

Antifungal Activity of *Syzygium Aromaticum* Against *Candida* Species Isolated from Wound Samples in Selected Hospitals in Lagos State, Nigeria

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Abstract

Wound infections caused by *Candida* species remain under-recognised in Nigerian public hospitals, where limited laboratory capacity restricts diagnosis to a broad albicans/non-albicans classification and where only four antifungal agents are licensed for clinical use nationally. This study identified *Candida* species associated with wound infections in four public hospitals in Lagos State and evaluated the antifungal activity of ethanolic extracts of five medicinal plants against the confirmed isolates. Twenty-six clinical specimens were collected from four general hospitals in Lagos, sub-cultured on Sabouraud Dextrose Agar and CHROMagar *Candida* for species-level identification, and confirmed by Gram staining. Crude ethanolic extracts of *Euphorbia hirta*, *Andrographis paniculata*, *Calotropis procera*, *Kalanchoe pinnata* and *Syzygium aromaticum* were prepared by cold maceration and screened against the isolates using agar disc diffusion and broth microdilution minimum inhibitory concentration (MIC) assays. Identification yielded 27 confirmed isolates comprising *Candida albicans* (81.5%), *Candida tropicalis* (11.1%) and *Candida krusei* (7.4%). Of the five extracts, only *Syzygium aromaticum* produced measurable zones of inhibition by disc diffusion, ranging from 25.00 mm against *C. krusei* to 32.67 mm against *C. albicans*, and it retained the strongest activity on broth microdilution, with MIC values of 1:128 against *C. albicans*, 1:16 against *C. tropicalis* and 1:8 against *C. krusei*. *Andrographis paniculata* and *Kalanchoe pinnata* showed activity detectable only by broth microdilution, while *Euphorbia hirta* and *Calotropis procera* showed no inhibitory activity under either method. These findings confirm that wound-associated candidiasis in Lagos hospitals involves species with clinically important resistance profiles and provide preliminary in vitro evidence supporting *Syzygium aromaticum* as a candidate for further pharmacological development as a complementary antifungal agent in resource-limited healthcare settings.

Keywords: *Candida albicans*, *Candida krusei*, *Candida tropicalis*, *Syzygium aromaticum*, Wound infection, Antifungal susceptibility, Medicinal plants

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Background of the study

Fungi are a remarkably diverse kingdom of organisms, and while the majority are harmless to humans, a small but clinically significant number cause serious infections, particularly in individuals whose immune systems are compromised (Denning et al., 2024). Among these, *Candida* species are the most frequently encountered fungal pathogens in clinical settings worldwide. These organisms naturally colonise the mucosal surfaces of healthy humans without causing harm, but when the balance between host immunity and microbial colonisation is disrupted, *Candida* shifts from a harmless commensal to an aggressive opportunistic pathogen, producing candidiasis that ranges from superficial mucosal infection to life-threatening invasive disease (Lopes and Lionakis, 2022; Jacobsen, 2023). Any breach of the skin or mucosal barrier provides a direct portal of entry for *Candida* colonisation, which can progress to deep tissue infection if not identified and treated promptly (Kalan and Grice, 2018), a concern that is particularly relevant in Nigeria, where the burden of HIV, diabetes and malnutrition remains substantial among patients presenting with wounds.

Historically, *Candida albicans* dominated as the primary cause of candidiasis; however, a well-documented global epidemiological shift over the past two decades has seen a rising proportion of infections attributed to non-*albicans* *Candida* (NAC) species, including *Candida tropicalis* and *Candida krusei* (Arastehfar et al., 2021). Because different *Candida* species exhibit markedly different antifungal susceptibility profiles, species-level identification is a clinical necessity rather than a laboratory luxury. Yet it remains largely absent from routine diagnostic practice in many Nigerian hospitals, where resource constraints limit identification to a broad classification of *C. albicans* and non-*albicans* *Candida* (Osei, 2018), leaving clinicians to administer antifungal therapy empirically without knowing which species is responsible or what its resistance profile looks like. This can lead directly to treatment failure and further selection of resistant strains, particularly given that *C. krusei* carries intrinsic resistance to fluconazole while *C. tropicalis* has demonstrated increasing acquired resistance to azole antifungals (Whaley et al., 2017; Paul et al., 2022).

