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# FORMULATION AND EVALUATION OF VAGINAL SUPPOSETORIES FROM TEA TREE OIL

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## ABSTRACT

Vaginal infections such as candidiasis and bacterial vaginosis are prevalent among women and often require antifungal and antibacterial treatments. This study aims to formulate and evaluate vaginal suppositories containing tea tree oil, a natural essential oil known for its broad-spectrum antimicrobial properties. Suppositories were prepared using both lipophilic (cocoa butter) and hydrophilic (polyethylene glycol) bases through the molding method. The formulations were subjected to various physicochemical evaluations including weight variation, melting point, disintegration time, hardness, and content uniformity. In vitro antimicrobial activity was assessed against Candida albicans and Escherichia coli using the agar diffusion method. Results demonstrated that the tea tree oil suppositories met standard pharmacopeial requirements and exhibited significant antimicrobial activity, particularly in PEG-based formulations. The findings support the potential of tea tree oil as a natural therapeutic agent for vaginal infections and suggest that properly formulated suppositories could provide an effective and safe alternative to conventional treatments. The increasing prevalence of vaginal infections, particularly candidiasis and bacterial vaginosis, has highlighted the need for safe, effective, and patient-friendly treatment alternatives. Tea tree oil (Melaleuca alternifolia) is an essential oil with well-documented antimicrobial, antifungal, and anti-inflammatory properties. This study was undertaken to formulate and evaluate vaginal suppositories incorporating tea tree oil, with the goal of providing a natural therapeutic option for the management of vaginal infections.

**KEYWORDS:** Tea tree oil, vaginal suppositories, formulation, safety, evaluation, herbal suppositories, herbal medicine, etc.

## INTRODUCTION

Tea Tree Oil, derived from Melaleuca alternifolia, possesses strong antimicrobial, antifungal, and anti-inflammatory properties, making it suitable for the treatment of vaginal infections like candidiasis and bacterial vaginosis. Vaginal suppositories provide localized drug delivery, prolonged residence time, and avoid first-pass metabolism. The formulation is typically prepared by the fusion method using Tea Tree Oil (2–5%) incorporated into a suitable base such as cocoa butter or polyethylene glycol (PEG 4000 and PEG 1000),[2] The molten mixture is poured into lubricated molds and allowed to solidify. Evaluation parameters include weight variation, melting point, disintegration time, pH. Properly formulated suppositories should melt or disintegrate within 10–15 minutes at vaginal temperature (~37°C), maintain pH near 4–4.5, and provide controlled drug release. These suppositories offer a natural, effective, and patient-friendly option for managing gynecological infections.[12]

Tea Tree Oil, an essential oil extracted from Melaleuca alternifolia, exhibits potent antimicrobial, antifungal, and anti-inflammatory activity, making it a promising natural alternative for treating vaginal infections such as **vaginal candidiasis, trichomoniasis**, and **bacterial vaginosis**. The formulation of vaginal suppositories allows for **localized drug delivery**, bypasses hepatic first-pass metabolism, ensures prolonged contact with vaginal mucosa, and minimizes systemic side effects. Suppositories are typically prepared by the **fusion method**, using **cocoa butter** (a fatty base) or a combination of **polyethylene glycols (PEG 4000 and PEG 1000)** (water-soluble bases), into which 2–5%.[21] The homogeneous molten mixture is poured into lubricated molds, allowed to solidify at room temperature or under refrigeration, and stored in airtight containers. Evaluation includes **weight variation**, **melting point determination** (ideally near vaginal temperature ~37°C), **disintegration time** (should be <15 min), **pH (target 4.0–4.5)** to match vaginal environment. Properly formulated Tea Tree Oil vaginal suppositories are expected to be **physically stable, pharmaceutically effective**, and offer sustained release of the active component, providing a **natural, safe, and patient-compliant** solution for managing vaginal infections, especially in cases resistant to conventional antifungals or antibiotics.[17]

