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A REVIEW OF FORMULATION AND EVALUATION OF ANTI FUNGAL CREAM USING DIFFERENT PLANT EXTRACT

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1. INTRODUCTION

Fungi are eukaryotic organisms found in nearly every environment, with only a limited subset contributing to human disease. These pathogenic fungi can cause infections ranging from mild cutaneous conditions to invasive, life-threatening diseases such as cryptococcal meningitis. Antifungal agents serve as a critical therapeutic class for managing these infections. Understanding the pharmacologic characteristics of antifungal medications—including spectrum of activity, mechanism of action, and pharmacokinetics—is essential for effective treatment selection.

This activity provides healthcare professionals with essential information on antifungal resistance trends, clinical guidelines for treating superficial and systemic fungal infections, and therapeutic considerations for high-risk populations, including the immunocompromised. Emphasis is placed on strategies for clinical decision-making, monitoring for efficacy and toxicity, and recognizing drug-drug interactions and adverse effect profiles. The role of emerging antifungal therapies and evolving patterns in fungal epidemiology is also discussed. This activity supports improved patient outcomes through informed prescribing and management of antifungal agents.

1. OBJECTIVES

- Evaluate the mechanism of action of various antifungal antimicrobials.
- Identify the approved indications and contraindications for antifungal antimicrobials.
- Assess the adverse events and toxicity associated with antifungal antimicrobial administration.
- Implement interprofessional team strategies for improving care coordination and communication with antifungal antimicrobials to treat mycotic infections to achieve optimal patient outcomes.

Indications

Fungi are eukaryotic organisms that exist in all environments worldwide. They exist in many forms, ranging from visible fungi, such as mushrooms, to microscopic yeasts and Molds. While most fungi do not play a significant role in human disease, there are several hundred fungi that do, resulting in fungal infection or disease. Fungal infections (mycoses) range from common benign infections like 'jock itch' to severe, life-threatening illnesses such as cryptococcal meningitis. The term 'antifungals' encompasses all chemical compounds, pharmacologic agents, and natural products used to treat mycoses.

Clinically, fungal infections are best categorized first by the site and extent of the infection, then by the route of acquisition, and finally, by the virulence of the causative organism. These classifications are essential when determining the most effective treatment regimen for a particular mycosis. Mycoses are classified as local (superficial, cutaneous, subcutaneous) or systemic (deep, bloodborne). The acquisition of the fungal infection can occur through either an exogenous (airborne/inhalation, cutaneous exposure, or percutaneous inoculation) or an endogenous process (normal flora or reactivation of an existing infection). The virulence of the organism is classified as either a primary infection (a disease arising in a healthy host) or an opportunistic infection (a disease arising in human hosts with a compromised immune system or other defences).[1]

Antifungal drugs represent a pharmacologically diverse group of drugs that are crucial components in the modern medical management of mycoses. While antimycotic

pharmacology has advanced significantly, particularly over the last 3 decades, common invasive fungal infections still carry a high mortality rate: *Candida albicans* (20% to 40% mortality), *Aspergillus fumigatus* (50% to 90%), and *Cryptococcus neoformans* (20% to 70%).[2][3]

Amphotericin B deoxycholate, a polyene antibiotic, was the first antimycotic agent introduced in 1958 to treat systemic mycoses. While this drug is an effective agent, the demand for other efficacious topical, oral, and intravenous agents was apparent. Griseofulvin was introduced in 1959, representing the second class of antifungals. The next significant introduction would not occur until 1971 when the antimetabolite drug flucytosine entered the market. Azoles first became available in 1973 with the arrival of clotrimazole; additional azoles that have the pharmaceutical industry has rolled out over the past 5 decades: miconazole (1979), ketoconazole (1981), fluconazole (1990), itraconazole (1992), voriconazole (2002), posaconazole (2006), and most recently isavuconazonium (2015).[4] Terbinafine, an allylamine antifungal, was approved by the FDA in 1996 and has indications for treating local, non-systemic fungal infections. The next breakthrough in systemic therapy would be based on amphotericin B lipid formulations, which have more favourable adverse effect profiles.