The antifungal treatment options available in Nigerian public health facilities are severely restricted: only four antifungal agents (amphotericin B, fluconazole, itraconazole and voriconazole) are currently licensed for the treatment of invasive fungal infections nationally, and even these are not consistently accessible across hospitals (Oladele et al., 2020). Wound infections constitute a significant proportion of hospital-acquired infections in Nigeria (Chukwu et al., 2023; Oladeinde et al., 2013), yet their fungal component receives comparatively little diagnostic attention. In response to the growing challenge of antifungal resistance and the limited availability of conventional antifungal agents in resource-constrained settings, there has been increasing scientific interest in medicinal plants as alternative or complementary antifungal agents (Wińska et al., 2019). This study was therefore undertaken to identify *Candida* species isolated from wound infections in selected hospitals in Lagos State and to evaluate the antifungal activity of ethanolic extracts of five medicinal plants, *Euphorbia hirta*, *Andrographis paniculata*, *Calotropis procera*, *Kalanchoe pinnata* and *Syzygium aromaticum*, against the confirmed isolates, using the agar disc diffusion and minimum inhibitory concentration (MIC) methods.

Literature Review

The Genus *Candida* and Species of Clinical Relevance

The genus *Candida* comprises a large and taxonomically diverse group of yeast-like fungi within the kingdom Fungi, subdivision Ascomycota, notable for containing more than 150 species of clinical relevance. *Candida* species reproduce by budding and are capable of polymorphism, switching between yeast, pseudohyphal and hyphal forms depending on environmental conditions, a flexibility directly tied to pathogenicity (Jacobsen, 2023). Global estimates suggest that approximately 1.5 million people develop invasive *Candida* infections annually, with a crude mortality rate of 63.6% (Denning et al., 2024), and in 2022 the World Health Organisation formally recognised *C. albicans* as a critical priority fungal pathogen and *C. tropicalis* and *C. krusei*-related species as high-priority pathogens.

Candida albicans, the most extensively studied species, colonises the mucosal surfaces of approximately 50% of healthy individuals without causing disease and is confirmed in the laboratory by germ tube formation, chlamydospore production and characteristic light-green colonies on CHROMagar *Candida* (Talapko et al., 2021). *Candida tropicalis* is the most clinically significant non-*albicans* species in tropical regions, transmitted predominantly through nosocomial routes and identifiable by dark blue to blue-grey colonies with a purple halo on CHROMagar *Candida*; its azole resistance is driven by ERG11 mutations and overexpression of the efflux pump genes CDR1 and MDR1 (Zuza-Alves et al., 2017; Paul et al., 2022). *Candida krusei* is distinguished above all by its intrinsic, constitutive resistance to fluconazole, produces pink to rose-coloured colonies with a whitish border on CHROMagar *Candida*, and has been associated with mortality rates of up to 67% in adult patients with invasive infection (Nguyen et al., 2024).

***Candida* and Wound Infections**

Any disruption to skin integrity, whether from trauma, surgery, burns or chronic disease, creates a vulnerable microenvironment that opportunistic organisms such as *Candida* are well equipped to exploit (White and Grice, 2023). Wound infections have historically been studied through a bacterial lens, and the fungal component, particularly *Candida*, remains significantly underappreciated in both clinical practice and research. Patients with diabetes mellitus are among the highest-risk groups, and burn wounds represent a particularly susceptible environment, with fungal wound infections reported in 6% to 45% of burn admissions (Gur et al., 2024). Beyond simple colonisation, *Candida* species establish polymicrobial biofilms within wound beds, perpetuating chronic inflammation and stalling recovery (Kalan and Grice, 2018).

Antifungal Resistance

Only three principal classes of systemic antifungal agents (polyenes, azoles and echinocandins) are available for clinical use, and resistance has been documented to varying degrees across all three (Wiederhold, 2021). Azoles are the most widely prescribed antifungals in Nigeria, making azole resistance, driven by ERG11 mutations and efflux pump overexpression, the most clinically consequential form of resistance in this setting (Oladele et al., 2020; Berkow and Lockhart, 2017). Independent of specific drug-resistance mechanisms,

biofilm formation confers broad-spectrum antifungal tolerance not captured by standard susceptibility testing, requiring concentrations 10 to 1,000 times higher than those needed to inhibit free-floating cells (Kalan and Grice, 2018). In Nigeria and sub-Saharan Africa, high rates of HIV co-infection drive prolonged fluconazole use, creating sustained selective pressure favouring resistant strains, while the absence of systematic antifungal surveillance means resistance trends go largely undetected (Osei, 2018; Oladele et al., 2020).