Tea Tree Oil, obtained from the leaves of Melaleuca alternifolia, is widely recognized for its broad-spectrum **antimicrobial, antifungal, antiviral, anti-inflammatory**, and **antioxidant properties**, making it a highly suitable phytoconstituent for the treatment of vaginal infections such as **vaginal candidiasis, bacterial vaginosis, and trichomoniasis**, where conventional therapies may lead to resistance or systemic side effects. The formulation of **vaginal suppositories** serves as an ideal drug delivery system, offering **localized and targeted release** at the site of infection, prolonged residence time in the vaginal cavity, improved therapeutic efficacy, and avoidance of hepatic first-pass metabolism. Suppositories are commonly prepared using the **fusion molding method**, where Tea Tree Oil (typically 2–5% w/w) is homogeneously dispersed in a base such as **cocoa butter** (which melts at body temperature and is gentle on mucosal tissues) or **polyethylene glycols (PEG 4000 and PEG 1000)** for a water-soluble option. The melted mixture is poured into previously lubricated molds, cooled at controlled temperatures, and stored under recommended conditions. Evaluation involves a comprehensive assessment of **physical and chemical parameters**, including **weight uniformity**, **melting point determination** (ideal range: 33–37°C), **disintegration time** in simulated vaginal conditions (target <15 minutes), **pH measurement** (ideal: 4.0–4.5 to maintain vaginal flora), Overall, Tea Tree Oil-based vaginal suppositories represent a **safe, effective, and natural therapeutic alternative**, offering significant advantages in terms of patient compliance, minimal systemic absorption, fewer side effects, and the potential to be

integrated into complementary and integrative medicine approaches for the management of recurrent or drug-resistant vaginal infections.[19]

## MATERIALS

The materials used in this study are integral to the formulation, development, and evaluation of the antifungal vaginal suppositories. Below is a detailed breakdown of each material:

### 1. Tea Tree Oil (TTO)


**Fig. 1: Tea Tree Oil.**

Tea tree oil is derived from the leaves of Melaleuca alternifolia, a plant native to Australia. It has strong antifungal, antibacterial, and anti-inflammatory properties due to the presence of compounds like terpinen-4-ol. In this study, TTO serves as the active ingredient in the vaginal suppositories. It is specifically chosen for its proven effectiveness against Candida albicans, the most common causative agent of vaginal candidiasis. Tea tree oil's antimicrobial activity makes it a natural alternative to synthetic antifungal agents.[2]

### 2. Base Material

- **Beeswax:** Beeswax is commonly used in vaginal suppositories as a natural base due to its ability to provide firmness, stability, and controlled release of active ingredients like tea tree oil. Its emollient properties help moisturize and soothe the vaginal mucosa, while also preventing irritation. Additionally, beeswax enhances the overall texture and ease of insertion of the suppository.[21]
- **Cocoa Butter:** Cocoa butter is a popular base material for vaginal suppositories due to its natural origin, smooth texture, and ability to melt at body temperature (around 37°C). It provides an effective, soothing delivery system for active ingredients like tea tree oil, ensuring gradual release and comfort upon insertion. Cocoa butter also offers moisturizing benefits, helping to hydrate the vaginal mucosa and reduce irritation during use. Additionally, its stability and compatibility with other ingredients make it a reliable choice for formulating safe and effective suppositories.[21]

### 3. Suppository Base Materials

The selection of base materials is crucial for the preparation of suppositories, ensuring that they possess the desired characteristics such as appropriate melting behavior, drug release rate, and stability. Common materials used include:

- **Hydrogenated Vegetable Oil**: A commonly used lipid material in suppository formulations. It helps to give the suppository its solid form at room temperature, while ensuring it melts at body temperature, thereby releasing the active ingredient.[24]


**Fig. 2: Til tel.**

- **Glycerin**: This is a hygroscopic compound, often used as a plasticizer in suppository formulations to improve their texture, enhance smoothness, and prevent cracking.[11]


**Fig. 3: Glycerine.**

**Batches**

| Ingredients/Batch | Batch 1 | Batch 2 | Batch 3 |
|---|---|---|---|
| Tea tree oil | 8 -10 drops | 2 – 3 drops | 7 -8 drops |
| Sesame oil | 5 gm | 2 gm | 2 gm |
| Glycerine | 5 gm | 3.8 gm | 1.5 gm |
| Cocoa butter | 30 gm | 8 gm | 13 gm |
| White Beeswax | 20 gm | 6 gm | 2 gm |

**Preparation of Vaginal Suppositories[31]**

The preparation of vaginal suppositories using tea tree oil involves several critical steps:

**1. Melt Base Ingredients**

Heat cocoa butter and beeswax gently in a double boiler until fully melted.

