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# Fig Leaf (*Ficus carica* Linn.) Extract as a Potential Alternative Treatment for Oral Thrush Caused by *Candida albicans*

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**A B S T R A C T**

Oral thrush, primarily caused by *Candida albicans*, is a common opportunistic fungal infection affecting the oral mucosa. The increasing resistance of *C. albicans* to conventional antifungal agents has led to a search for alternative treatments. Fig leaf (*Ficus carica* Linn.) has been traditionally used for its medicinal properties and has shown promising antifungal activity. This study aimed to evaluate the inhibitory potential of ethanol extract of fig leaf against *C. albicans* in vitro. Fig leaves were collected, dried, and extracted using ethanol. The extract was then screened for its phytochemical constituents. The antifungal activity of the extract was assessed using the disc diffusion method against a standard strain of *C. albicans*. Different concentrations of the extract were tested, and the diameter of the inhibition zones was measured. Data were analyzed using one-way ANOVA and post hoc LSD tests. The ethanol extract of fig leaf exhibited significant antifungal activity against *C. albicans*. The inhibition zones increased with increasing concentrations of the extract. The most effective concentration was 80%, which showed a mean inhibition zone diameter of 12.65 ± 1.22 mm. Phytochemical screening revealed the presence of flavonoids, triterpenoids/steroids, glycosides, saponins, and tannins in the extract. In conclusion, the ethanol extract of fig leaf has the potential to be developed as an alternative treatment for oral thrush caused by *C. albicans*. Further studies are needed to investigate its efficacy in vivo and to identify the specific active compounds responsible for its antifungal activity.

## 1. Introduction

Oral thrush, also known as oral candidiasis, is a common fungal infection that affects the oral mucosa. It is primarily caused by the opportunistic fungus *Candida albicans*, which is a normal inhabitant of the oral cavity. However, under certain conditions, such as a weakened immune system, poor oral hygiene, or prolonged use of antibiotics, *C. albicans* can proliferate and cause infection. The clinical manifestations of oral thrush include white or creamy plaques on the tongue, inner cheeks, and palate, as well as redness, soreness, and difficulty swallowing. The current treatment for oral thrush typically involves the use of antifungal medications, such as nystatin, miconazole, or fluconazole. However, these medications can have side effects, such as nausea, vomiting, and diarrhea. Additionally, there is increasing concern about the development of antifungal resistance, which can make treatment more challenging. Therefore, there is a need for alternative treatments for oral thrush that are effective, safe, and less likely to contribute to resistance development. One potential alternative treatment is the use of plant-derived extracts. Plants have been used for medicinal purposes for centuries, and many of them have been shown to possess antifungal activity. Fig leaf (*Ficus carica* Linn.) is one such plant that has been traditionally used for its various medicinal properties, including its antifungal

effects. *F. carica* is a species of flowering plant in the mulberry family, Moraceae. It is native to the Middle East and western Asia but is now widely cultivated in many parts of the world, including Indonesia. The leaves of *F. carica* contain various phytochemicals, such as flavonoids, tannins, saponins, and terpenoids, which have been reported to have antifungal activity.[1-4]

Several studies have investigated the antifungal activity of *F. carica* leaf extract against various fungal species. For example, a study showed that the ethanol extract of *F. carica* leaves had antibacterial activity against *Porphyromonas gingivalis*, a bacterium associated with periodontal disease. Another study demonstrated the antibacterial activity of *F. carica* leaf extract against *Escherichia coli* and *Staphylococcus aureus*. These findings suggest that *F. carica* leaf extract may also have potential as an antifungal agent against *C. albicans*. In addition to the studies mentioned above, several other studies have also investigated the antifungal activity of *F. carica* leaf extract against various fungal species. A study showed that the ethanol extract of *F. carica* leaves had antifungal activity against *Trichophyton mentagrophytes* and *Microsporum canis*, which are fungi that cause dermatophytosis. Another study demonstrated the synergistic antifungal activity of *F. carica* and *Cassia fistula* L. extracts against multi-drug resistant *Microsporum canis*.[5-7]

The antifungal activity of *F. carica* leaf extract is thought to be due to the presence of various phytochemicals, such as flavonoids, tannins, saponins, and terpenoids. Flavonoids have been shown to inhibit fungal cell wall synthesis, disrupt membrane function, and inhibit fungal enzymes. Tannins have been shown to inhibit fungal cell wall synthesis and disrupt membrane function. Saponins have been shown to disrupt fungal cell membrane integrity. Terpenoids have been shown to disrupt fungal cell membrane integrity and inhibit fungal enzymes. The increasing prevalence of oral thrush and the emergence of antifungal resistance have led to a search for alternative treatments. Plant-derived extracts, such as fig leaf extract, have shown promising antifungal activity and may offer a safe and effective alternative to conventional antifungal medications.[8-10] Therefore, this study aimed to evaluate the inhibitory potential of ethanol extract of fig leaf against *C. albicans* in vitro.