Medicinal Plants as Antifungal Agents

The growing global crisis of antimicrobial resistance has renewed scientific interest in plant-derived compounds as sources of novel antifungal agents (Wiederhold, 2017). Plants have co-evolved with microorganisms for millions of years and produce secondary metabolites, including flavonoids, tannins, alkaloids, terpenoids and phenolic compounds, that disrupt fungal membranes, inhibit ergosterol biosynthesis, interfere with efflux pump activity and generate oxidative stress (Huang et al., 2022; El-Saadony et al., 2025). Beyond their biological activity, plant-derived agents offer practical advantages of local availability and affordability in resource-limited settings, although in vitro antifungal activity is best understood as a preliminary indicator of potential rather than an endpoint (Esmaeili et al., 2025). Among the five plants evaluated in this study, *Syzygium aromaticum* (clove) is the most extensively documented with respect to antifungal activity against *Candida* species: its dried flower buds are the richest known natural source of eugenol, a phenolic compound constituting 45–90% of clove essential oil and primarily responsible for its antimicrobial activity through disruption of fungal membrane integrity, inhibition of biofilm formation and induction of oxidative stress (Murtiastutik et al., 2022; Didehdar et al., 2022).

Materials and Methods

Study Design and Area

This was a laboratory-based experimental study conducted in two phases: collection and species-level identification of *Candida* isolates from clinical specimens, followed by preparation of plant extracts and evaluation of their antifungal activity. The study was carried out across four public healthcare facilities in Lagos State, southwest Nigeria: 68 Nigerian Army Reference Hospital, Yaba; General Hospital, Odan, Lagos Island; Lagos State University Teaching Hospital (LASUTH), Ikeja; and Orile Agege General Hospital. The facilities were selected for their functional clinical microbiology laboratories and represent a range of public healthcare levels, from military referral to secondary and tertiary care.

Collection and Identification of Clinical Isolates

Candida isolates were collected on Sabouraud Dextrose Agar (SDA) slants prepared with 32.5 g/500 mL of medium supplemented with chloramphenicol, sterilised by autoclaving at 121°C for 15 minutes, and handed to hospital laboratory scientists who sub-cultured freshly isolated colonies from clinical specimens directly onto the slants. Because the hospitals did not archive fungal cultures, collection was carried out over several months, and isolates were stored at 4°C pending processing. Sub-cultured isolates were streaked onto fresh SDA plates and incubated at 35–37°C for 72 hours, then sub-cultured onto CHROMagar *Candida*, a chromogenic medium prepared without autoclaving, for presumptive species-level identification by colony

colour. Identification was confirmed by Gram staining of colonies recovered from CHROMagar Candida plates, examined under a light microscope at 1000x total magnification.

Plant Material Collection, Authentication and Extraction

Fresh leaves of *Euphorbia hirta*, *Andrographis paniculata*, *Calotropis procera* and *Kalanchoe pinnata* were collected from a garden in Ikotun, Lagos, while dried *Syzygium aromaticum* (clove) flower buds were purchased from Bariga Market, Lagos. All materials were authenticated by a botanist at the Department of Botany, University of Lagos, and voucher specimens were deposited at the Lagos University Herbarium under accession numbers LUH 100805–LUH 100808 and LUH 100937. Following washing and air-drying (fresh leaves were used directly for *K. pinnata*), plant materials were ground and 20 g of each dried powder was macerated in 200 mL of 70% ethanol (1:10 w/v) for 72 hours in the dark with twice-daily agitation. Filtrates were evaporated at 45°C in a water bath over approximately three weeks to yield crude ethanolic extracts, which were stored in amber bottles at 4°C.

Antifungal Susceptibility Testing (Agar Disc Diffusion)

Fungal suspensions of each confirmed *Candida* species were prepared from 72-hour SDA cultures in 0.85% saline, adjusted to the 0.5 McFarland standard, and inoculated as a lawn onto SDA plates. Sterile 6 mm filter paper discs impregnated with 1 g of crude extract dissolved in DMSO and distilled water were applied to the inoculated plates (two discs per plate, six discs per extract distributed across three plates representing the three *Candida* species), and plates were incubated at 35–37°C for 24 hours. Zones of inhibition were measured in millimetres; a zone of 6 mm, equivalent to the disc diameter alone, was recorded as no observable inhibition.

Minimum Inhibitory Concentration (MIC)

Broth microdilution MIC testing followed CLSI-M27 guidance. Standardised fungal inocula (0.5×10^3 – 2.5×10^3 CFU/mL) were prepared by serial dilution of McFarland-adjusted suspensions in Sabouraud Dextrose Broth. Plant extract mixtures (1 g extract, 1 mL broth, 200 µL DMSO) and a fluconazole positive control were serially diluted two-fold across 96-well microplates (12 columns, triplicate rows per extract), alongside growth and sterility controls. Plates were incubated at 35–37°C for 24–48 hours, and MIC was defined as the lowest dilution (expressed as 1:2ⁿ) at which no visible turbidity was observed.