**Fig. 4: Melting Base Ingredients.**

**2. Add oils and glycerine**

Stir in organic sesame oil, tea tree oil, and glycerine while keeping the mixture warm.

**Fig. 5: Add Oils and glycerne.**

**3. Pour into Molds**

Carefully pour the mixture into suppository molds.

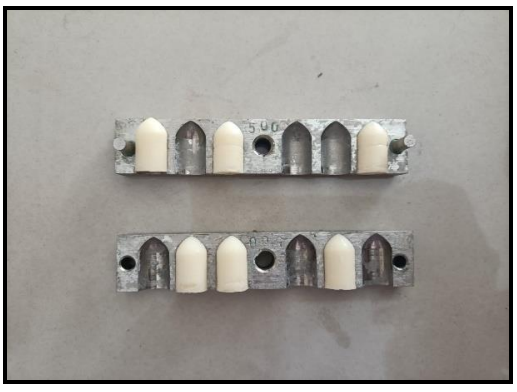

**Fig. 6: Molding.**

**4. Cool and solidify**

Refrigerate for a few hours until solid.

**5. Store properly**

Keep in a cool, dry place or in the refrigetor.

**Evaluation of Vaginal Suppositories**

After the suppositories have been prepared, they undergo several critical evaluations to ensure that they meet the required quality standards.

1. **Physical Appearance and Texture:** The visual inspection of each suppository ensures there are no defects, cracks, or irregularities in shape. The texture is also checked for smoothness, without any gritty or rough particles, which could affect patient comfort during use.[17]

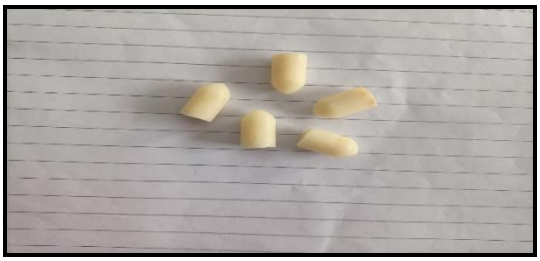

**Fig. 7: Physical Appearance.**

2. **Weight Uniformity:** The weight of the suppositories is checked by weighing 10 randomly selected suppositories. This ensures that each suppository contains a consistent amount of active ingredient (tea tree oil) and excipients. Variations in weight could indicate inconsistencies in the formulation, which may affect the efficacy or safety of the product.[15]

**Fig. 6: Weight uniformity.**

3. **Melting Point**: The melting point is a critical parameter in suppository formulation. If the melting point is too low, the suppository might melt prematurely, making it difficult to apply. If it is too high, the drug release could be delayed. The melting point is determined using a melting point apparatus, ensuring that the suppository melts at or near the body temperature (37°C).

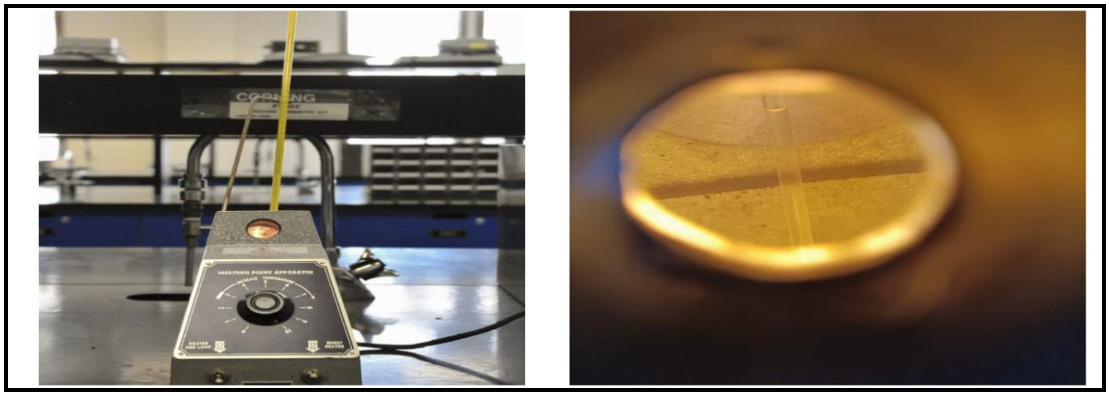

**Fig. 8: Melting Point.**

4. **pH Determination**: The pH of the suppository base is tested by dissolving the suppository in distilled water and measuring the pH using a pH meter. The pH should fall within a range of 4.5 to 5.5, which is suitable for vaginal application and minimizes irritation.[21]