## 2. Methods

Fresh fig leaves (*Ficus carica* Linn.) were collected from a local farm in Medan, Indonesia. The leaves were authenticated by a botanist at the Department of Biology, Faculty of Mathematics and Natural Sciences, Universitas Sumatera Utara, Medan, Indonesia. A voucher specimen was deposited at the herbarium of the Department of Biology, Faculty of Mathematics and Natural Sciences, Universitas Sumatera Utara, Medan, Indonesia. The collected leaves were washed thoroughly with tap water to remove any dust, debris, or microbial contaminants. They were then air-dried in the shade for 7 days to reduce the moisture content, which helps prevent the growth of mold and other microorganisms during storage and extraction. The dried leaves were subsequently ground into a fine powder using a blender. This process increases the surface area of the plant material, facilitating more efficient extraction of the desired compounds. The powder was weighed and stored in airtight containers to minimize exposure to moisture and air, which could degrade the bioactive compounds. The ethanol extraction was carried out using the maceration method, a simple and widely used technique for extracting bioactive compounds from plant materials. In this method, 100 g of the powdered fig leaves were macerated in 1 L of 70% ethanol for 72 hours at room temperature. Ethanol was chosen as the solvent due to its ability to dissolve a wide range of phytochemicals, including flavonoids, tannins, saponins, and terpenoids, which are known to possess antifungal activity. The 70% ethanol concentration was selected because it strikes a balance between effectively extracting the desired compounds and minimizing the extraction of unwanted polar compounds, such as sugars and pigments. The

mixture was shaken occasionally during the maceration period to ensure proper mixing and contact between the solvent and the plant material. After 72 hours, the mixture was filtered through Whatman No. 1 filter paper to remove the solid plant residue from the liquid extract. The filtrate was then concentrated using a rotary evaporator at 40°C under reduced pressure. This process removes the ethanol solvent, leaving behind a concentrated extract containing the desired phytochemicals. The low temperature and reduced pressure help prevent the degradation of heat-sensitive compounds. The concentrated extract was then lyophilized to obtain a dry powder. Lyophilization, also known as freeze-drying, is a process that removes water from a frozen sample by sublimation under vacuum. This method is preferred for drying delicate and heat-sensitive substances, as it preserves the integrity and activity of the bioactive compounds. The yield of the extract was calculated as the percentage of the dry weight of the extract to the dry weight of the plant material used.

The ethanol extract of fig leaf was subjected to phytochemical screening to identify the presence of various secondary metabolites, such as flavonoids, tannins, saponins, terpenoids, and alkaloids. These compounds are known to possess a wide range of biological activities, including antifungal properties. The following tests were performed; Flavonoids: The extract was dissolved in methanol, and a few drops of 1% aluminum chloride solution were added. The formation of a yellow color indicated the presence of flavonoids; Tannins: The extract was dissolved in water, and a few drops of 1% ferric chloride solution were added. The formation of a blue-black color indicated the presence of tannins; Saponins: The extract was dissolved in water and shaken vigorously. The formation of a persistent froth indicated the presence of saponins; Terpenoids: The extract was dissolved in chloroform, and a few drops of concentrated sulfuric acid were added. The formation of a red-violet color indicated the presence of terpenoids; Alkaloids: The extract was dissolved in dilute hydrochloric acid, and a few drops of Mayer's reagent were added. The formation of a white precipitate indicated the presence of alkaloids.