In 2021, the FDA approved ibrexafungerp, a triterpenoid fungicidal agent, making it the first oral non-azole treatment option for vulvovaginal candidiasis.[5] Following lipid formulations of azoles, a new class of antifungal agents that are highly effective in treating some systemic mycoses, is the recently developed echinocandin class. While the echinocandins demonstrate less renal toxicity than amphotericin B, they cause significant hepatotoxicity and are more expensive than azoles; this effectively relegates this class to second- or third-line agents. Rezafungin was approved by the FDA in 2023.[6][7] Mechanistically, antifungal agents are diverse, yet due to the alarming and rapid increase in drug-resistant systemic fungal infections, new agents are more necessary than ever.[8][9][10][11] This discussion will focus on the currently available antifungal agents.[12][13][14][15]

Common, medically relevant fungal infections include, but are not limited to, the conditions and causative organisms listed below.[16][17][18][19]

- Aspergillosis - *Aspergillus fumigatus, A. flavus*
- Blastomycosis - *Blastomyces dermatitidis*
- Candidiasis - *Candida albicans, C glabrata, C krusei, C parasilosis, C tropicalis*
- Chromoblastomycosis (Chromomycosis) - *Cladosporium carrionii, Phialophora verrucosa, Fonsecaea pedrosoi*
- Coccidioidomycosis - *Coccidioides imitis, C posadasii*
- Cryptococcosis - *Cryptococcus neoformans, C gattii*
- Dermatophytosis (Tinea) - *Microsporum spp, Epidermophyton spp, Trichophyton spp*
- Fusariosis - *Fusarium oxysporum, F proliferatum, F verticillioides*
- Histoplasmosis - *Histoplasma capsulatum*
- Mucormycosis (Zygomycosis) - *Mucor spp, Rhizopus spp*
- Paracoccidioidomycosis - *Paracoccidioides brasiliensis*
- Pneumocystis pneumonia - *Pneumocystis jirovecii* (formerly called *P. carinii*)*

*While this is an essential and prevalent fungal disease, it is not treated with typical antifungal agents.

- Sporotrichosis - *Sporothrix schenckii*
- Tinea (Pityriasis) Versicolor - *Malassezia furfur* (also called *Pityrosporum orbiculare), M globosa*

Antifungal Drug Classification and Common Specific Drugs:

- Loss of cell membrane integrity: Polyenes: amphotericin B deoxycholate, liposomal amphotericin B, amphotericin B lipid complex, nystatin
- Azoles: ketoconazole, miconazole, clotrimazole, itraconazole, isavuconazonium sulfate (isavuconazole), fluconazole, voriconazole, posaconazole
- Allylamines: terbinafine, naftifine[20]
- Loss of cell wall integrity: Echinocandins: anidulafungin, caspofungin, micafungin, rezafungin
- Mitotic inhibitors: griseofulvin
- Antimetabolites: flucytosine
- Ciclopirox
- Quinoline derivatives: iodoquinol, clioquinol
- Potassium iodide: saturated solution of potassium iodide (SSKI)
- Zinc pyrithione
- Triterpenoid antifungal agent: Ibrexafungerp[21]

Indications

Various antifungal agents are indicated for the situations discussed below.[22][23][24][25]

Amphotericin B deoxycholate (AMB-d) is FDA indicated for treating life-threatening or potentially life-threatening fungal infections: aspergillosis, cryptococcosis, blastomycosis, systemic candidiasis, coccidioidomycosis, histoplasmosis, and mucormycosis. AMB-d is also approved for treating the parasitic disease American mucocutaneous leishmaniasis. AMB-d has an off-label use for esophageal candidiasis (both HIV infected and non-HIV-infected adults and adolescents; HIV-exposed and or infected infants and children), fluconazole-refractory oropharyngeal candidiasis, candidal endophthalmitis, candidal urinary tract infections, visceral leishmaniasis, and ophthalmic aspergillosis.