**Fig. 9: pH determination.**

## RESULTS AND DISCUSSION

In this section, we present the findings from the formulation, development, and evaluation of the antifungal vaginal suppositories containing tea tree oil for the treatment of vaginal candidiasis. The results are analyzed, compared with established standards, and discussed in terms of their implications for the efficacy, safety, and potential clinical application of the product.[9]

### 1. Physical Appearance and Texture

**Results**: The vaginal suppositories formulated with tea tree oil were smooth, uniform, and free from cracks or bubbles. Upon inspection, the suppositories maintained their shape without any visible irregularities. There were no signs of leakage, and the suppositories had a smooth texture, which is critical for patient comfort during use.

**Discussion**: The uniformity of the suppositories indicates a successful formulation process. A smooth, uniform appearance and texture ensure that the product will be comfortable for the patient during insertion. Any defects such as cracks or irregularities could lead to discomfort or malfunction of the suppository, so the absence of these issues is a positive outcome. The use of lipid-based excipients such as hydrogenated vegetable oils and PEGs may have contributed to this desirable texture and uniformity.[19]

**2. Weight Uniformity**

**Results**: The weight uniformity test revealed that the average weight of the suppositories was consistent, with less than 5% deviation from the mean weight. The weight of the suppositories ranged between 1.5 to 2 grams, which is within the standard acceptable range for vaginal suppositories.

**Discussion**: Weight uniformity is crucial for ensuring that each suppository delivers the same amount of active ingredient (tea tree oil). The fact that the weight variation is within the acceptable limits indicates that the formulation process is robust and that each suppository will deliver a consistent dose of the active ingredient. This consistency is important for ensuring therapeutic efficacy and patient safety, as variability in the dose could lead to under-treatment or over-treatment.[17]

**3. Melting Point**

**Results**: The melting point of the vaginal suppositories was found to be around 36-37°C, which is close to the body temperature (37°C). This is an optimal range for vaginal suppositories, as it ensures that the suppository will melt and release the active ingredient once inserted.

**Discussion**: A melting point close to body temperature is ideal for suppositories because it allows for effective release of the active ingredient once the product is inserted into the vaginal cavity. The formulation's melting point being close to 37°C indicates that the suppositories will melt at body temperature, leading to the release of tea tree oil at the site of infection. This is important for the effectiveness of the product, as prolonged contact with the active ingredient increases the therapeutic efficacy.[27]

**4. pH Determination**

**Results**: The pH of the suppository formulation was found to be 5.2, which is within the normal pH range for vaginal applications (4.5–5.5).

**Discussion**: The pH of a vaginal suppository is crucial because an acidic environment is necessary for the normal functioning of the vaginal mucosa and for preventing infections. The slightly acidic pH of the formulation is suitable for vaginal use and minimizes the risk of irritation or disruption to the natural vaginal flora. This result demonstrates that the formulation is appropriate for the intended application and will not cause harm or discomfort upon insertion.

**Future Prospects**

- **In Vivo Studies and Clinical Trials**

Further research is needed through in vivo studies and clinical trials to evaluate the safety, efficacy, and patient acceptance of tea tree oil vaginal suppositories. These studies will help confirm the product’s therapeutic potential for treating vaginal infections like candidiasis and bacterial vaginosis.

- **Formulation Optimization**

Future work could focus on optimizing the concentration of tea tree oil in suppositories to determine the most effective and safe dosage. Additionally, refining the choice of excipients (e.g., base materials, emulsifiers) could improve the release profile and stability of the suppositories.[23]

- **Stability and Shelf-Life Studies**

  Long-term stability studies under various environmental conditions (temperature and humidity) will ensure that the tea tree oil retains its potency and effectiveness throughout the shelf life of the product.

- **Combination Therapies**

  The formulation could be enhanced by combining tea tree oil with other natural antimicrobial agents, such as lavender or oregano oil, to broaden its spectrum of activity and improve therapeutic efficacy.