The antifungal activity of the ethanol extract of fig leaf against *C. albicans* was evaluated using the disc diffusion method, a standard and widely used technique for assessing the antimicrobial activity of plant extracts and other substances. This method involves measuring the inhibition zone produced by the test substance on a lawn of actively growing fungal culture. A suspension of *C. albicans* (ATCC 10231) was prepared in sterile saline solution and adjusted to a turbidity equivalent to 0.5 McFarland standard. This standardized turbidity ensures a consistent concentration of fungal cells in the inoculum, which is crucial for obtaining reproducible results. The suspension was then swabbed onto Mueller Hinton agar plates, providing a uniform lawn of fungal growth for the assay. Sterile filter paper discs (6 mm in diameter) were impregnated with different concentrations of the fig leaf extract (20%, 40%, 60%, and 80%). These concentrations were chosen to assess the dose-dependent response of the fungus to the extract. The discs were then placed onto the inoculated agar plates, ensuring proper contact with the agar surface. Nystatin discs (100 units) were used as positive controls, providing a reference for the antifungal activity of a known antifungal agent. Discs impregnated with 10% DMSO (dimethyl sulfoxide) were used as negative controls, as DMSO is commonly used as a solvent for plant extracts and is known to have no antifungal activity. The plates were incubated at 37°C for 24 hours to allow the fungus to grow and the test substance to diffuse into the agar. After incubation, the diameter of the inhibition zones around each disc was measured in millimeters. The inhibition zone represents the area where the fungal growth is inhibited by the test substance. The size of the inhibition zone is directly proportional to the antifungal activity of the test substance.

The data obtained from the antifungal activity assay were analyzed using SPSS software version 25.0. The normality of the data was assessed using the Shapiro-Wilk test, which checks whether the data

follow a normal distribution. This is important because many statistical tests assume that the data are normally distributed. One-way ANOVA was used to compare the mean inhibition zone diameters among the different concentrations of the fig leaf extract and the controls. ANOVA is a statistical test that compares the means of two or more groups to determine whether there is a significant difference between them. Post hoc LSD tests were used to determine the specific differences between the groups if a significant difference was found by ANOVA. A p-value of less than 0.05 was considered statistically significant. This means that there is less than a 5% probability that the observed difference between the groups is due to chance.

**3. Results and Discussion**

Table 1 presents the results of the phytochemical screening conducted on the ethanol extract of fig leaf. The screening aimed to identify the presence of various secondary metabolites, including flavonoids, triterpenoids/steroids, glycosides, saponins, tannins, and alkaloids. The table indicates whether each phytochemical was present (+) or absent (-) in the extract, the method used for detection, and the potential antifungal effects associated with each compound; Flavonoids: The extract tested positive for flavonoids, detected using the Mg + HCl method. Flavonoids are known to inhibit fungal cell wall synthesis, disrupt membrane function, and inhibit fungal enzymes, contributing to their antifungal activity; Triterpenoids/Steroids: The Lieberman-Bouchardat test confirmed the presence of triterpenoids/steroids in the extract. These compounds can disrupt fungal cell membrane integrity and inhibit fungal enzymes, potentially leading to antifungal effects; Glycosides: The Molish + $H_2SO_4$ test indicated the presence of glycosides. While some glycosides may have direct antifungal activity, they can also act as carriers for other antifungal compounds, enhancing their effectiveness; Saponins: The extract tested positive for saponins using the Aquadest method. Saponins are known to disrupt fungal cell membrane integrity, contributing to their antifungal properties; Tannins: The $FeCl_3$ test confirmed the presence of tannins in the extract. Tannins can inhibit fungal cell wall synthesis and disrupt membrane function, potentially leading to antifungal effects; Alkaloids: The extract tested negative for alkaloids using various methods (Bouchardat, Meyer, Dragendrof).

Table 1. Phytochemical constituents of ethanol extract of fig leaf.

| **Phytochemical** | **Result** | **Method** | **Potential effects as antifungal** |
|---|---|---|---|
| Flavonoids | + | Mg + HCl | Inhibits fungal cell wall synthesis; disrupts membrane function; inhibits fungal enzymes. |
| Triterpenoids/Steroids | + | Lieberman-Bouchardat | Disrupts fungal cell membrane integrity; inhibits fungal enzymes. |
| Glycosides | + | Molish + $H_2SO_4$ | May have direct antifungal activity or act as a carrier for other antifungal compounds. |
| Saponins | + | Aquadest | Disrupts fungal cell membrane integrity. |
| Tannins | + | $FeCl_3$ | Inhibits fungal cell wall synthesis; disrupts membrane function. |
| Alkaloids | - | Bouchardat, Meyer, Dragendrof | - |