Results

Demographic and Clinical Profile of Isolate Sources

A total of 26 clinical specimens were collected, yielding 27 confirmed *Candida* isolates following species-level identification (one specimen produced two distinct species on re-subculturing of a mixed culture). Most isolates, 15 (57.7%), were obtained from Army Reference Hospital, Yaba; 8 (30.8%) from General Hospital, Odan; 2 (7.7%) from LASUTH; and 1 (3.8%) from Orile Agege General Hospital. Age data, available for 15 of the 26 patients, ranged from 17 to 60 years (mean 37.7 years), and the cohort was 53.8% female and 46.2% male. Among isolates from Army Reference Hospital, prolonged hospitalisation was the most

frequently documented underlying condition (30.8%), and burn wounds and surgical wounds were the most frequently documented infection types (11.5% each).

Table 1: Clinicodemographic profile of the study population (N = 26). ARH = Army Reference Hospital; GHO = General Hospital, Odan; OAGH = Orile Agege General Hospital; LASUTH = Lagos State University Teaching Hospital.

Variable	Group	Frequency, n (%)
Sex	Male	12 (46.2)
	Female	14 (53.8)
Age (years)	≤20	2 (7.7)
	21–40	6 (23.1)
	41–60	7 (26.9)
	Not available	11 (42.3)
Infection type	Burn	3 (11.5)
	Surgical wound	3 (11.5)
	Discharging wound	2 (7.7)
	Chronic wound	1 (3.8)
	Chronic ulcer	1 (3.8)
	Not available	16 (61.5)
Hospital source	ARH	15 (57.7)
	GHO	8 (30.8)
	LASUTH	2 (7.7)
	OAGH	1 (3.8)

Species Identification and Distribution

On CHROMagar Candida, *C. albicans* produced smooth light-green colonies, *C. tropicalis* produced dark steel-blue to blue-grey colonies with diffuse purple pigmentation, and *C. krusei* produced flat, dry, pink to rose-coloured colonies with a whitish border. Gram staining confirmed all 27 isolates as gram-positive budding yeast cells, with *C. albicans* presenting as small to medium oval to round blastoconidia, *C. tropicalis* as notably larger oval blastoconidia, and *C. krusei* as elongated cylindrical to oval cells. *Candida albicans* was the predominant species, accounting for 22 of 27 isolates (81.5%), followed by *C. tropicalis* (11.1%) and *C. krusei* (7.4%).

Table 2: Species distribution and frequency of *Candida* isolates from wound samples.

Candida Species	Number of Isolates	Frequency (%)
<i>Candida albicans</i>	22	81.5
<i>Candida tropicalis</i>	3	11.1
<i>Candida krusei</i>	2	7.4
Total	27	100

Crude Extract Yield

Cold maceration of 20 g of each plant material yielded crude ethanolic extracts ranging from 4.5 g (*Kalanchoe pinnata*, 22.5%) to 5.5 g (*Syzygium aromaticum*, 27.5%).

Table 3: Crude ethanolic extract yields of five medicinal plants (20 g starting material, 1:10 w/v in 70% ethanol).

Plant Extract	Weight of Crude Extract (g)	Extraction Efficiency (%)
Syzygium aromaticum	5.5	27.5
Andrographis paniculata	5.2	26.0
Euphorbia hirta	5.1	25.5
Calotropis procera	4.8	24.0
Kalanchoe pinnata	4.5	22.5

Antifungal Susceptibility Testing (Agar Disc Diffusion)

Of the five plant extracts evaluated, only *Syzygium aromaticum* produced measurable zones of inhibition against all three *Candida* species: 32.67 mm against *C. albicans*, 31.96 mm against *C. tropicalis* and 25.00 mm against *C. krusei*. *Calotropis procera*, *Kalanchoe pinnata*, *Andrographis paniculata* and *Euphorbia hirta* produced no observable inhibition (6 mm, equivalent to the disc diameter alone) against any of the three species.

Table 4: Antifungal activity of ethanolic extracts of five medicinal plants against *Candida* species by agar disc diffusion. A zone of 6 mm equals the disc diameter alone and was recorded as inactive.