Liposomal amphotericin B (L-AMB) has FDA approval

for treating systemic aspergillosis, candidiasis, and cryptococcosis in patients with renal impairment and those refractory to AMB-d therapy. Additionally, L-AMB is an empiric antifungal therapy in patients with febrile neutropenia or HIV with cryptococcal meningitis. Visceral leishmaniasis is a parasitic infection that is also treated with this agent. L-AMB has extensive off-label usage for patients infected or exposed to HIV, including candidiasis, coccidioidomycosis, cryptococcosis, and histoplasmosis.[26][27][28][29]

Amphotericin B lipid complex (ABLC), like L-AMB, is indicated for treating invasive mycoses in patients unable to tolerate AMB-d. Off-label use of ABLC is an indicated agent in HIV infected patients with coccidioidomycosis, cryptococcal meningitis, and histoplasmosis; empiric therapy for candidiasis and neutropenic fever; and in the treatment of the parasitic infection, visceral leishmaniasis.[30][31][32][33]

Nystatin has been approved as an oral "swish-and-swallow" suspension for treating cutaneous, mucocutaneous, and oral *Candida* infections. Topically, nystatin has been approved for treating mucocutaneous and cutaneous infections with *Candida spp* (most commonly *C. albicans).*

Ketoconazole, when applied topically, has been approved for the treatment of tinea corporis, tinea cruris, tinea pedis, tinea versicolor, cutaneous candidiasis, and seborrheic dermatitis. Off-label, topical ketoconazole is used to treat several oral candidal pathologies, including chronic mucocutaneous candidiasis and oral thrush. Ketoconazole is also a systemic agent, approved for treating blastomycosis, coccidioidomycosis, chromomycosis, histoplasmosis, and paracoccidioidomycosis. Off-label oral ketoconazole treatment is used to treat Cushing syndrome and prostate cancer.[34][35]

Miconazole in its topical form is approved to treat cutaneous and mucocutaneous mycoses, particularly vulvovaginal candidiasis. Oral formulations of miconazole are indicated for the treatment of oropharyngeal candidiasis.

Clotrimazole, in topical forms, is approved to treat tinea corporis, tinea pedis, tinea versicolor, cutaneous candidiasis, and vaginal yeast infections. Oral clotrimazole is indicated for the treatment of oropharyngeal candidiasis.

Itraconazole is an oral drug approved to treat aspergillosis (pulmonary and extrapulmonary), blastomycosis (pulmonary and extrapulmonary), and histoplasmosis (systemic/disseminated not involving the CNS, cavitary pulmonary histoplasmosis) in patients who are immunocompromised and immunocompetent. In immunocompetent patients, this drug is also approved for the treatment of oropharyngeal candidiasis, esophageal candidiasis, and onychomycosis (involving the toenails or fingernails).

Fluconazole indications include the treatment of esophageal, oropharyngeal, peritoneal, urinary tract, and vaginal candidiasis. Fluconazole may also help treat systemic fungal infections, including candidemia, candida pneumonia, and cryptococcal meningitis. Fluconazole serves as a first-line agent in prophylaxis for mycoses in allogeneic hematopoietic stem cell transplant patients. Off-label, fluconazole has a variety of applications, including blastomycosis, empiric antifungal therapy in non-neutropenic ICU patients, Candida prophylaxis (in ICU patients with a high risk of invasive *Candida spp and* transplant patients), and tinea.[36]

Voriconazole has approval for the following indications: invasive aspergillosis, candidemia in patients without neutropenia, oesophageal candidiasis, and disseminated candidiasis. This drug also treats life-threatening mycoses caused by fungi, such as *Fusarium spp* Off-label uses for voriconazole are primarily aimed at prophylactic and suppressive therapy for fungal infections, including but not limited to aspergillosis, candidiasis, hematopoietic stem cell transplant patients with or without graft-versus-host disease, acute myelogenous leukemia, and empiric therapy in neutropenic fever.

Isavuconazole is approved to treat invasive aspergillosis and invasive mucormycosis in adult populations.

Posaconazole is approved for prophylaxis of both invasive aspergillosis and invasive candidiasis. Additionally, it is used to treat oropharyngeal candidiasis, typically for patient populations refractory to treatment with fluconazole and itraconazole.

Terbinafine is approved for both topical and systemic (oral) use. Topical terbinafine is approved to treat tinea pedis, cruris, and corporis. When administered orally, this drug is indicated for the systemic treatment of onychomycosis (tinea unguium) and tinea capitis. Common off-label uses of oral formulations include treating tinea (cruris, corporis, penis, and manuum) as well as lymphocutaneous and cutaneous sporotrichosis.

Anidulafungin is an echinocandin that is administered intravenously only. This drug has been approved for the treatment of *Candida spp* infections (esophageal candidiasis, candidemia, *Candida spp* peritonitis, and intrabdominal abscesses when *Candida spp* is grown in culture or the suspected organism).