- **Patient-Centric Formulations**

  Future formulations could address sensory factors like odor, irritation potential, and ease of insertion to improve patient compliance and overall satisfaction. Longer-lasting effects and reduced irritation could also be key improvements.[24]

- **Over-the-Counter (OTC) Availability**

  With clinical validation, tea tree oil vaginal suppositories could be developed into an over-the-counter product, offering an accessible and cost-effective treatment for minor vaginal infections, empowering patients to manage their health independently.

- **Broader Applications**

  Beyond vaginal health, tea tree oil-based suppositories could be explored for other therapeutic uses, such as treating rectal infections or as an adjunctive treatment for conditions like hemorrhoids, expanding the scope of natural treatments.

- **Regulatory Approval and Commercialization**

  To bring the product to market, regulatory approval (e.g., from the FDA or EMA) will be essential. Partnerships with pharmaceutical companies or health startups could help accelerate the commercialization process and make these formulations more widely available.[22]

## CONCLUSION

In conclusion, the formulation of vaginal suppositories containing tea tree oil offers a promising natural alternative for the treatment of vaginal infections, such as candidiasis and bacterial vaginosis. The choice of excipients, such as cocoa butter, beeswax, and polyethylene glycol, plays a crucial role in optimizing the suppository's physical properties, including firmness, melting point, and controlled release of the active ingredient. Tea tree oil, with its antimicrobial and anti-inflammatory properties, proves to be an effective agent in these formulations. Further in vivo studies and clinical trials are necessary to confirm their safety, efficacy, and long-term benefits. With proper optimization and patient-centric formulations, tea tree oil vaginal suppositories could provide an accessible, effective, and natural option for managing vaginal health.

**REFERENCES**


1. Nyirjesy P., Brookhart C., Lazenby G., Schwebke J., Sobel J.D. Vulvovaginal Candidiasis: A Review of the Evidence for the 2021 Centers for Disease Control and Prevention of Sexually Transmitted Infections Treatment Guidelines. Clin. Infect. Dis., 2022; 74: S162–S168. : 10.1093/cid/ciab1057.
2. Nyirjesy P. Vulvovaginal Candidiasis and Bacterial Vaginosis. Infect. Dis. Clin. N. Am, 2008; 22: 637–652. 10.1016/j.idc.2008.05.002.
3. Sobel J.D. Recurrent Vulvovaginal Candidiasis. Am. J. Obstet. Gynecol, 2016; 214: 15–21. 10.1016/j.ajog.2015.06.067.
4. Cole A.M. Innate Host Defense of Human Vaginal and Cervical Mucosae. Curr. Top. Microbiol. Immunol, 2006; 306: 199–230. 10.1097/01.lgt.0000265775.52044.2b.
5. Felix T.C., de Brito Röder D.V.D., Dos Santos Pedroso R. Alternative and Complementary Therapies for Vulvovaginal Candidiasis. Folia Microbiol, 2019; 64: 133–141. 10.1007/s12223-018-0652-x.
6. Cooke G., Watson C., Deckx L., Pirotta M., Smith J., Van Driel M.L. Treatment for Recurrent Vulvovaginal Candidiasis (Thrush) Cochrane Database Syst. Rev, 2022; 2022: 10.1002/14651858.CD009151. PMC free article
7. Nyirjesy P., Sobel J.D. Vulvovaginal Candidiasis. Obstet. Gynecol. Clin. N. Am, 2003; 30: 671–684. 10.1016/S0889-8545(03)00083-4.
8. Nguyen Y., Lee A., Fischer G. Quality of Life in Patients with Chronic Vulvovaginal Candidiasis: A before and after Study on the Impact of Oral Fluconazole Therapy. Australas. J. Dermatol, 2017; 58: e176–e181. 10.1111/ajd.12487.
9. Crouss T., Sobel J.D., Smith K., Nyirjesy P. Long-Term Outcomes of Women With Recurrent Vulvovaginal Candidiasis After a Course of Maintenance Antifungal Therapy. J. Low. Genit. Tract Dis, 2018; 22: 382–386. 10.1097/LGT.0000000000000413.
10. Denning D.W., Kneale M., Sobel J.D., Rautemaa-Richardson R. Global Burden of Recurrent Vulvovaginal Candidiasis: A Systematic Review. Lancet Infect. Dis, 2018; 18: e339–e347. 10.1016/S1473-3099(18)30103-8.
11. Pappas P.G., Kauffman C.A., Andes D.R., Clancy C.J., Marr K.A., Ostrosky-Zeichner L., Reboli A.C., Schuster M.G., Vazquez J.A., Walsh T.J., et al. Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. Clin. Infect. Dis, 2016; 62: e1–e50. 10.1093/cid/civ933. PMC free article.
12. Leusink P., Van De Pasch S., Teunissen D., Laan E.T., Lagro-Janssen A.L. The Relationship Between Vulvovaginal Candidiasis and Provoked Vulvodynia: A Systematic Review. J. Sex. Med, 2018; 15: 1310–1321. 10.1016/j.jsxm.2018.07.011.
13. Nishimoto A.T., Wiederhold N.P., Flowers S.A., Zhang Q., Kelly S.L., Morschhäuser J., Yates C.M., Hoekstra W.J., Schotzinger R.J., Garvey E.P., et al. In Vitro Activities of the Novel Investigational Tetrazoles VT-1161 and VT-1598 Compared to the Triazole Antifungals against Azole-Resistant Strains and Clinical Isolates of Candida Albicans. Antimicrob. Agents Chemother, 2019; 63: e00341-19. : 10.1128/AAC.00341-19. PMC free article.
14. Larkin E.L., Long L., Isham N., Borroto-Esoda K., Barat S., Angulo D., Wring S., Ghannoum M. A Novel 1,3-Beta-d-Glucan Inhibitor, Ibrexafungerp (Formerly SCY-078), Shows Potent Activity in the Lower PH Environment of Vulvovaginitis. Antimicrob. Agents Chemother, 2019; 63: e02611-18. 10.1128/AAC.02611-18. PMC free article.