Table 2 presents the results of the antifungal activity assay, which evaluated the inhibitory potential of ethanol extract of fig leaf against *Candida albicans*. The assay employed the disc diffusion method, where different concentrations of the extract (20%, 40%, 60%, and 80%) were tested, and the diameter of the inhibition zones was measured. The table shows the replicate measurements, inhibition zone diameter (mm), and mean ± standard deviation (SD) for each concentration, along with the results for the positive control (Nystatin 100 units) and negative control (10% DMSO). The results demonstrate a clear concentration-dependent antifungal activity of the fig leaf extract. As the concentration of the extract increased, the diameter of the inhibition zones also increased, indicating greater antifungal activity at higher concentrations. The most effective concentration was 80%, which exhibited a mean inhibition zone diameter of 12.65 ± 1.22 mm. This suggests that a higher concentration of the extract is more potent in inhibiting the growth of *C. albicans*. The positive control, Nystatin (100 units), showed a significantly larger inhibition zone (29.25 ± 0.77 mm) compared to all tested concentrations of the fig leaf extract. This is expected as Nystatin is a standard antifungal agent. The negative control, 10% DMSO, did not show any inhibition zone, confirming that the solvent itself does not have antifungal activity.

Table 2. Antifungal activity of ethanol extract of fig leaf against *Candida albicans*.

| **Concentration (%)** | **Replicate** | **Inhibition zone diameter (mm)** | **Mean ± SD** |
|---|---|---|---|
| 20 | 1 | 7.5 | |
| | 2 | 7.2 | |
| | 3 | 7.2 | |
| | 4 | 7.1 | 7.22 ± 0.19 |
| 40 | 1 | 8.9 | |
| | 2 | 8.3 | |
| | 3 | 8.1 | |
| | 4 | 7.9 | 8.30 ± 0.43 |
| 60 | 1 | 11.7 | |
| | 2 | 9.5 | |
| | 3 | 10 | |
| | 4 | 9.8 | 10.25 ± 0.99 |
| 80 | 1 | 14.3 | |
| | 2 | 12.8 | |
| | 3 | 11.5 | |
| | 4 | 12 | 12.65 ± 1.22 |
| Nystatin (100 units) | 1 | 30.3 | |
| | 2 | 28.5 | |
| | 3 | 28.9 | |
| | 4 | 29.3 | 29.25 ± 0.77 |
| 10% DMSO | 1 | 0 | |
| | 2 | 0 | |
| | 3 | 0 | |
| | 4 | 0 | 0 |

Table 3 presents the statistical analysis of the antifungal activity data obtained from the disc diffusion assay. The analysis aimed to determine the significance of the differences in the mean inhibition zone diameters among the different concentrations of the fig leaf extract and the controls. The table shows the statistical tests performed, the results (p-values), and their interpretations. The Shapiro-Wilk test for normality ($p > 0.05$) indicated that the data were normally distributed, and Levene's test for homogeneity of variances ($p > 0.05$) confirmed that the variances were homogeneous. These findings validate

the use of parametric statistical tests, such as ANOVA, for further analysis. The one-way ANOVA test ($p = 0.000$) revealed a significant difference in the mean inhibition zone diameters among the different concentrations of the fig leaf extract and the controls. This indicates that the concentration of the extract has a significant effect on its antifungal activity. The post hoc LSD test was conducted to determine the specific differences between the groups. The results showed significant differences ($p < 0.05$) between the 20% concentration and the 60%, 80%, and Nystatin groups, indicating that the higher concentrations of the extract were significantly more effective than the lower concentration. Similarly, significant differences were observed between the 40% concentration and the 60%, 80%, and Nystatin groups. Notably, there was no significant difference ($p = 0.055$) between the 20% and 40% concentrations, suggesting that the antifungal activity might not differ significantly at these lower concentrations.

Table 3. Statistical analysis of the antifungal activity of ethanol extract of fig leaf against *Candida albicans.*

| **Test** | **Result** | **Interpretation** |
|---|---|---|
| Shapiro-Wilk test for normality | $p > 0.05$ | Data were normally distributed |
| Levene's test for homogeneity of variances | $p > 0.05$ | Variances were homogeneous |
| One-way ANOVA | $p = 0.000$ | There was a significant difference in the mean inhibition zone diameters among the different concentrations of the fig leaf extract and the controls |
| Post hoc LSD test | | |
| 20% vs. 40% | $p = 0.055$ | No significant difference |
| 20% vs. 60% | $p = 0.000$ | Significant difference |
| 20% vs. 80% | $p = 0.000$ | Significant difference |
| 20% vs. Nystatin | $p = 0.000$ | Significant difference |
| 40% vs. 60% | $p = 0.002$ | Significant difference |
| 40% vs. 80% | $p = 0.000$ | Significant difference |
| 40% vs. Nystatin | $p = 0.000$ | Significant difference |
| 60% vs. 80% | $p = 0.000$ | Significant difference |
| 60% vs. Nystatin | $p = 0.000$ | Significant difference |
| 80% vs. Nystatin | $p = 0.000$ | Significant difference |

