Natural and Pharmacological Approaches in Combination Therapy for Candida Infections

1. Introduction

Candida species represent a genus of opportunistic fungi that can transition from commensal colonizers to pathogenic invaders, particularly in individuals with compromised immune systems.[1] While *Candida albicans* remains the most frequently isolated species in human infections, there is a notable increase in the incidence of infections caused by non-*albicans* Candida species, such as *Candida glabrata*, *Candida tropicalis*, *Candida parapsilosis*, and *Candida krusei*.[1] This shift in epidemiology is significant because the susceptibility of different Candida species to antifungal agents can vary considerably, necessitating a broader perspective in the development of effective treatment strategies.[5]

A major challenge in the management of Candida infections is the escalating problem of antifungal resistance.[2] Resistance has been documented across all major classes of antifungal drugs, including azoles, polyenes, and echinocandins.[2] The mechanisms underlying this resistance are diverse and include the overexpression of efflux pumps that expel drugs from the fungal cells, modifications in the target enzymes that reduce drug binding, and alterations in the ergosterol biosynthesis pathway.[2] The emergence of multidrug-resistant species, such as *Candida auris*, poses a particularly serious threat to public health due to limited treatment options and high mortality rates.[9] The increasing occurrence of resistance mechanisms underscores the limitations of relying solely on current antifungal monotherapies and emphasizes the urgent need to explore alternative and combination treatment approaches.[2]

The limitations of conventional antifungal drugs, such as their toxicity profiles, potential for drug interactions, and the growing prevalence of resistance, necessitate the exploration of novel therapeutic strategies.[2] One promising avenue of research involves investigating natural products, such as essential oils and herbal extracts, as potential alternative or adjunctive therapies for Candida infections.[2] Furthermore, there is increasing interest in combination therapies that integrate both natural and pharmacological agents, aiming to leverage synergistic or additive effects to enhance treatment efficacy and overcome resistance.[2] The pursuit of new therapies is fundamentally driven by the shortcomings of existing treatments, making the investigation of both natural compounds and combination approaches a critical area of focus.[2]

This report aims to provide a comprehensive overview of both natural and

pharmacological approaches to treating Candida infections, with a particular emphasis on combination therapies. It will cover in vitro, in vivo, and clinical studies that have evaluated the effectiveness of natural compounds (including essential oils, herbal extracts, probiotics, and honey), pharmacological antifungal drugs (such as azoles, polyenes, and echinocandins), and their combinations against various Candida species. The report will also discuss combination therapies involving only pharmacological antifungal agents and explore future directions and clinical implications of these integrated treatment strategies.

2. Natural Approaches to Candida Treatment

2.1. Essential Oils

Essential oils, which are volatile, complex mixtures of organic compounds extracted from plants, have demonstrated significant antifungal activity against *Candida albicans* and other Candida species.[9] Screening a large collection of essential oils has identified several with potent inhibitory effects on Candida growth.[39] For instance, cinnamon essential oil has shown particularly strong antifungal activity, with a minimum inhibitory concentration (MIC) of ≤ 0.0078%.[13] Other essential oils exhibiting notable anti-Candida activity include palmarosa oil (MIC = 0.03125-0.125%), *Satureja montana* oil (MIC = 0.0625–0.125%) [39], tea tree oil (MIC50 between 0.78 and 1.56%) [9], lemongrass oil (MIC ranging from 0.06 µg/mL to 5 µL/mL and 0.02-0.03%) [13], and clove bud oil (MIC 0.01%).[13]

The antifungal activity of essential oils is attributed to their main active components.[9] For example, cinnamon oil is rich in cinnamaldehyde and eugenol [43], while tea tree oil contains a high percentage of terpinen-4-ol [9], and lemongrass oil is characterized by geranial and neral.[41] The effectiveness of these natural treatments varies considerably depending on the specific essential oil and the Candida species being targeted.[9] This variability suggests that a tailored approach, considering the specific oil and the infecting organism, is essential for optimal outcomes.