Caspofungin is only administered intravenously. This agent is approved for treating invasive aspergillosis in patient populations refractory to amphotericin B and itraconazole. Caspofungin has also received approval for treating *Candida spp* infections (candidemia, esophageal, intra-abdominal abscess, peritonitis, and empiric therapy

in patients with neutropenia). Off-label, this agent is used as an adjunct in the treatment of other severe *Candida spp* infections not listed above.

Micafungin is also approved for intravenous administration to treat esophageal candidiasis and or the prophylaxis of Candida spp infections, including candidemia, Candida spp peritonitis, Candida spp abscesses, and disseminated candidiasis.

Griseofulvin is only approved as a systemic (oral) agent. This drug is indicated for treating dermatophytoses of the skin, hair, and nails, which are severe or refractory to topical therapy. Specifically, this drug treats tinea (corporis, pedis, cruris, barbae, capitis, and unguium).

Flucytosine has been approved as an adjunct antifungal agent for treating systemic infections caused by *Candida spp* or *Cryptococcus spp* infections. Off-label, flucytosine is administered to treat pediatric endocarditis caused by *Aspergillus spp*; however, other antifungal agents, such as amphotericin B or voriconazole, are preferred for Aspergillus infections.

Ciclopirox is FDA-approved for the topical treatment of tinea corporis, tinea pedis, tinea cruris, tinea unguium (onychomycosis), tinea (pityriasis) versicolor, and *Candida spp* infection with moniliasis.

Iodoquinol (discontinued in the USA) was a topical agent approved for treating tinea capitis, tinea cruris, tinea corporis, tinea pedis, moniliasis, and candidal intertrigo.

Clioquinol is a combination product with hydrocortisone (availability in the U.S. is unclear). This combination topical agent was approved to treat the same spectrum of dermatoses as iodoquinol: tinea capitis, tinea cruris, tinea corporis, tinea pedis, moniliasis, and candidal intertrigo.

Potassium iodide, formulated as a saturated solution of potassium iodide (SSKI), has no official antifungal approvals, but is used in the off-label treatment of both cutaneous and lymphocutaneous sporotrichosis.

Zinc pyrithione is not officially approved for antifungal purposes but has been utilized as primary or adjunct therapy in the treatment of mycoses leading to hyperkeratotic skin conditions. A common off-label use is in treating tinea (pityriasis) versicolor.

Mechanism of Action

Polyene antifungals (eg, amphotericin B) bind to ergosterol, a steroid-alcohol unique to fungi. The polyene-ergosterol complex creates pores in the fungal cell membrane, ultimately leading to electrolyte leakage, cell lysis, and cell death.[37]

Azole (eg, miconazole) antifungal compounds are non-competitive inhibitors of the fungal enzyme lanosterol 14-α-demethylase, a rate-limiting enzyme in the fungal biosynthetic ergosterol pathway. This action destabilizes the fungal cell membrane, leading to leakage of cell content, lysis, and ultimately, cell death.[38]

Allylamines (eg, terbinafine) inhibit the rate-limiting enzyme squalene epoxidase, which is responsible for synthesizing precursors to ergosterol. This type of drug is another antifungal compound whose mechanism of action is the loss of cell membrane integrity.[39]

Echinocandins (eg, caspofungin) inhibit the fungal β-(1,3)-D-glucan synthase, which is the enzyme responsible for synthesizing β-(1,3)-D-glucan, a key component of fungal cell walls. Losing this cell wall component leads to osmotic instability and cell death.

Griseofulvin is a mitotic inhibitor that binds to polymerized fungal microtubules, thereby inhibiting depolymerization and leading to the failure of fungal cell replication.[40]

Flucytosine is an antimetabolite compound absorbed into fungal cells via cytosine permease. Within the fungal cell, flucytosine gets converted to 5-fluorouracil, which interferes with fungal RNA biosynthesis.[41]

Ciclopirox has a poorly understood mechanism of action but is believed to interfere with the structural integrity of the fungal cell membrane.[42]

Quinoline antifungal (eg, clioquinol) compound derivatives also have a mechanism of action that is poorly understood.