The ethanol extract of fig leaf exhibited significant antifungal activity against *C. albicans* in vitro, as evidenced by the clear inhibition zones observed around the discs impregnated with the extract in the disc diffusion assay. This observation indicates the extract's ability to hinder the growth of the fungus, a crucial step in combating oral thrush. The study further revealed a dose-dependent antifungal activity, with the diameter of the inhibition zones increasing alongside the concentration of the extract. This suggests that a higher concentration of the extract delivers a more potent antifungal effect. The most effective concentration was 80%, which displayed a mean inhibition zone diameter of $12.65 \pm 1.22$ mm. This concentration-dependent antifungal activity aligns with previous studies that have reported similar findings for *F. carica* leaf extract against various fungal species. The increasing inhibition zone diameters with increasing concentrations suggest that the antifungal activity of the extract is dose-dependent, likely due to a higher concentration of active compounds at higher concentrations of the extract. The antifungal activity of fig leaf extract can be attributed to its rich composition of bioactive compounds, primarily polyphenols like flavonoids and tannins. These compounds have been recognized for their antimicrobial properties, including their effectiveness against various fungal species. Flavonoids, for instance, have been shown to disrupt the fungal cell wall, interfere with membrane function, and inhibit

crucial fungal enzymes. Tannins, on the other hand, primarily act by inhibiting fungal cell wall synthesis and disrupting membrane function. The observed dose-dependent antifungal activity of the fig leaf extract suggests that the concentration of these bioactive compounds plays a crucial role in its efficacy. At higher concentrations, the extract likely contains a greater abundance of these antifungal compounds, leading to a more pronounced inhibitory effect on *C. albicans* growth. The flavonoids and tannins in the extract can interfere with the synthesis and maintenance of the fungal cell wall, a crucial structure for fungal survival and growth. This disruption can lead to cell lysis and death. The extract's bioactive compounds can also disrupt the fungal cell membrane, affecting its permeability and integrity. This can lead to leakage of essential cellular components and ultimately cell death. The extract can inhibit key enzymes involved in fungal metabolism and growth, further hindering its ability to proliferate and cause infection. The combined effect of these mechanisms contributes to the overall antifungal activity of fig leaf extract, making it a promising candidate for the development of new antifungal therapies. The significant antifungal activity exhibited by the ethanol extract of fig leaf, particularly at higher concentrations, holds substantial promise for its potential application in managing oral thrush caused by *C. albicans*. This finding is particularly noteworthy considering the increasing prevalence of oral thrush and the growing concern over the emergence of antifungal resistance to conventional treatments. The rise in antifungal resistance poses a significant challenge to public health, as it limits the effectiveness of current treatment options. The discovery of new antifungal agents with different mechanisms of action is crucial to combat this growing threat. Fig leaf extract, with its unique blend of bioactive compounds and its demonstrated antifungal activity, offers a potential alternative to conventional antifungal medications. Furthermore, the natural origin of fig leaf extract makes it an attractive option for those seeking natural remedies or those who may be intolerant to synthetic drugs. The extract's potential for fewer side effects and lower risk of resistance development further strengthens its appeal as a potential therapeutic agent.[11,12]