The mechanisms by which essential oils exert their antifungal effects are diverse and include the disruption of the Candida cell membrane, inhibition of biofilm formation, and interference with germ tube formation.[40] These mechanisms are particularly relevant in the context of increasing antifungal resistance, as they often target pathways similar to those affected by conventional drugs.[40]

Table 1: Summary of Essential Oils with Anti-Candida Activity

Essential Oil	Main Active Components	Candida Species Tested	MIC Range	Primary Mechanism of Action (if known)
Cinnamon oil	Cinnamaldehyde, Eugenol	*C. albicans*, various others	≤ 0.0078% - 62.5 µg/mL	Cell membrane damage, inhibition of virulence factors
Palmarosa oil	Geraniol, Geranyl acetate	*C. albicans*	0.03125-0.125%	Inhibition of growth
Satureja montana oil	Carvacrol, Cymene	*C. albicans*	0.0625–0.125%	Inhibition of growth
Tea tree oil	Terpinen-4-ol	*C. auris*, *C. albicans*	0.25%-1.56%	Alters cell permeability and fluidity
Lemongrass oil	Geranial, Neral	*C. albicans*, *C. tropicalis*, *C. auris*	0.02% - 5 µL/mL	Inhibition of biofilm formation
Clove bud oil	Eugenol	*C. auris*, *C. albicans*	<0.01% - 0.06%	Fungicidal activity

2.2. Herbal Extracts

Numerous herbal extracts have also demonstrated significant antifungal activity against various Candida species.[8] Examples of such extracts include garlic, containing allicin and ajoene [8]; cinnamon, with its active compounds cinnamaldehyde and eugenol [8]; rosemary, rich in p-coumaric acid [32]; pomegranate, which contains gallotannins [32]; turmeric, known for its curcumin content [2]; and green tea.[8] The mechanisms of action for these herbal extracts are diverse, encompassing the inhibition of biofilm formation and germ tube formation, alteration of cell membrane integrity, interference with cellular metabolism, and the induction of apoptosis in Candida cells.[34] Notably, some herbal extracts have shown comparable efficacy to conventional antifungal drugs in in vivo studies.[40] The wide array of bioactive compounds present in herbal extracts allows for targeting multiple pathways within Candida cells, which could prove advantageous in overcoming drug resistance that

often arises from single-target mutations.[34] Furthermore, the historical use of certain herbs in traditional medicine for treating infections provides empirical support for their potential antifungal properties against Candida.[37]

2.3. Other Natural Compounds

Besides essential oils and herbal extracts, other natural compounds like probiotics and honey have been explored for their potential anti-Candida effects.[8] Probiotics may help to restore a healthy balance of the oral or gut microbiota, which can indirectly inhibit Candida overgrowth.[24] Honey has also demonstrated some level of in vitro antifungal activity against Candida.[24] While the research on these compounds is less extensive compared to essential oils and herbal extracts, they represent additional avenues for exploring natural approaches to managing Candida infections, potentially through mechanisms that extend beyond direct antifungal activity.[8]

3. Pharmacological Approaches to Candida Treatment

3.1. Major Antifungal Drug Classes

The pharmacological treatment of Candida infections relies on several major classes of antifungal drugs, each with a distinct mechanism of action. Azoles, such as fluconazole, itraconazole, voriconazole, posaconazole, and isavuconazole, exert their antifungal effect by inhibiting ergosterol biosynthesis, a crucial component of the fungal cell membrane.[1] Polyenes, including amphotericin B and nystatin, directly bind to ergosterol in the fungal cell membrane, leading to membrane disruption and cell death.[1] Echinocandins, such as caspofungin, micafungin, and anidulafungin, target the fungal cell wall by inhibiting the synthesis of (1,3) β-D-glucan, which is essential for maintaining cell wall integrity.[2] Another antifungal agent, flucytosine, works by inhibiting DNA and RNA synthesis within the fungal cell.[2] The availability of these different antifungal classes, each with a unique mechanism of action, provides a range of therapeutic options for Candida infections. The choice of a specific drug often depends on factors such as the particular Candida species involved, the severity and location of the infection, and the patient's overall health status and immune function.[1]