Potassium iodide exerts its effects directly on *Sporothrix spp*, yet the exact mechanism of action remains unproven. Leading theories suggest that human polymorphonuclear cells convert potassium iodide to iodine through the action of myeloperoxidase. Iodine inhibits fungal germination and reduces structural integrity through the intracytosolic destruction of structural components.[43]

Zinc pyrithione has a poorly understood mechanism of action against fungi. Still, leading theories suggest that this agent modifies fungal cellular membrane transport, decreasing the concentrations of critical metabolic substrates, inhibiting protein synthesis, and limiting ATP production.[44] These metabolic changes are likely due to increased intracellular copper and iron-sulfur cluster formation, which leads to protein damage.[45]

Administration

Amphotericin B has several formulations, including amphotericin B deoxycholate (d-AMB, or AMB-d), liposomal amphotericin B (L-AMB), amphotericin B lipid complex (ABLC), and amphotericin B colloidal dispersion (ABCD; not available in the United States). All approved indications require intravenous

administration. Off-label administration of AMB-d is also given intraventricularly and as an irrigation solution.

Nystatin, the other polyene drug, is only approved for topical and oral "swish-and-swallow' applications. Nystatin is available as a powder, cream, and oral solution.

Azole preparations for systemic azole antifungals include tablets, capsules, oral, and IV solutions. Azole drugs for local or topical use include powders, creams, ointments, gels, shampoos, and lozenges.

Terbinafine, a member of the allylamine class of antifungals, can be administered topically or orally, depending on whether the fungal infection is local or systemic.

Caspofungin, anidulafungin, and micafungin, the 3 primary echinocandin medications, are all given intravenously as a reconstituted solution.

Griseofulvin is administered orally as a tablet or suspension and should be taken with a fatty meal to enhance absorption.

Flucytosine, also commonly known as 5-fluorocytosine, is almost always administered intravenously as a combination therapy with amphotericin B to treat mycoses.

Ciclopirox is approved for topical use only, not intracavitary or ophthalmic applications. This drug is available as a compounded gel, cream, lacquer, shampoo, and suspension.

Quinolines, iodoquinol, and clioquinol had approval for topical administration. Clioquinol is combined with hydrocortisone in a compounded cream.

Potassium iodide is most commonly administered topically as a saturated solution of potassium iodide (SSKI).

Zinc pyrithione, a compound used to treat topical fungal infections, is applied topically as a shampoo, a solid soap-like bar, or a non-shampoo liquid.

Adverse Effects

The systemic polyene antifungal amphotericin B (formulated as AMB-d, L-AMB, ABLC, and ABCD) has the potential for severe adverse reactions. AMB-d therapy carries the risk of hypotension, chills, headache, hypokalemia, hypomagnesemia, anemia, renal insufficiency, renal function abnormalities, injection site pain, nausea, vomiting, rigors, and fever.[46] L-AMB therapy has decreased the incidence of renal function abnormalities when compared to AMB-d, yet it still carries a risk of nephrotoxicity. The most common adverse events caused by L-AMB therapy include hypertension, hypotension, tachycardia, localized phlebitis, chills, headache, skin rash, electrolyte abnormalities (hypokalemia, hypomagnesemia, hyponatremia), hyperglycemia, and abnormal liver function tests. ABLC also carries a risk of nephrotoxicity, leading to increased serum creatinine, fever related to infusion, rigors, and chills; however, these risks are less than those associated with treatment regimens, including AMB-d.

Nystatin is approved only for topical and oral "swish-and-swallow" applications due to the potential for severe systemic adverse effects. Adverse events related to topical nystatin include mild contact dermatitis, with the most severe adverse effect being Stevens-Johnson syndrome. Oral "swish-and-swallow" nystatin carries a lower risk of hypersensitivity reactions than topical formulations; there are also reports of diarrhea, nausea, vomiting, and abdominal pain.

Azoles, while typically well-tolerated, frequently cause nausea, vomiting, diarrhea, and abdominal pain. Hepatotoxicity (elevated liver function tests, hepatitis, cholestasis, and or fulminant liver failure) is a common adverse reaction associated with all azoles. Each of the azole drugs has unique adverse events as well:

- Ketoconazole is associated with orthostatic hypotension, thrombocytopenia, pruritis, rash, myalgias, and a rare suppression of glucocorticoid production in the adrenal glands. Of note, ketoconazole also correlates with significantly more gastrointestinal distress than other azoles.
- Fluconazole has been shown to cause mild headaches, dizziness, and alopecia in high doses.[47]
- Itraconazole has a triad of heart failure-like symptoms, hypertension, peripheral edema, and hypokalemia. There are reports of an increased risk of herpes zoster activation or reactivation, headache, dizziness, and fatigue.
- Voriconazole has the most numerous and unique adverse effects in the azole class. These include vision changes, auditory and/or visual hallucinations, neurotoxicity, photosensitivity rash, photophobia, periostitis, cardiotoxicity, and alopecia.
- Posaconazole most commonly causes thrombophlebitis secondary to peripheral intravenous catheters, hypertension, hypotension, headache, rash, hypokalemia, and thrombocytopenia. Another reported adverse event is a rare prolongation of the QTc interval.[48]
- Isavuconazole has more severe gastrointestinal adverse effects than most of the other azoles. Other reported adverse events include a headache, hypokalemia, dyspnea, cough, and peripheral edema.
- Miconazole has no reported serious adverse events; however, it commonly causes contact dermatitis, burning, stinging, and pruritus at the application site.

- Clotrimazole has no severe adverse reactions but commonly causes irritation, burning, or stinging, pruritus, urticaria, and possible blistering at the application site.

Terbinafine, an allylamine, most commonly results in central nervous system adverse effects, with a headache being the most frequently reported symptom. Other manifestations of adverse events include rashes, diarrhea, dyspepsia, and upper respiratory inflammation or infection.

Echinocandins, like many other antifungal agents, can cause hepatotoxicity.

- Anidulafungin is associated with hypotension, peripheral edema, insomnia, hypokalemia, hypomagnesemia, increased risk of urinary tract infections, dyspnea, and fever.
- Caspofungin can cause hypotension, peripheral edema, tachycardia, chills, headache, rash, anemia, localized phlebitis, respiratory failure, and infusion-related reactions.
- Micafungin can cause phlebitis, anemia, transaminitis, hyperbilirubinemia, renal failure, and fever.
- Rezafungin can cause hypomagnesemia, vomiting, hypokalemia, diarrhea, pyrexia, abdominal pain, constipation, anemia, hypophosphatemia, and hepatotoxicity.[49]

Griseofulvin has numerous potential adverse events, with the most commonly reported adverse events being rash and urticaria. More severe complications can occur and include an erythema multiforme-like drug reaction, skin photosensitivity, leukopenia (rare), granulocytopenia, and hepatotoxicity.

Flucytosine can cause adverse reactions to all body systems but is most commonly associated with the following: cardiovascular (cardiotoxicity, chest pain), central and peripheral nervous systems (confusion, headache hallucination, parkinsonian-like syndrome, peripheral neuropathy), dermatologic (pruritis, urticaria, rash), gastrointestinal (abdominal pain, nausea, vomiting, GI hemorrhage), hematologic (agranulocytosis, aplastic anemia, pancytopenia, eosinophilia), hepatic (acute hepatic injury/insufficiency/necrosis), and renal (acute kidney injury, renal failure).

Ciclopirox has no significant associated severe adverse reactions; however, common benign reactions include skin irritation, burning, contact dermatitis, and pruritus.

Quinolines (clioquinol and iodoquinol) are most commonly associated with dry skin, contact dermatitis, allergic reactions, rapid hair growth in areas where the agent is applied, and folliculitis.

Potassium iodide (as a saturated solution of potassium iodide) has several reported severe adverse reactions, including arrhythmias, GI bleeding, angioedema, parotitis, thyroid adenoma, and goiter. More frequent and less severe reactions include a possible metallic taste, urticaria, acne, cutaneous hemorrhage, numbness, and paresthesias.

Zinc pyrithione has no reported serious adverse reactions and most commonly can cause mild skin irritation.

Contraindications

Amphotericin B: All formulations (AMB-d, L-AMB, ABLC, and ABCD) are contraindicated for patients with a known or likely hypersensitivity to amphotericin B or any components of the L-AMB, ABLC, or ABCD formulations.

- AMB-d carries 2 FDA boxed warnings: 1) amphotericin B deoxycholate should be used for invasive, potentially life-threatening mycoses and avoided in non-invasive fungal infections (oral thrush, esophageal candidiasis, and vaginal candidiasis in patients with neutrophil counts within normal limits); 2) risk of accidental overdose. The use of this agent should also exercise extreme caution in patients with renal impairment and or electrolyte abnormalities.
- L-AMB, ABLC, and ABCD do not carry FDA boxed warnings; however, they require caution when administered to patients with renal impairment.

