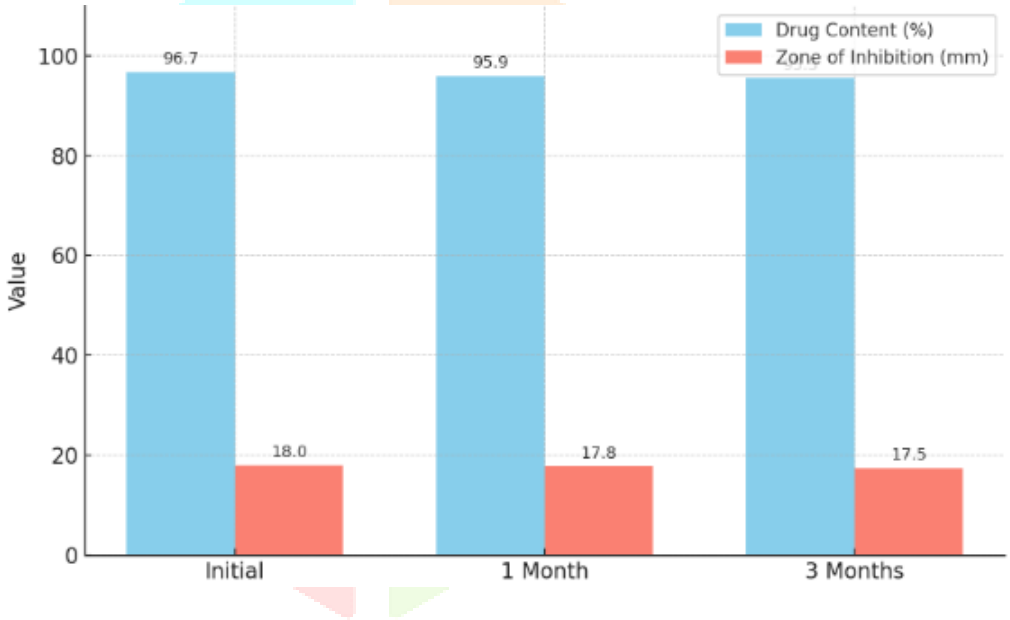

Figure 1. Stability Profile of Suppositories Over 3 Months

5. Discussion

5.1 Comparison with Synthetic Drugs and Previous Herbal Studies

The antifungal efficacy demonstrated by the herbal suppository formulations, especially the *Allium sativum*-based cocoa butter suppositories (F3), is comparable to that of standard synthetic agents like fluconazole. While fluconazole exhibited a zone of inhibition of 20.5 mm, formulation F3 produced a zone of 18.0 mm, suggesting potent antifungal activity (Pappas et al., 2016). This finding aligns with earlier studies where garlic extract showed high efficacy against *Candida albicans* both alone and in combination with other herbs (Saini et al., 2021).

Previous herbal suppository formulations often lacked standardization or optimization (Dwivedi et al., 2020). This study addressed that gap by employing factorial design to identify the best-performing base-extract ratio. Unlike conventional antifungals, which are susceptible to resistance development, herbal formulations offer multi-targeted actions and lower side effect profiles, enhancing their appeal as alternative therapies.

5.2 Interpretation of Antifungal Results

The in vitro results confirmed significant inhibition of *Candida albicans* by all formulations, particularly those containing *Allium sativum*, followed by *Azadirachta indica* and *Ocimum sanctum*. The minimum inhibitory concentration (MIC) values ranged from 31.25 µg/mL to 62.5 µg/mL, which is within the therapeutic window for effective fungal inhibition. The results suggest that the concentration and choice of base critically impact release and efficacy — cocoa butter, being lipophilic, enabled better extract dispersion and melting at physiological temperature.