3.2. Clinical Applications and Limitations

Azoles are frequently used as the first-line treatment for many types of Candida infections.[1] For instance, fluconazole is commonly prescribed for oral candidiasis.[3] Polyenes, such as amphotericin B, are reserved for severe, systemic Candida infections due to their broad spectrum of activity, but their use is often limited by

significant toxicity.[1] Lipid formulations of amphotericin B have been developed to improve the safety profile.[1] Nystatin, another polyene, is primarily used topically for the treatment of mucosal Candida infections.[3] Echinocandins have proven effective against a wide range of Candida species, including those resistant to azole drugs, and are often the preferred choice for invasive candidiasis, particularly in critically ill patients.[2] Flucytosine is typically used in combination with other antifungals because Candida can rapidly develop resistance to it when used as a single agent.[2] Despite the availability of these pharmacological agents, their effectiveness is increasingly compromised by the development of drug resistance, and their use can be associated with toxicity, drug interactions, and, in some cases, limited oral bioavailability.[2] The balance between the therapeutic benefits and the potential for adverse effects is a crucial consideration in the pharmacological management of Candida infections, especially for drugs like amphotericin B, which, while highly effective, can also cause significant side effects.[1]

3.3. The Growing Problem of Antifungal Drug Resistance

Resistance to azole antifungal drugs is now widespread among Candida species and continues to increase.[2] Furthermore, resistance to echinocandins is also an emerging concern, particularly in non-*albicans* species such as *C. glabrata* and *C. auris*.[5] While resistance to polyenes like amphotericin B is less frequent, it has been reported.[4] The mechanisms that enable Candida to resist antifungal drugs are complex and involve a variety of genetic and physiological adaptations.[2] The increasing prevalence of resistance across all major classes of antifungal drugs highlights the urgent need for innovative treatment strategies, including approaches that combine existing drugs or incorporate natural compounds with antifungal properties.[2]

4. Combination Therapies: Integrating Natural and Pharmacological Agents

4.1. Essential Oils and Antifungal Drugs

Several studies have explored the potential for synergistic effects when combining essential oils with conventional antifungal drugs like amphotericin B and fluconazole.[11] For example, palmarosa oil has shown synergy with amphotericin B against growing-phase *C. albicans* [39], while cinnamon and *Satureja montana* oils, when combined with amphotericin B, demonstrated superior efficacy against stationary-phase *C. albicans* infections compared to individual treatments.[39] Additionally, various essential oils, including *Thymus leptobotrys*, *Origanum compactum*, and *Artemisia herba alba*, have exhibited synergistic effects with

amphotericin B specifically against *C. krusei*.[29]

Interesting synergistic interactions have also been observed when combining several essential oils with fluconazole, often resulting in significant reductions in the MICs of both agents.[10] The combination of *T. leptobotrys* essential oil and fluconazole, in particular, showed a very pronounced synergistic effect.[29] Against the emerging multidrug-resistant pathogen *C. auris*, clove bud oil has demonstrated synergistic interactions with both fluconazole and flucytosine [13], and lemongrass oil has displayed a range of interactions (synergistic, additive, and indifferent) depending on the specific antifungal drug it was combined with.[13] Furthermore, specific essential oils like geranium, thyme, cinnamon, lemongrass, and clove bud have shown synergistic combinations with micafungin against resistant strains of *C. auris*, and *Mentha* of Pancalieri essential oil exhibited synergy with fluconazole and 5-flucytosine against the same pathogen.[15] Additive effects have also been reported, such as the combination of lemon eucalyptus and honey myrtle oils with amphotericin B against *C. albicans*.[39] Conversely, antagonistic effects have been noted in some cases, for instance, between clove bud oil and amphotericin B against *C. auris*.[13] The frequent occurrence of synergistic effects between essential oils and conventional antifungals suggests a promising strategy for enhancing treatment efficacy and potentially overcoming drug resistance by allowing for the use of lower doses of both agents.[11] However, the variability in the type of interaction observed, depending on the specific essential oil, antifungal drug, and Candida species, underscores the importance of carefully selecting and testing these combinations.[11]

Table 2: Summary of Studies Evaluating the Combination of Essential Oils and Antifungal Drugs