Nystatin is contraindicated for patients with hypersensitivity to the drug or any additional components in the dosage formulation.

Azoles: All should be avoided in patients with hypersensitivity to azole drugs or components of the dosage form, and used with caution in patients with renal impairment or failure, or hepatic impairment or failure.

- Fluconazole requires cautious administration in patients with electrolyte abnormalities, torsades de pointes, and or medical history, family history, or current QTc prolongation.
- Itraconazole has an FDA boxed warning against the use in treating onychomycosis in patients with CHF. Itraconazole is contraindicated in pregnancy, left ventricular dysfunction, and current or active congestive heart failure. This drug should be used cautiously in patients with cystic fibrosis, cardiovascular disease, pulmonary disease, and older adults.
- Ketoconazole carries several FDA boxed warnings:
  - This agent should be used only when another effective antifungal, such as azoles, cannot be tolerated or is unavailable.
  - This agent carries a significant risk of hepatotoxicity, even in patients without predisposing factors, and thus, any treatment with ketoconazole should include close liver function monitoring.

- Ketoconazole is a cytochrome P450 inhibitor. It has several contraindications for coadministration with drugs that result in QTc prolongation, as it causes increasing concentrations of cisapride, disopyramide, dofetilide, dronedarone, methadone, quinidine, or ranolazine.
- Voriconazole oral formulation is contraindicated in galactose malabsorption/intolerance, lactase deficiency, glucose malabsorption, uncorrected electrolyte abnormalities, and pregnancy. Clinicians should use this agent with caution in patients with a medical or family history of QTc prolongation, history of torsades de pointes, and or hematologic malignancy.
- Isavuconazole is contraindicated in patients with familial short QTc syndrome and should be used with caution in patients with hematologic malignancies.
- Posaconazole is contraindicated in pregnancy. Caution is advisable in patients with electrolyte abnormalities; renal insufficiency; cardiomyopathy; torsades de pointes; or a medical history, family history, or congenital prolonged QTc interval.

Terbinafine should be utilized with caution or avoided in patients with hypersensitivity reactions, depression, gastrointestinal issues, liver failure, and immune suppression secondary to hematologic effects.

All echinocandins are contraindicated in patients with a history of hypersensitivity to any echinocandin drug or its components. Caspofungin should be used with caution in hepatic impairment.

Treatment with griseofulvin should include consideration of potential adverse events in susceptible patients and those with existing disease states, particularly patients with a history of hypersensitivity to griseofulvin, hypersensitivity to penicillins (due to a possible cross-reaction between penicillins and griseofulvin), hepatic failure, known porphyrias, and pregnant or nursing patients.

Flucytosine carries an FDA boxed warning that it should be used with extreme caution in patients with renal impairment, and hematologic, hepatic, and renal function should be closely monitored. This agent is contraindicated in patients with hypersensitivity to this drug or its components, first-trimester pregnancies, and breastfeeding women. Caution is advisable with this agent in patients with renal impairment, hepatic impairment, bone marrow depression, and pregnant patients in their second or third trimester.

The quinolines iodoquinol and clioquinol are contraindicated in patients with hypersensitivities to the drugs or their components.

Antifungals, including ciclopirox, potassium iodide, and zinc pyrithione, are used only as topical agents and should be avoided in patients with hypersensitivities to them.

Monitoring

Polyenes lack supporting evidence or indications to justify the use of therapeutic drug level monitoring (TDM) in patients treated with AMB-d, L-AMB, and ABLC.[50] All patients receiving amphotericin B formulations should have their BUN and creatinine levels assessed at baseline and then monitored frequently; additionally, CBC, electrolytes, and LFTs should be monitored regularly. Nystatin does not have supporting evidence for TDM or routine laboratory monitoring.

Azole antifungals, which are generally indicated for therapeutic drug concentration monitoring (TDM), all belong to the triazole subclass. These include itraconazole, voriconazole, and posaconazole. Laboratory monitoring is necessary for the use of fluconazole, isavuconazonium sulfate, and ketoconazole; however, there is no current indication for monitoring with clotrimazole or miconazole.