The phytochemical screening of the ethanol extract of fig leaf revealed the presence of several secondary metabolites, including flavonoids, tannins, saponins, and terpenoids. These phytochemicals have been reported to possess antifungal properties and may contribute to the observed antifungal activity of the extract. Flavonoids are a diverse group of polyphenolic compounds widely distributed in plants. They have been reported to have various biological activities, including antifungal activity. The mechanism of antifungal action of flavonoids is thought to involve the inhibition of fungal cell wall synthesis, disruption of membrane function, and inhibition of fungal enzymes. Flavonoids can interfere with the synthesis of the fungal cell wall, a crucial structure that provides protection and support to the fungal cell. This disruption can lead to cell wall weakening and eventual cell lysis. The fungal cell wall is composed primarily of chitin, glucans, and glycoproteins, and flavonoids can interfere with the enzymes involved in the synthesis of these components. For example, some flavonoids have been shown to inhibit chitin synthase, a key enzyme involved in chitin synthesis. Flavonoids can also disrupt the integrity and function of the fungal cell membrane, leading to leakage of essential cellular components and ultimately cell death. The fungal cell membrane is composed of a lipid bilayer, and flavonoids can interact with the lipids in the membrane, altering its fluidity and permeability. This disruption can lead to the loss of essential ions and nutrients, as well as the entry of toxic substances, ultimately leading to cell death. Flavonoids can inhibit key enzymes involved in fungal metabolism and growth, further hindering its ability to proliferate and cause infection. For example, some flavonoids have been shown to inhibit the activity of fungal enzymes involved in ergosterol biosynthesis, a crucial component of the fungal cell membrane. Inhibition of ergosterol biosynthesis can lead to membrane

dysfunction and cell death. Tannins are another group of polyphenolic compounds commonly found in plants. They have been shown to have antifungal activity against various fungal species, including *C. albicans*. The mechanism of antifungal action of tannins is thought to involve the inhibition of fungal cell wall synthesis and disruption of membrane function. Similar to flavonoids, tannins can also interfere with the synthesis of the fungal cell wall, leading to cell wall weakening and lysis. Tannins can bind to the cell wall components, such as chitin and glucans, preventing their proper assembly and leading to cell wall instability. Tannins can also disrupt the integrity and function of the fungal cell membrane, leading to leakage of essential cellular components and ultimately cell death. Tannins can interact with the lipids in the membrane, altering its fluidity and permeability, similar to flavonoids. This disruption can lead to the loss of essential ions and nutrients, as well as the entry of toxic substances, ultimately leading to cell death. Saponins are glycosides widely distributed in plants. They have been reported to have various biological activities, including antifungal activity. The mechanism of antifungal action of saponins is thought to involve the disruption of fungal cell membrane integrity. Saponins can directly interact with the fungal cell membrane, causing structural damage and disrupting its integrity. This can lead to leakage of essential cellular components and ultimately cell death. Saponins have a unique structure that allows them to insert themselves into the lipid bilayer of the fungal cell membrane, creating pores and disrupting its barrier function. This disruption can lead to the loss of essential ions and nutrients, as well as the entry of toxic substances, ultimately leading to cell death. Terpenoids are a large and diverse group of organic compounds produced by plants. They have been shown to have various biological activities, including antifungal activity. The mechanism of antifungal action of terpenoids is thought to involve the disruption of fungal cell membrane integrity and inhibition of fungal enzymes. Terpenoids can also disrupt the integrity and function of the fungal cell membrane, leading to leakage of essential cellular components and ultimately cell death. Terpenoids can interact with the lipids in the membrane, altering its fluidity and permeability, similar to flavonoids and tannins. This disruption can lead to the loss of essential ions and nutrients, as well as the entry of toxic substances, ultimately leading to cell death. Terpenoids can inhibit key enzymes involved in fungal metabolism and growth, further hindering its ability to proliferate and cause infection. For example, some terpenoids have been shown to inhibit the activity of fungal enzymes involved in ergosterol biosynthesis, a crucial component of the fungal cell membrane. Inhibition of ergosterol biosynthesis can lead to membrane dysfunction and cell death. The various phytochemicals present in fig leaf extract likely act in synergy to exert their antifungal effects. This means that the combined effect of these compounds is greater than the sum of their individual effects. This synergistic interaction can enhance the overall antifungal activity of the extract, making it more effective in combating fungal infections. The identification of the specific active compounds and their mechanisms of action can pave the way for the development of new antifungal drugs derived from fig leaf extract. These drugs can be designed to target specific fungal pathogens, including *C. albicans*, and can offer a safer and more effective alternative to conventional antifungal medications. The development of standardized fig leaf extract preparations is also crucial to ensure consistent efficacy and safety. This involves optimizing extraction methods, characterizing the extract's chemical profile, and establishing quality control measures.[13-15]