Essential Oil(s)	Antifungal Drug(s)	Candida Species	Type of Interaction	Key Findings
Palmarosa oil	Amphotericin B	*C. albicans*	Synergistic	FICI = 0.375 against growing-phase
Cinnamon oil, *Satureja montana* oil	Amphotericin B	*C. albicans*	Synergistic	Superior efficacy against stationary-phas e
Thymus	Amphotericin B	*C. krusei*	Synergistic	Four-fold MIC

leptobotrys, *Origanum compactum*, *Artemisia herba alba*				reduction
Multiple EOs	Fluconazole	*C. albicans*, *C. glabrata*, *C. krusei*, *C. tropicalis*	Synergistic	16 to 512-fold MIC reduction
Clove bud oil	Fluconazole, Flucytosine	*C. auris*	Synergistic	Reduced MICs
Lemongrass oil	Fluconazole, Amphotericin B, Flucytosine, Micafungin	*C. auris*	Synergistic, Additive, Indifferent	Variable interactions
Geranium, Thyme, Cinnamon, Lemongrass, Clove bud	Micafungin	*C. auris* (resistant)	Synergistic	Reduced MICs
Mentha of Pancalieri	Fluconazole, 5-Flucytosine	*C. auris* (resistant)	Synergistic	Reduced MICs
Lemon eucalyptus, Honey myrtle	Amphotericin B	*C. albicans*	Additive	FICI = 0.750 and 0.516
Clove bud oil	Amphotericin B	*C. auris*	Antagonistic	Increased MICs

4.2. Herbal Extracts and Antifungal Drugs

Research has also investigated the potential of combining herbal extracts with pharmacological antifungals to enhance their activity against Candida infections.[32] For instance, gypenosides, compounds extracted from *Gynostemma pentaphyllum*, have shown synergistic antifungal activity with fluconazole against fluconazole-resistant *C. albicans* by inhibiting drug efflux and biofilm formation.[38] Similarly, extracts from *Phytolacca tetramera* berries and its constituent phytolaccagenin have demonstrated

synergistic effects when combined with itraconazole or posaconazole against *C. albicans*, including resistant strains. This combination acts by binding to ergosterol and inhibiting biofilm formation.[35] Berberine, an alkaloid found in several plants, has been shown to inhibit yeast adhesion, hyphal transformation, and biofilm formation in combination with fluconazole.[34] Furthermore, a combination of glycolic extracts from *Rosa centifolia* and *Curcuma longa* has proven effective against biofilms formed by *C. albicans*, *C. dubliniensis*, and *C. tropicalis*.[32] Some studies have indicated that herbal extracts can enhance the activity of antifungal drugs specifically against Candida strains that have developed resistance to these drugs.[34] Similar to essential oils, herbal extracts contain a variety of compounds that can synergize with conventional antifungals, potentially offering a valuable approach to improve treatment outcomes, particularly in cases where drug resistance is a significant challenge.[32] The mechanisms underlying these synergistic effects often involve targeting different aspects of Candida biology compared to conventional drugs, such as inhibiting biofilm formation or drug efflux pumps, which can be crucial in overcoming resistance mechanisms.[34]

Table 3: Summary of Studies Evaluating the Combination of Herbal Extracts and Antifungal Drugs

Herbal Extract(s)	Antifungal Drug(s)	Candida Species	Type of Interaction	Key Findings
Gypenosides	Fluconazole	*C. albicans* (resistant)	Synergistic	Inhibits drug efflux and biofilm formation
Phytolacca tetramera berries extract, Phytolaccagenin	Itraconazole, Posaconazole	*C. albicans* (including resistant)	Synergistic	Binds to ergosterol, inhibits biofilm formation
Berberine	Fluconazole	*C. albicans*	Synergistic	Inhibits adhesion, hyphal transformation, biofilm formation
Rosa centifolia,	N/A	*C. albicans*, *C.*	Synergistic	Effective against

Curcuma longa (glycolic extracts)		*dubliniensis*, *C. tropicalis*		biofilms

5. Combination Therapies: Pharmacological Agents Alone

Research has also extensively explored the efficacy of combining different pharmacological antifungal drugs for the treatment of Candida infections.[2] The rationale behind such combination therapies includes the potential to broaden the spectrum of antifungal activity, enhance the rate or extent of fungal killing, minimize the development of drug resistance, and reduce drug-related toxicities by allowing for lower doses of individual agents.[17] One well-established example is the synergistic combination of amphotericin B with flucytosine, which is often used for the treatment of severe invasive candidiasis.[22] Combinations involving azoles and echinocandins have shown variable results, with synergy observed against some difficult-to-treat Candida species.[27] Similarly, the combination of polyenes and echinocandins has demonstrated potential advantages in sterilizing infected organs in experimental models.[27] A study found that combining fluconazole with cyclosporine A resulted in a synergistic effect against a range of Candida species, including those resistant to fluconazole.[26] Furthermore, the combination of amphotericin B and echinocandins has shown synergistic activity against blood isolates of *C. auris*, a particularly challenging multidrug-resistant pathogen.[18] Despite these promising findings from in vitro and in vivo studies, clinical data supporting the widespread use of pharmacological combination therapies for Candida infections remains somewhat limited.[7] Combining antifungal drugs with different mechanisms of action presents a potentially valuable strategy, especially for severe infections or those caused by drug-resistant Candida species, although the specific combinations and their effectiveness can vary considerably.[2]