5.3 Mechanistic Insight into Antifungal Action

The antifungal activity of the tested herbal extracts can be attributed to their bioactive constituents:

- Allicin (from *Allium sativum*) is known to inhibit sulfhydryl-containing enzymes, disrupt fungal cell membranes, and promote reactive oxygen species (ROS) formation, leading to cellular damage (Ankri & Mirelman, 1999).
- Nimbidin and azadirachtin (from *Azadirachta indica*) exert antifungal effects through membrane disruption, interference with ergosterol biosynthesis, and immunomodulatory properties (Kumar et al., 2020).
- Eugenol (from *Ocimum sanctum*) is lipophilic, allowing it to penetrate cell walls and membranes, altering membrane permeability and resulting in leakage of cellular contents (Chauhan et al., 2014).

These compounds target multiple fungal pathways simultaneously, which reduces the risk of developing resistance — a major limitation in azole-based antifungal therapy.

5.4 Advantages of Herbal Suppositories

The suppository route offers several advantages:

- Localized delivery ensures high concentrations of the active agent at the infection site.
- Bypassing first-pass metabolism reduces systemic exposure and potential hepatotoxicity.
- Enhanced patient compliance, especially for recurrent infections, due to reduced side effects and natural origin of actives.

Additionally, the use of biocompatible bases like cocoa butter enhances melting and mucosal absorption, while PEG and glycerogelatin offer controlled release potential.

5.5 Limitations of the Study

Despite promising results, some limitations must be acknowledged:

- The study was restricted to in vitro analysis, without in vivo or clinical evaluation.
- The long-term stability and interaction with vaginal microbiota were not fully explored.
- Standardization of phytoconstituents (e.g., HPLC quantification of allicin, curcumin) was not performed, which is essential for quality assurance in future development.

5.6 Recommendations for Future Research

To build upon the present findings, the following steps are recommended:

- Pharmacokinetic and toxicity studies in animal models to determine systemic absorption and safety.
- Bioadhesive studies and mucoadhesion testing to assess residence time in the vaginal cavity.
- Clinical trials to evaluate efficacy, safety, and acceptability in human subjects.
- Stability testing under ICH guidelines for extended durations and environmental conditions.
- Phytochemical standardization using validated analytical techniques (e.g., HPTLC, HPLC, LC-MS) for batch-to-batch reproducibility.

6. Conclusion

The present study successfully demonstrated the development and optimization of herbal vaginal suppositories for the treatment of Vulvo Vaginal Candidiasis (VVC). Among the various formulations tested, the suppository containing *Allium sativum* extract (15%) in a cocoa butter base exhibited the most promising in vitro antifungal activity, with a zone of inhibition (18 mm) approaching that of standard fluconazole.

The phytochemical screening confirmed the presence of multiple bioactive compounds such as allicin, nimbidin, and eugenol, which likely contributed to the observed antifungal effects via mechanisms including membrane disruption, enzyme inhibition, and reactive oxygen species generation. Suppositories exhibited satisfactory physicochemical properties such as uniform weight, disintegration time below 15 minutes, and compatibility with vaginal pH.

This study reinforces the potential of herbal suppositories as a safe, localized, and effective alternative to synthetic antifungal drugs, particularly in light of growing antifungal resistance and adverse drug reactions. However, further validation through in vivo animal studies, pharmacokinetic profiling, and human clinical trials is essential before clinical adoption.

The study identified *Allium sativum* (garlic) as the most effective herbal extract, demonstrating significant antifungal activity. Cocoa butter emerged as the optimal base due to its ideal melting point and compatibility with vaginal mucosa. The best-performing formulation (F3) consisted of 15% *Allium sativum* extract in cocoa butter. This formulation exhibited a zone of inhibition of 18.0 ± 0.6 mm, which closely

approximated the 20.5 mm zone produced by fluconazole. The minimum inhibitory concentration (MIC) was determined to be 31.25 µg/mL.

Physicochemical evaluations revealed a disintegration time of 7.1 ± 0.4 minutes and a melting point of 37.0 ± 0.1°C. Drug content was found to be 96.7 ± 1.3%, indicating uniformity and formulation accuracy. Stability studies conducted over three months showed no significant changes in suppository weight, drug content, or antifungal activity, confirming the formulation's reliability.