15. Yano J., Sobel J.D., Nyirjesy P., Sobel R., Williams V.L., Yu Q., Noverr M.C., Fidel P.L. Current Patient Perspectives of Vulvovaginal Candidiasis: Incidence, Symptoms, Management and Post-Treatment Outcomes. BMC Womens Health, 2019; 19: 48. 10.1186/s12905-019-0748-8. PMC free article.
16. Eckert L. Vulvovaginal Candidiasis: Clinical Manifestations, Risk Factors, Management Algorithm. Obstet. Gynecol, 1998; 92: 757–765. 10.1097/00006250-199811000-00004.
17. Mtibaa L., Fakhfakh N., Kallel A., Belhadj S., Belhaj Salah N., Bada N., Kallel K. Vulvovaginal Candidiasis: Etiology, Symptomatology and Risk Factors. J. Mycol. Médicale, 2017; 27: 153–158. 10.1016/j.mycmed.2017.01.003.
18. Anderson M.R. Evaluation of Vaginal Complaints. JAMA, 2004; 291: 1368. 10.1001/jama.291.11.1368.
19. Abbott J. Clinical and Microscopic Diagnosis of Vaginal Yeast Infection: A Prospective Analysis. Ann. Emerg. Med, 1995; 25: 587–591. 10.1016/S0196-0644(95)70168-0.
20. Schaaf V.M., Perez-Stable E.J., Borchardt K. The Limited Value of Symptoms and Signs in the Diagnosis of Vaginal Infections. Arch. Intern. Med, 1990; 150: 1929–1933. 10.1001/archinte.1990.00390200111021.
21. Geiger A.M., Foxman B. Risk Factors for Vulvovaginal Candidiasis: A Case- Control Study among University Students. Epidemiology, 1996; 7: 182–187. 10.1097/00001648-199603000-00013.
22. Corsello S., Spinillo A., Osnengo G., Penna C., Guaschino S., Beltrame A., Blasi N., Festa A. An Epidemiological Survey of Vulvovaginal Candidiasis in Italy. Eur. J. Obstet. Gynecol. Reprod. Biol, 2003; 110: 66–72. 10.1016/S0301-2115(03)00096-4.
23. Linhares I.M., Witkin S.S., Miranda S.D., Fonseca A.M., Pinotti J.A., Ledger W.J. Differentiation Between Women With Vulvovaginal Symptoms Who Are Positive or Negative for Candida Species by Culture. Infect. Dis. Obstet. Gynecol, 2001; 9: 221–225. 10.1155/S1064744901000369. PMC free article
24. Aniebue U.U., Nwankwo T.O., Nwafor M.I. Vulvovaginal Candidiasis in Reproductive Age Women in Enugu Nigeria, Clinical versus Laboratory-Assisted Diagnosis. Niger. J. Clin. Pract, 2018; 21: 1017–1022. 10.4103/njcp.njcp_25_16.
25. Schwebke J.R., Gaydos C.A., Nyirjesy P., Paradis S., Kodsi S., Cooper C.K. Diagnostic Performance of a Molecular Test versus Clinician Assessment of Vaginitis. J. Clin. Microbiol, 2018; 56: e00252-18. 10.1128/JCM.00252-18. PMC free article.
26. Farr A., Effendy I., Frey Tirri B., Hof H., Mayser P., Petricevic L., Ruhnke M., Schaller M., Schaefer A.P.A., Sustr V., et al. Guideline: Vulvovaginal Candidosis (AWMF 015/072, Level S2k) Mycoses, 2021; 64: 583–602. 10.1111/myc.13248. PMC free article.
27. Naglik J.R., Gaffen S.L., Hube B. Candidalysin: Discovery and Function in Candida Albicans Infections. Curr. Opin. Microbiol, 2019; 52: 100–109. 10.1016/j.mib.2019.06.002. PMC free article.
28. Jafarzadeh L., Ranjbar M., Nazari T., Naeimi Eshkaleti M., Aghaei Gharehbolagh S., Sobel J.D., Mahmoudi S. Vulvovaginal Candidiasis: An Overview of Mycological, Clinical, and Immunological Aspects. J. Obstet. Gynaecol. Res, 2022; 48: 1546–1560. 10.1111/jog.15267.
29. Sobel J.D. Vaginitis. N. Engl. J. Med. 1997; 337: 1896–1903. 10.1056/NEJM199712253372607.
30. Morton R.S., Rashid S. Candidal Vaginitis: Natural History, Predisposing Factors and Prevention. Proc. R. Soc. Med, 1977; 70(Suppl. S4): 3–6. 10.1177/00359157770700S402. PMC free article
31. Wiesenfeld H.C., Macio I. The Infrequent Use of Office-Based Diagnostic Tests for Vaginitis. Am. J. Obstet. Gynecol, 1999; 181: 39–41. 10.1016/S0002-9378(99)70433-3.