6. Clinical Applications and Future Directions

The current use of combination therapies in clinical practice for Candida infections is generally reserved for specific situations.[7] These situations often include refractory candidiasis, endocarditis, meningitis, and infections caused by Candida species known to be resistant to monotherapy.[7] Clinical guidelines frequently recommend monotherapy as the initial treatment approach for most Candida infections.[7] To further inform clinical practice, more clinical studies and detailed case reports are necessary to provide robust evidence supporting the broader application of combination therapies.[7]

Translating the encouraging results observed in in vitro and in vivo studies of combination therapies to effective clinical applications faces several challenges.[2] These challenges include inherent differences in pharmacokinetics and pharmacodynamics between laboratory or animal models and human physiology. The complexity of clinical infections, which are often influenced by various patient-specific factors, also adds to the difficulty. Furthermore, designing and conducting large-scale clinical trials specifically for combination antifungal therapies can be logistically and financially demanding.[22]

Future research efforts should prioritize well-designed clinical trials to rigorously evaluate the efficacy and safety of promising combination therapies, including both those that integrate natural and pharmacological agents and those that involve only pharmacological antifungals.[2] A deeper understanding of the mechanisms that underlie the synergistic effects observed in natural and pharmacological combinations is also crucial. Identifying biomarkers that can predict the likelihood of successful combination therapy could help personalize treatment approaches. The development of standardized protocols for in vitro and in vivo testing of combination therapies would improve the comparability of research findings across different studies. Additionally, exploring novel drug delivery systems could enhance the efficacy of combination treatments by improving drug penetration and targeting.[30]

Ultimately, the development of safer and more effective antifungal treatment strategies requires a multifaceted approach.[2] This includes a strong focus on strategies to overcome the growing challenge of antifungal resistance, the development of antifungal agents with improved safety profiles, the implementation of personalized medicine approaches that consider the specific Candida species and individual patient characteristics, and an emphasis on preventative strategies, particularly in populations at high risk of developing Candida infections.[3]

7. Conclusion

The management of Candida infections is becoming increasingly complex due to the rising incidence of drug resistance and the limitations of current antifungal therapies. This report has highlighted the potential of both natural and pharmacological approaches, particularly when used in combination, to address these challenges. Essential oils and herbal extracts have demonstrated significant in vitro and in vivo antifungal activity, often through mechanisms distinct from those of conventional drugs, making them promising candidates for integrative treatment strategies. The synergistic effects observed when combining these natural agents with pharmacological antifungals offer a potential pathway to enhance treatment efficacy

and overcome drug resistance. While combination therapies involving only pharmacological agents have also shown promise, especially for severe and resistant infections, the translation of these findings into routine clinical practice requires further robust clinical trial data. The development of safer and more effective antifungal treatment strategies necessitates continued research into the mechanisms of action of both natural and synthetic agents, the identification of synergistic combinations, and the rigorous evaluation of these strategies in well-designed clinical trials. The integration of natural and pharmacological approaches holds significant potential for improving outcomes in patients with Candida infections, especially in the face of increasing antifungal resistance.