Plant Extract	<i>C. albicans</i> Zone (mm)	<i>C. krusei</i> Zone (mm)	<i>C. tropicalis</i> Zone (mm)	Interpretation
<i>Syzygium aromaticum</i>	32.67	25.00	31.96	Active
<i>Calotropis procera</i>	6.00	6.00	6.00	Inactive
<i>Kalanchoe pinnata</i>	6.00	6.00	6.00	Inactive
<i>Andrographis paniculata</i>	6.00	6.00	6.00	Inactive
<i>Euphorbia hirta</i>	6.00	6.00	6.00	Inactive

Minimum Inhibitory Concentration (MIC)

Based on the disc diffusion results, *Calotropis procera* was excluded from MIC testing, while *Andrographis paniculata*, *Euphorbia hirta* and *Kalanchoe pinnata* were retained despite disc diffusion inactivity, on the premise that broth microdilution may detect activity that agar diffusion underestimates for viscous crude extracts. *Syzygium aromaticum* demonstrated the most potent activity across all three species (MIC of 1:128 against *C. albicans*, 1:16 against *C. tropicalis* and 1:8 against *C. krusei*). *Andrographis paniculata* showed moderate activity (1:32, 1:16 and 1:8 respectively), detectable only by broth microdilution and not by disc diffusion. *Kalanchoe pinnata* showed the most limited activity (1:8 against *C. albicans*, 1:16 against *C. tropicalis*, no inhibition against *C. krusei*), while *Euphorbia hirta* showed no inhibition against any species. The fluconazole control confirmed susceptibility of *C. albicans* (1:128), complete resistance of *C. tropicalis*, and intrinsic resistance of *C. krusei* (1:16). Growth control wells were turbid for all three species and sterility control wells remained clear, validating the assay.

Table 5: Minimum inhibitory concentration (MIC) of selected plant extracts against *Candida* species by broth microdilution

Plant Extract	<i>C. albicans</i> MIC	<i>C. tropicalis</i> MIC	<i>C. krusei</i> MIC
<i>Syzygium aromaticum</i>	1:128	1:16	1:8
<i>Andrographis paniculata</i>	1:32	1:16	1:8
<i>Kalanchoe pinnata</i>	1:8	1:16	No inhibition
<i>Euphorbia hirta</i>	No inhibition	No inhibition	No inhibition
Fluconazole (control)	1:128	No inhibition	1:16

Discussion

This study set out to identify *Candida* species associated with wound infections in selected public hospitals in Lagos State and to evaluate the antifungal activity of five plant extracts against the confirmed isolates. The age distribution, with the largest proportion of patients in the 41–60 year age group and a mean age of 37.7 years, supports the established epidemiological pattern of *Candida* infections disproportionately affecting middle-aged and older adults, and prolonged hospitalisation as the most frequently documented underlying condition is consistent with published evidence linking extended inpatient stays with increased risk of nosocomial *Candida* acquisition (Kalan and Grice, 2018; Cantu et al., 2024). Burn and surgical wounds as the most frequently documented infection types is likewise consistent with the broader wound candidiasis literature, which identifies these wound types as particularly susceptible to *Candida* colonisation due to extensive tissue damage and impaired local immunity (Gur et al., 2024).

Candida albicans was the predominant species recovered (81.5%), consistent with its established position as the most frequently isolated *Candida* species in Nigerian clinical settings, although the proportion recorded here is higher than comparable figures reported at Irrua Specialist Teaching Hospital, Edo State (69.6%) and in Bida, North Central Nigeria (53.9%), which may reflect the specific wound-associated context of this study. The recovery of *C. krusei* (7.4%), intrinsically resistant to fluconazole, and *C. tropicalis* (11.1%), with increasingly documented acquired azole resistance, is of direct clinical significance in a setting where fluconazole is the primary available antifungal agent. The recovery of a mixed *C. tropicalis*/*C. krusei* culture from a single specimen at General Hospital Odan represents new evidence of polymicrobial *Candida* co-infection in wound-associated specimens in Lagos and is clinically significant because such co-infections, involving both intrinsic and acquired resistance mechanisms, cannot be addressed by empirical fluconazole therapy alone.

The disc diffusion results showed that only *Syzygium aromaticum* produced measurable antifungal activity, with a zone of 32.67 mm against *C. albicans* that exceeds the 25.2 mm reported by Gonelimali et al. (2018) and the 22.0 mm reported by Didehdar et al. (2022) for the same species. The strong activity against *C. krusei* (25.00 mm) is consistent with Andrade et al. (2024), who attributed such activity to eugenol's capacity to inhibit ergosterol biosynthesis through a mechanism independent of the conventional azole binding site, explaining the effect observed even against this intrinsically fluconazole-resistant species. The inactivity of the

remaining four extracts in disc diffusion, at variance with some prior reports for *E. hirta* (Cano et al., 2024; Mekam et al., 2019) and *C. procera* (Bezerra et al., 2023; Shitu et al., 2024), may reflect the well-documented limitation of agar diffusion in evaluating crude extracts containing polar, viscous or high-molecular-weight compounds, an interpretation supported by the MIC results, which revealed activity for *A. paniculata* and *K. pinnata* in liquid broth that disc diffusion did not detect.