32. Gaydos C.A., Beqaj S., Schwebke J.R., Lebed J., Smith B., Davis T.E., Fife K.H., Nyirjesy P., Spurrell T., Furgerson D., et al. Clinical Validation of a Test for the Diagnosis of Vaginitis. Obstet. Gynecol, 2017; 130: 181–189. : 10.1097/AOG.0000000000002090. PMC free article
33. Workowski K.A., Bolan G.A. Centers for Disease Control and Prevention Sexually Transmitted Diseases Treatment Guidelines, 2015. MMWR Recomm. Rep. Morb. Mortal. Wkly. Rep. Recomm. Rep. 2015; 64: S759–S762. 10.1093/cid/civ771.
34. Sobel J.D., Wiesenfeld H.C., Martens M., Danna P., Hooton T.M., Rompalo A., Sperling M., Livengood C., Horowitz B., Von Thron J., et al. Maintenance Fluconazole Therapy for Recurrent Vulvovaginal Candidiasis. N. Engl. J. Med. 2004; 351: 876–883. 10.1056/NEJMoa033114.
35. Denison H.J., Worswick J., Bond C.M., Grimshaw J.M., Mayhew A., Gnani Ramadoss S., Robertson C., Schaafsma M.E., Watson M.C. Oral versus Intra-Vaginal Imidazole and Triazole Anti-Fungal Treatment of Uncomplicated Vulvovaginal Candidiasis (Thrush) Cochrane Database Syst. Rev, 2020; 8: CD002845. : 10.1002/14651858.CD002845.pub3. PMC free article
36. Sexually Transmitted Infections Treatment Guidelines. Vulvovaginal Candidiasis (VVC) (accessed on 22 July 2023); 2021 Available online: https://www.cdc.gov/std/treatment-guidelines/candidiasis.htm.
37. Mendling W. Guideline: Vulvovaginal Candidosis (AWMF 015/072), S2k (Excluding Chronic Mucocutaneous Candidosis) Mycoses, 2015; 58: 1–15. : 10.1111/myc.12292.