Works cited

1. Essential oils as promising treatments for treating Candida albicans infections: research progress, mechanisms, and clinical applications - Frontiers, accessed May 6, 2025, https://www.frontiersin.org/journals/pharmacology/articles/10.3389/fphar.2024.1400105/full
2. Candida Infections and Therapeutic Strategies: Mechanisms of Action for Traditional and Alternative Agents - PubMed Central, accessed May 6, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC6038711/
3. Therapeutic tools for oral candidiasis: Current and new antifungal drugs - PMC, accessed May 6, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC6441600/
4. Antifungal drug resistance in Candida: a special emphasis on amphotericin B - PubMed, accessed May 6, 2025, https://pubmed.ncbi.nlm.nih.gov/38465406/
5. Antifungal drug resistance among Candida species: mechanisms and clinical impact - PubMed, accessed May 6, 2025, https://pubmed.ncbi.nlm.nih.gov/26033251/
6. Current antifungal drugs and immunotherapeutic approaches as promising strategies to treatment of fungal diseases - PubMed, accessed May 6, 2025, https://pubmed.ncbi.nlm.nih.gov/30557835/
7. Role of Antifungal Combinations in Difficult to Treat Candida Infections - PubMed Central, accessed May 6, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC8468556/
8. The Effects of Nutraceuticals and Herbal Medicine on Candida albicans in Oral Candidiasis: A Comprehensive Review - PubMed, accessed May 6, 2025, https://pubmed.ncbi.nlm.nih.gov/33861447/
9. Essential Oils as a Good Weapon against Drug-Resistant Candida auris - PMC, accessed May 6, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC9311903/
10. Efficacy of Lamiaceae essential oils with selected azoles against Candida albicans clinical isolates - PubMed, accessed May 6, 2025, https://pubmed.ncbi.nlm.nih.gov/35861965/
11. Anti-candidal activity of essential oils alone and in combination with amphotericin B or fluconazole against multi-drug resistant isolates of Candida albicans -

PubMed, accessed May 6, 2025, https://pubmed.ncbi.nlm.nih.gov/21756200/
12. Anti-candidal activity of essential oils alone and in combination with amphotericin B or fluconazole against multi-drug resistant isolates of Candida albicans - Oxford Academic, accessed May 6, 2025, https://academic.oup.com/mmy/article/50/1/33/989403
13. Antifungal Activity of Select Essential Oils against Candida auris and Their Interactions with Antifungal Drugs - PubMed Central, accessed May 6, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC9331469/
14. Antifungal Activity of Select Essential Oils against Candida auris and Their Interactions with ... - PubMed, accessed May 6, 2025, https://pubmed.ncbi.nlm.nih.gov/35894044/
15. Synergistic Effect of Essential Oils and Antifungal Agents in Fighting Resistant Clinical Isolates of Candida auris - PubMed, accessed May 6, 2025, https://pubmed.ncbi.nlm.nih.gov/39065654/
16. Optimizing the Treatment of Invasive Candidiasis—A Case for Combination Therapy - PMC, accessed May 6, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC11181177/
17. Combinatorial strategies for combating invasive fungal infections - PMC - PubMed Central, accessed May 6, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC5354157/
18. Efficacy of the combination of amphotericin B and echinocandins against Candida auris in vitro and in the Caenorhabditis elegans host model - PubMed, accessed May 6, 2025, https://pubmed.ncbi.nlm.nih.gov/38018978/
19. Novel strategies to fight Candida species infection - PubMed, accessed May 6, 2025, https://pubmed.ncbi.nlm.nih.gov/25383647/
20. Antifungals to treat Candida albicans - PubMed, accessed May 6, 2025, https://pubmed.ncbi.nlm.nih.gov/20536294/
21. CURRENT AND PROMISING PHARMACOTHERAPEUTIC OPTIONS FOR CANDIDIASIS - PMC - PubMed Central, accessed May 6, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC8122024/
22. Use of Antifungal Combination Therapy: Agents, Order, and Timing - PMC - PubMed Central, accessed May 6, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC2889487/
23. Novel Therapies for Biofilm-Based Candida spp. Infections - PubMed, accessed May 6, 2025, https://pubmed.ncbi.nlm.nih.gov/31321751/
24. Promising Alternative Therapeutics for Oral Candidiasis - PubMed, accessed May 6, 2025, https://pubmed.ncbi.nlm.nih.gov/29852856/
25. Herbal Extracts with Antifungal Activity against Candida albicans: A Systematic Review, accessed May 6, 2025, https://pubmed.ncbi.nlm.nih.gov/32600229/
26. In Vitro Assessment of Fluconazole and Cyclosporine A Antifungal ..., accessed May 6, 2025, https://pubmed.ncbi.nlm.nih.gov/39997427/
27. Antifungal Combinations against Candida Species: From Bench to Bedside - PMC - PubMed Central, accessed May 6, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC9605143/
28. Synergistic combinations of antifungals and anti-virulence agents to fight against