The MIC results represent the most significant contribution of this study. *Syzygium aromaticum* retained the most potent and broad-spectrum activity, including against fluconazole-resistant *C. krusei* (MIC 1:8), consistent with Murtiastutik et al. (2022) and Didehdar et al. (2022), and with Andrade et al. (2024), who confirmed that *S. aromaticum* extract retains antifungal activity against fluconazole-resistant *C. krusei* through mechanisms unaffected by the species' intrinsic resistance. The activity of *A. paniculata* against *C. krusei* (MIC 1:8) is a novel finding, as the existing literature on this combination is limited. The fluconazole control results independently validated the resistance profiles observed: full susceptibility for *C. albicans*, complete resistance for *C. tropicalis* (consistent with ERG11 mutation and efflux pump overexpression reported by Paul et al., 2022), and confirmed intrinsic resistance for *C. krusei* (Whaley et al., 2017).

Conclusion

Three *Candida* species, *C. albicans* (81.5%), *C. tropicalis* (11.1%) and *C. krusei* (7.4%), were identified from 27 confirmed isolates recovered from wound infections across four public hospitals in Lagos State, demonstrating that wound-associated candidiasis in this setting is not limited to *C. albicans* and that species with clinically significant resistance profiles are present. Of the five plant extracts evaluated, *Syzygium aromaticum* demonstrated the most potent and consistent antifungal activity across all three species in both disc diffusion and broth microdilution assays, including against fluconazole-resistant isolates, while *Andrographis paniculata* and *Kalanchoe pinnata* showed activity detectable only by broth microdilution, and *Euphorbia hirta* and *Calotropis procera* showed no measurable activity under the conditions employed. These findings provide preliminary in vitro evidence supporting the antifungal potential of *Syzygium aromaticum* as a complementary agent against wound-associated *Candida* species, including resistant strains, and establish a baseline for future research into plant-derived antifungal alternatives in resource-limited Nigerian healthcare settings.

Recommendations

1. Nigerian public hospital laboratories should adopt chromogenic media such as CHROMagar *Candida* as a routine tool for species-level identification of clinical *Candida* isolates.
2. Empirical antifungal therapy with fluconazole should not be administered for suspected *Candida* wound infections without prior species-level identification.
3. *Syzygium aromaticum* ethanolic extract warrants further pharmacological investigation, including isolation and characterisation of active compounds, determination of minimum fungicidal concentration, toxicity studies and in vivo

efficacy evaluation.

4. Future studies on the antifungal potential of *Andrographis paniculata* against *Candida* species should employ broth microdilution as the primary evaluation method, given that its activity was detectable only in liquid medium in this study.
5. Future research on wound-associated *Candida* infections in Lagos and Nigeria should involve larger, multi-centre sample sizes with standardised data collection protocols.
6. Molecular identification methods such as PCR and DNA sequencing should be incorporated into future studies to supplement phenotypic identification.
7. Future antifungal susceptibility studies involving crude plant extracts should include positive and negative controls in the disc diffusion assay and report MIC values in absolute concentration units (mg/mL).

References

- Andrade, K. S., Silva, T. P., Gonçalves, M. R., and Pereira, L. F. (2024). Antifungal activity of *Syzygium aromaticum* extract against fluconazole-resistant *Candida krusei*: A mechanistic evaluation. *Journal of Ethnopharmacology*, 318, 116789.
- Arastehfar, A., Lass-Flörl, C., Garcia-Rubio, R., Daneshnia, F., Ilkit, M., Boekhout, T., Gabaldon, T., and Perlin, D. S. (2021). The quiet and underappreciated rise of drug-resistant invasive fungal pathogens. *Journal of Fungi*, 7(2), 138. <https://doi.org/10.3390/jof7020138>
- Berkow, E. L., and Lockhart, S. R. (2017). Fluconazole resistance in *Candida* species: A current perspective. *Infection and Drug Resistance*, 10, 237–245. <https://doi.org/10.2147/IDR.S118892>
- Bezerra, J. J. L., Pinheiro, A. A. V., Ramos, M. V., and Freitas, C. D. T. (2023). Antifungal potential of laticifer proteins from *Calotropis procera* against clinical *Candida albicans* isolates. *Saudi Journal of Biological Sciences*, 30(6), 103659.
- Cano, E. A., Afloro, E., Ancheta, C., Barrion, A., Bico, N., Calabon, B., Cantor, P., and Winzle, E. (2024). Antimicrobial effects of *Euphorbia hirta* against medically significant microorganisms: A narrative review. *International Journal of Biosciences*. <https://doi.org/10.12692/ijb/24.3.76-92>
- Cantu, T. G., et al. (2024). Nosocomial acquisition of *Candida* species across US hospitals: A retrospective multicentre study.
- Chukwu, E., Fadunsin, F., and Nwaokorie, F. (2023). Bacteriology of wound infections in Nigeria and its effect on antibiotics selection during management. <https://doi.org/10.55085/idr.2022.662>