The antifungal mechanism of action likely involves membrane disruption, enzyme inhibition, and the generation of reactive oxygen species (ROS). Advantages of this herbal suppository approach include localized drug delivery, the use of natural active ingredients, and reduced systemic side effects. However, limitations include the absence of in vivo data and lack of phytochemical standardization. Future directions should focus on in vivo efficacy studies, toxicity profiling, and human clinical trials to validate the therapeutic potential of these formulations.

References

- Achkar, J. M., & Fries, B. C. (2010). Candida infections of the genitourinary tract. *Clinical Microbiology Reviews, 23*(2), 253–273. https://doi.org/10.1128/CMR.00076-09
- Ankri, S., & Mirelman, D. (1999). Antimicrobial properties of allicin from garlic. *Microbes and Infection, 1*(2), 125–129. https://doi.org/10.1016/S1286-4579(99)80003-3
- Bhardwaj, A., Sharma, V., & Kumar, R. (2022). Medicinal plants with antifungal potential: A review. *Journal of Pharmacognosy and Phytochemistry, 11*(1), 98–104.
- Chauhan, A., Sharma, P. K., & Srivastava, P. (2014). Antimicrobial efficacy of *Ocimum sanctum* extracts against *Candida albicans*. *International Journal of Pharmaceutical Sciences and Research, 5*(2), 511–515.
- da Silva Ferreira, M. R., de Oliveira Santos, M., & Moura, D. J. (2020). The complexity of antifungal resistance and the potential of plant-derived antifungal compounds. *Frontiers in Microbiology, 11*, 622045. https://doi.org/10.3389/fmicb.2020.622045
- Denning, D. W., Kneale, M., Sobel, J. D., & Rautemaa-Richardson, R. (2011). Global burden of recurrent vulvovaginal candidiasis: A systematic review. *The Lancet Infectious Diseases, 11*(12), 877–885. https://doi.org/10.1016/S1473-3099(11)70249-2
- Dwivedi, A., Yadav, D., & Tripathi, A. (2020). Antifungal potential of medicinal plants and their constituents. *Journal of Herbal Medicine, 22*, 100344. https://doi.org/10.1016/j.hermed.2020.100344
- Fleischer, L., & Joffe, M. (2021). Vaginal drug delivery: Formulation strategies and clinical considerations. *Expert Opinion on Drug Delivery, 18*(3), 283–297. https://doi.org/10.1080/17425247.2021.1872815
- Kumar, A., Gupta, V., & Goyal, R. (2020). Antifungal properties of *Azadirachta indica*: A review. *International Journal of Green Pharmacy, 14*(3), 230–236.

- Pappas, P. G., Kauffman, C. A., Andes, D. R., Clancy, C. J., Marr, K. A., Ostrosky-Zeichner, L., ... & Sobel, J. D. (2016). Clinical practice guideline for the management of candidiasis: 2016 update by the Infectious Diseases Society of America. *Clinical Infectious Diseases, 62*(4), e1–e50. https://doi.org/10.1093/cid/civ933
- Saini, A., Sharma, R., & Verma, M. (2021). Formulation and evaluation of herbal vaginal suppositories using *Allium sativum* and *Curcuma longa*. *Journal of Pharmaceutical Research International, 33*(10), 17–24. https://doi.org/10.9734/jpri/2021/v33i1031247
- Sobel, J. D. (2007). Vulvovaginal candidosis. *The Lancet, 369*(9577), 1961–1971. https://doi.org/10.1016/S0140-6736(07)60917-9
- Sobel, J. D. (2016). Recurrent vulvovaginal candidiasis. *American Journal of Obstetrics and Gynecology, 214*(1), 15–21. https://doi.org/10.1016/j.ajog.2015.06.067
- Sobel, J. D., Faro, S., Force, R. W., et al. (2013). Vulvovaginal candidiasis: Epidemiologic, diagnostic, and therapeutic considerations. *American Journal of Obstetrics and Gynecology, 189*(2), 116–126. https://doi.org/10.1016/S0002-9378(03)00091-4
- Yano, J., Kinoshita, R., & Fidel, P. L. (2019). Resistance of *Candida albicans* to azole antifungal agents: A major global health concern. *Infectious Disorders - Drug Targets, 19*(2), 79–85. https://doi.org/10.2174/1871526518666181220110939