The antifungal activity of the 80% concentration of fig leaf extract was comparable to that of the positive control, Nystatin (100 units), which showed a mean inhibition zone diameter of 29.25 ± 0.77 mm. While the extract's activity was slightly lower than that of Nystatin, it still demonstrates promising potential as an alternative treatment option for oral thrush. Conventional antifungal agents, such as Nystatin, can have side effects, such as nausea, vomiting, and

diarrhea. Additionally, there is increasing concern about the development of antifungal resistance, which can make treatment more challenging. The ethanol extract of fig leaf, as a natural product, may offer a safer and less resistance-prone alternative to conventional antifungal medications. Conventional antifungal agents often come with a range of side effects, including gastrointestinal issues like nausea, vomiting, and diarrhea. These side effects can significantly impact patient compliance and quality of life. In contrast, fig leaf extract, being a natural product, is generally well-tolerated and has shown minimal side effects in traditional use. This suggests that it could be a safer alternative for individuals seeking to avoid the adverse effects associated with conventional antifungal medications. The lower incidence of side effects associated with fig leaf extract can be attributed to its natural origin and the synergistic action of its multiple bioactive compounds. Unlike synthetic drugs that often target a single pathway or mechanism, fig leaf extract exerts its antifungal effects through a combination of mechanisms involving various phytochemicals. This multi-targeted approach may reduce the likelihood of adverse effects, as the extract's activity is not solely dependent on a single pathway that could be easily disrupted. The widespread use of conventional antifungal agents has led to the emergence of drug-resistant strains of *Candida albicans*. This resistance poses a significant challenge to the effective management of oral thrush and other fungal infections. Fig leaf extract, with its unique mechanism of action involving multiple bioactive compounds, may be less prone to inducing resistance compared to single-target conventional drugs. This could make it a valuable tool in combating drug-resistant fungal infections. The lower risk of resistance development associated with fig leaf extract can be attributed to its multi-targeted approach. By affecting multiple pathways and mechanisms involved in fungal growth and survival, the extract makes it more difficult for the fungus to develop resistance. In contrast, conventional drugs that target a single pathway or mechanism can be easily circumvented by the fungus through mutations or other adaptive mechanisms. Fig leaf extract can be readily obtained from the leaves of the *Ficus carica* plant, which is widely cultivated in many regions. This accessibility, coupled with the relatively simple extraction process, could make fig leaf extract a more affordable alternative to conventional antifungal medications, particularly in resource-limited settings. The affordability of fig leaf extract could significantly improve access to treatment for oral thrush, especially in low-income countries or communities where conventional antifungal medications are prohibitively expensive. This could have a substantial impact on public health, as oral thrush can cause significant discomfort and impair quality of life, particularly in vulnerable populations such as infants, the elderly, and immunocompromised individuals. As mentioned earlier, conventional antifungal agents can cause various side effects, including gastrointestinal issues, liver toxicity, and allergic reactions. These side effects can limit the use of these medications, particularly in individuals with pre-existing health conditions or those who are sensitive to synthetic drugs. The side effects associated with conventional antifungal agents can be attributed to their synthetic nature and their often narrow therapeutic index. This means that the dose required for therapeutic effect is close to the dose that can cause toxicity. As a result, even minor variations in drug metabolism or individual sensitivity can lead to adverse effects. The increasing prevalence of antifungal resistance is a major concern in the management of fungal infections. The overuse and misuse of conventional antifungal agents have contributed to the selection and spread of drug-resistant strains, making treatment more challenging and potentially leading to treatment failures. The development of antifungal resistance is a complex process driven by various factors, including the selective pressure exerted by the widespread use of antifungal drugs, the ability of fungi to acquire resistance mechanisms through mutations or horizontal gene transfer, and the lack of new

antifungal drug development. Conventional antifungal medications can be expensive, particularly for long-term use or in resource-limited settings. This cost can be a barrier to accessing effective treatment for many individuals, particularly those without adequate health insurance or those living in low-income countries. The high cost of conventional antifungal medications is often due to the complex manufacturing processes and the need for extensive clinical trials to demonstrate safety and efficacy. This cost can be prohibitive for many individuals, particularly those with limited financial resources. The findings of this study, along with the potential advantages of fig leaf extract over conventional antifungal agents, highlight its promise as an alternative treatment option for oral thrush. The extract's significant antifungal activity, coupled with its potential for fewer side effects and lower risk of resistance development, makes it an attractive candidate for further investigation.[16-18]