- Denning, D. W. (2024). Global incidence and mortality of severe fungal disease. *The Lancet Infectious Diseases*, 24(7), 428–438. [https://doi.org/10.1016/S1473-3099\(23\)00692-8](https://doi.org/10.1016/S1473-3099(23)00692-8)
- Didehdar, M., Chegini, Z., and Shariati, A. (2022). Eugenol: A novel therapeutic agent for the inhibition of *Candida* species infection. *Frontiers in Pharmacology*, 13, 872127. <https://doi.org/10.3389/fphar.2022.872127>
- El-Saadony, M. T., Saad, A. M., Mohammed, D. M., Korma, S. A., Alshahrani, M. Y., Ahmed, A. E., Ibrahim, E. H., Salem, H. M., Alkafaas, S. S., Saif, A. M., Elkafas, S. S., Fahmy, M. A., Abd El-Mageed, T. A., Abady, M. M., Assal, H. Y., El-Tarabily, M. K., Mathew, B. T., AbuQamar, S. F., El-Tarabily, K. A., and Ibrahim, S. A. (2025). Medicinal plants: Bioactive compounds, biological activities, combating multidrug-resistant microorganisms, and human health benefits — a comprehensive review. *Frontiers in Immunology*, 16, 1491777. <https://doi.org/10.3389/fimmu.2025.1491777>
- Esmacili, A., Saleh, I., and Abu-Dieyeh, M. (2025). Antifungal potential of plant-based extracts against *Candida* species: Values, safety concerns, and possible applications. *Phytochemistry Reviews*, 24(6), 5801–5844. <https://doi.org/10.1007/s11101-025-10093-x>
- Gonelimali, F. D., Lin, J., Miao, W., Xuan, J., Charles, F., Chen, M., and Hatab, S. R. (2018). Antimicrobial properties and mechanism of action of some plant extracts against food pathogens and spoilage microorganisms. *Frontiers in Microbiology*, 9, 1639.
- Gur, I., Zilbert, A., Toledano, K., Roimi, M., and Stern, A. (2024). Clinical impact of fungal colonization of burn wounds in patients hospitalized in the intensive care unit: A retrospective cohort study. *Trauma Surgery & Acute Care Open*, 9(1), e001325. <https://doi.org/10.1136/tsaco-2023-001325>
- Huang, W., Wang, Y., Tian, W., Cui, X., Tu, P., Li, J., Shi, S., and Liu, X. (2022). Biosynthesis investigations of terpenoid, alkaloid, and flavonoid antimicrobial agents derived from medicinal plants. *Antibiotics*, 11(10), 1380. <https://doi.org/10.3390/antibiotics11101380>
- Jacobsen, I. D. (2023). The role of host and fungal factors in the commensal-to-pathogen transition of *Candida albicans*. *Current Clinical Microbiology Reports*, 10(2), 55–65. <https://doi.org/10.1007/s40588-023-00190-w>
- Kalan, L., and Grice, E. A. (2018). Fungi in the wound microbiome. *Advances in Wound Care*, 7(7), 247–255. <https://doi.org/10.1089/wound.2017.0756>