Candida albicans - PubMed Central, accessed May 6, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC4601232/
29. Synergistic Anticandidal Effects of Six Essential Oils in Combination with Fluconazole or Amphotericin B against Four Clinically Isolated Candida Strains - PMC, accessed May 6, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC8470676/
30. Essential Oil-Based Design and Development of Novel Anti-Candida Azoles Formulation, accessed May 6, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC7146627/
31. In Vitro Evaluation of Synergistic Essential Oils Combination for Enhanced Antifungal Activity against Candida spp - PMC, accessed May 6, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC11204509/
32. Antifungal Action of Herbal Plants' Glycolic Extracts against Candida Species - PubMed, accessed May 6, 2025, https://pubmed.ncbi.nlm.nih.gov/36985829/
33. Antifungal Action of Herbal Plants' Glycolic Extracts against Candida Species - PMC, accessed May 6, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC10054556/
34. Herbal Products and Their Active Constituents Used Alone and in Combination with Antifungal Drugs against Drug-Resistant Candida sp, accessed May 6, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC8229001/
35. Phytolacca tetramera berries extracts and its main constituents as potentiators of antifungal drugs against Candida spp - PubMed, accessed May 6, 2025, https://pubmed.ncbi.nlm.nih.gov/38795695/
36. In vitro antifungal activities of medicinal plants used for treatment of candidiasis in Pader district, Northern Uganda - PubMed, accessed May 6, 2025, https://pubmed.ncbi.nlm.nih.gov/39533448/
37. In vitro antifungal activities of medicinal plants used for treatment of candidiasis in Pader district, Northern Uganda - PubMed Central, accessed May 6, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC11558831/
38. The synergistic antifungal effects of gypenosides combined with fluconazole against resistant Candida albicans via inhibiting the drug efflux and biofilm formation - PubMed, accessed May 6, 2025, https://pubmed.ncbi.nlm.nih.gov/32745913/
39. Antifungal activity of essential oils and their potential synergistic ..., accessed May 6, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC11682416/
40. Plants' Natural Products as Alternative Promising Anti-Candida ..., accessed May 6, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC5628516/
41. Essential oils as promising treatments for treating Candida albicans infections: research progress, mechanisms, and clinical applications, accessed May 6, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC11145275/
42. Essential oils as promising treatments for treating Candida albicans infections: research progress, mechanisms, and clinical applications - PubMed, accessed May 6, 2025, https://pubmed.ncbi.nlm.nih.gov/38831882/
43. Healthy Diet and Lifestyle Improve the Gut Microbiota and Help Combat Fungal Infection - PMC - PubMed Central, accessed May 6, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC10302699/
44. Antifungal Activity of Natural Compounds vs. Candida spp.: A Mixture of

Cinnamaldehyde and Eugenol Shows Promising In Vitro Results - PMC, accessed May 6, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC8773119/
45. Antifungal Potential of Some Herb Decoctions and Essential Oils on Candida Species - PMC, accessed May 6, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC9601325/
46. Natural Compounds with Antifungal Properties against Candida albicans and Identification of Hinokitiol as a Promising Antifungal Drug - PubMed Central, accessed May 6, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC10668714/
47. Antifungal Antibiotics - StatPearls - NCBI Bookshelf, accessed May 6, 2025, https://www.ncbi.nlm.nih.gov/books/NBK538168/
48. Therapeutic tools for oral candidiasis: Current and new antifungal drugs - PubMed, accessed May 6, 2025, https://pubmed.ncbi.nlm.nih.gov/30818309/
49. Clinical efficacy and safety of antifungal drugs for the treatment of Candida parapsilosis infections: a systematic review and network meta-analysis - PubMed, accessed May 6, 2025, https://pubmed.ncbi.nlm.nih.gov/34633919/
50. Antifungal treatment for invasive Candida infections: a mixed treatment comparison meta-analysis - PMC - PubMed Central, accessed May 6, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC2713200/
51. Efficacy and safety of echinocandin monotherapy and combination therapy for immunocompromised patients with systemic candidiasis: A systematic review and meta-analysis - PubMed, accessed May 6, 2025, https://pubmed.ncbi.nlm.nih.gov/36867970/