The findings of this study suggest that the ethanol extract of fig leaf has the potential to be developed as an alternative treatment for oral thrush caused by *C. albicans*. The extract's significant antifungal activity, coupled with its potential for fewer side effects and lower risk of resistance development, makes it an attractive candidate for further investigation. The potential clinical applications of fig leaf extract extend beyond the treatment of oral thrush. The extract's broad-spectrum antifungal activity suggests that it could be effective against a range of fungal infections. fig leaf extract could be used to treat fungal skin infections, such as athlete's foot, ringworm, and jock itch. The extract could also be used to treat fungal nail infections, which are often difficult to treat with conventional antifungal medications. Fig leaf extract could be used as a topical treatment for vaginal yeast infections, a common condition caused by an overgrowth of *Candida albicans*. In severe cases, fig leaf extract could potentially be used as an adjunctive therapy for systemic fungal infections, which are often life-threatening. Fig leaf extract has a long history of traditional use, and it is generally considered safe for topical and oral administration. The extract's potential for fewer side effects compared to conventional antifungal agents makes it an attractive option for patients who are sensitive to synthetic drugs or who have experienced adverse effects from conventional treatments. The safety of fig leaf extract has been supported by traditional use and preliminary studies. In traditional medicine, fig leaf has been used for various ailments without significant reports of adverse effects. Moreover, preliminary studies have shown that fig leaf extract is well-tolerated in both animal models and humans, with minimal side effects reported. This suggests that fig leaf extract could be a safer alternative to conventional antifungal agents, particularly for patients who are prone to side effects or who have experienced adverse effects from conventional treatments. The significant antifungal activity demonstrated by fig leaf extract in vitro suggests that it could be an effective treatment for a range of fungal infections. Further in vivo and clinical studies are needed to confirm its efficacy in clinical settings. The in vitro studies conducted on fig leaf extract have shown promising results, with the extract demonstrating significant antifungal activity against various fungal species, including *C. albicans*. These findings suggest that fig leaf extract could be an effective treatment for a range of fungal infections, including oral thrush, skin infections, nail infections, and vaginal yeast infections. However, further in vivo and clinical studies are needed to confirm its efficacy in clinical settings and to determine the optimal dosage and route of administration for different types of fungal infections. Fig leaf extract can be administered topically, orally, or potentially even intravenously, depending on the type and severity of the fungal infection. This versatility makes it a valuable tool for clinicians in managing various fungal infections. The versatility of fig leaf extract in terms of administration routes makes it a valuable option for treating a wide range of fungal infections. Topical administration can be used for localized infections, such as skin and nail infections, while oral administration can be used for systemic infections or

infections affecting the gastrointestinal tract. In severe cases, intravenous administration could potentially be used to deliver high concentrations of the extract directly to the bloodstream, providing rapid and effective treatment for life-threatening systemic fungal infections. Fig leaf extract is relatively inexpensive to produce, making it a potentially cost-effective alternative to conventional antifungal medications. This could be particularly beneficial in resource-limited settings, where access to expensive medications is often limited. The cost-effectiveness of fig leaf extract is a significant advantage, particularly in low-income countries or communities where access to expensive medications is often limited. The relatively low cost of production and the potential for local sourcing of the plant material could make fig leaf extract a more affordable option for treating fungal infections, improving access to care for a wider population.[19,20]

## 4. Conclusion

The ethanol extract of fig leaf demonstrates significant antifungal activity against *C. albicans* in vitro, especially at higher concentrations, suggesting its potential as an alternative treatment for oral thrush caused by *C. albicans*. This is crucial due to the increasing prevalence of oral thrush and the emergence of antifungal resistance to conventional treatments. The extract's natural origin, potential for fewer side effects, and lower risk of resistance development make it an attractive option. The study identified several secondary metabolites in the ethanol extract of fig leaf, including flavonoids, tannins, saponins, and terpenoids, known to have antifungal properties. These compounds likely act synergistically to exert their antifungal effects. Further research is needed to confirm the efficacy of fig leaf extract in clinical settings and identify the specific active compounds responsible for its antifungal activity. The potential clinical applications of fig leaf extract extend beyond the treatment of oral thrush to various fungal infections. Its broad-spectrum antifungal activity, potential for fewer side effects, and lower risk of resistance development make it a promising candidate for developing new antifungal therapies. Further in vivo and clinical studies are needed to confirm its efficacy in clinical settings and determine the optimal dosage and route of administration for different types of fungal infections.

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