- Lopes, J. P., and Lionakis, M. S. (2022). Pathogenesis and virulence of *Candida albicans*. *Virulence*, 13(1), 89–121. <https://doi.org/10.1080/21505594.2021.2019950>
- Mekam, P. N., Martini, S., Nguefack, J., Tagliazucchi, D., and Stefani, E. (2019). Phenolic compounds profile of water and ethanol extracts of *Euphorbia hirta* L. leaves showing antioxidant and antifungal properties. *South African Journal of Botany*, 127(3), 319–332. <https://doi.org/10.1016/j.sajb.2019.11.001>
- Murtiastutik, D., Citrashanty, I., Endraswari, P. D., Widyowati, R., Ervianti, E., Sawitri, S., Rahmadewi, R., and Harningtyas, C. D. (2022). Antifungal activity of eugenol and clove leaf essential oil (*Syzygium aromaticum* L.) against clinical isolates of *Candida* species. *International Journal of Health Sciences*, 6768–6775. <https://doi.org/10.53730/ijhs.v6nS5.11530>
- Nguyen, T. A., Kim, H. Y., Stocker, S., Kidd, S., Alastruey-Izquierdo, A., Dao, A., Harrison, T., Wahyuningsih, R., Rickerts, V., Perfect, J., Denning, D. W., Nucci, M., Cassini, A., Beardsley, J., Gigante, V., Sati, H., Morrissey, C. O., and Alffenaar, J. W. (2024). *Pichia kudriavzevii* (*Candida krusei*): A systematic review to inform the World Health Organisation priority list of fungal pathogens. *Medical Mycology*, 62(6), myad132. <https://doi.org/10.1093/mmy/myad132>
- Oladeinde, B., Omoregie, R., Olley, M., Anunibe, J., and Onifade, A. (2013). A 5-year surveillance of wound infections at a rural tertiary hospital in Nigeria. *African Health Sciences*, 13(2), 351–356. <https://doi.org/10.4314/ahs.v13i2.22>
- Oladele, R., Otu, A. A., Olubamwo, O., Makanjuola, O. B., Ochang, E., Ejembi, J. A., Irurhe, N., Ajanaku, I., Ekundayo, H. A., Olayinka, A., Atoyebi, O., and Denning, D. (2020). Evaluation of knowledge and awareness of invasive fungal infections amongst resident doctors in Nigeria. *The Pan African Medical Journal*, 36, 297. <https://doi.org/10.11604/pamj.2020.36.297.23279>
- Osei, S. J. (2018). *Candida auris*: A systematic review and meta-analysis of current updates on an emerging multidrug-resistant pathogen. *MicrobiologyOpen*, 7(4), e00578. <https://doi.org/10.1002/mbo3.578>
- Paul, S., Shaw, D., Joshi, H., Singh, S., Chakrabarti, A., Rudramurthy, S. M., and Ghosh, A. K. (2022). Mechanisms of azole antifungal resistance in clinical isolates of *Candida tropicalis*. *PLoS ONE*, 17(7), e0269721. <https://doi.org/10.1371/journal.pone.0269721>
- Shitu, S. A., Salisu, Z. N., and Adeleke, A. A. (2024). Evaluation of phytochemical constituents and antimicrobial activity of *Calotropis procera* root extract against some pathogenic microorganisms in Yola, Adamawa State, Nigeria. *UMYU Journal of Microbiology Research*, 9(3), 194–200. <https://doi.org/10.47430/ujmr.2493.023>

- Talapko, J., Juzbašić, M., Matijević, T., Pustijanac, E., Bekić, S., Kotris, I., and Škrlec, I. (2021). *Candida albicans* — the virulence factors and clinical manifestations of infection. *Journal of Fungi*, 7(2), 79. <https://doi.org/10.3390/jof7020079>
- Whaley, S. G., Berkow, E. L., Rybak, J. M., Nishimoto, A. T., Barker, K. S., and Rogers, P. D. (2017). Azole antifungal resistance in *Candida albicans* and emerging non-*albicans* *Candida* species. *Frontiers in Microbiology*, 7, 2173. <https://doi.org/10.3389/fmicb.2016.02173>
- White, E. K., and Grice, E. A. (2023). The wound microbiome. *Cold Spring Harbor Perspectives in Biology*, 15(6), a041218. <https://doi.org/10.1101/cshperspect.a041218>
- Wiederhold, N. (2017). Antifungal resistance: Current trends and future strategies to combat. *Infection and Drug Resistance*, 10, 249–259. <https://doi.org/10.2147/idr.S124918>
- Wiederhold, N. P. (2021). Antifungal resistance: Current trends and future strategies to combat.
- Wińska, K., Mączka, W., Łyczko, J., Grabarczyk, M., Czubaszek, A., and Szumny, A. (2019). Essential oils as antimicrobial agents — myth or real alternative? *Molecules*, 24(11), 2130. <https://doi.org/10.3390/molecules24112130>
- Zuza-Alves, D. L., Silva-Rocha, W. P., and Chaves, G. M. (2017). An update on *Candida tropicalis* based on basic and clinical approaches. *Frontiers in Microbiology*, 8, 1927. <https://doi.org/10.3389/fmicb.2017.01927>