- Patients receiving itraconazole should receive TDM. Therapeutic drug concentrations range from 0.5 to 1 μg/mL. Trough concentrations should be assessed after the first administration, around the steady-state time (approximately 5 to 7 days), and reassessed before each consecutive dose. Adverse reactions are more likely to occur if concentrations exceed 5 μg/mL. Additionally, LFTs should undergo an assessment at baseline and be periodically evaluated in patients with hepatic impairment or treatment regimens lasting longer than one month.
- Therapeutic drug concentrations in voriconazole-containing regimens are recommended to be between 1 and 1.5 μg/mL; this requires assessment at the time of steady-state (which varies, approximately 4 to 7 days) and before subsequent administrations. Toxic concentrations are concentrations greater than 5 μg/mL, at which CNS toxicity tends to occur. Monitoring includes LFTs, creatinine, and electrolytes (including magnesium and calcium) at baseline, and LFT levels are frequently checked after that (every week for 4 weeks, then once every 4 weeks thereafter). Lipase should be assessed if a patient is at risk of pancreatitis. Finally, an ophthalmic examination is necessary for patients receiving voriconazole for more than 28 days.
- Posaconazole is administered to achieve therapeutic drug concentrations of greater than 0.7 μg/mL in prophylaxis and greater than 1.0 μg/mL in salvage therapy. Trough serum concentration should be measured on day 7 and before doses or after dose adjustments. Creatinine, electrolytes (including magnesium and calcium), and LFTs should be checked at baseline and then frequently during treatment.

- Monitoring parameters for fluconazole entail checking creatinine at baseline and monitoring LFTs.
- Administering is a vuconazonium sulfate requires checking LFTs and baseline, then periodically during treatment.
- Monitoring of ketoconazole-containing regimens should include LFTs at baseline and during therapy, with ALT checked weekly. If the patient is at risk of adrenal insufficiency, their adrenal function should be monitored.

Terbinafine has no supporting evidence to suggest that TDM is necessary for its utilization in prophylaxis, treatment, or toxicity. Monitoring creatinine and LFTs is, however, a baseline indication. Immunodeficient patients receiving terbinafine for longer than 6 weeks should have a CBC checked.

Griseofulvin does not have supporting evidence for TDM, but laboratory monitoring includes BUN, creatinine, CBC, and LFTs.

Patients on echinocandin therapy should be regularly monitored for hepatotoxicity via measurement of hepatic aminotransferases (AST, ALT), with consideration also given to alkaline phosphatase. There is currently no supporting evidence for TDM. Micafungin regimens should include routine laboratory monitoring of BUN and creatinine.

Patients receiving flucytosine-containing combination therapy require TDM. Patients should have serum concentration measured 2 to 4 hours after each dose; the trough concentration should be between 20 and 40 μg/L (some sources state 50 to 100 μg/mL). Toxic concentrations occur when serum drug concentrations exceed 100 μg/mL. Other indications for TDM in flucytosine therapy include when a drug with a known drug interaction is started or stopped, when adherence for oral therapy is uncertain, or when manifestations of toxicity occur.

Enhancing Healthcare Team Outcomes

Pragmatic management of mycoses is dependent on the interprofessional healthcare team characterizing the fungal infection as discussed in the introduction, then selecting the most effective antifungal treatment regimen; this requires a strong understanding of public health/epidemiology, medical microbiology/mycology, clinical pharmacology, and healthcare infrastructure which dictates the application of the first 3. There is currently a diverse and effective arsenal of antifungal agents. Still, the alarming global rise in drug-resistant fungi warrants judicious antifungal prescribing by clinicians, the development of combinatorial strategies, the utilization of antifungal adjuvants, and continued antifungal drug discovery and development.

Judicious prescribing begins with the healthcare team selecting the proper regimen based on culture and sensitivity data, patient history, and socioeconomic factors. Providers should work closely with pharmacists and, when appropriate, public health officials to provide therapy that appropriately treats infections. Nurses can also assess patient adherence, help administer the drug in the inpatient setting, answer patient questions, and monitor for adverse drug reactions. The ultimate goal is to provide antifungal therapy without unnecessarily creating drug-resistant organisms, limiting adverse events, and reducing drug-drug interactions. Antifungal stewardship is crucial for preserving the effectiveness of current antifungal agents.[51]

Combination therapy comprises treatment regimens that incorporate multiple antifungals from different classes and antifungal agents combined with non-antifungal agents. Non-antifungal drug targets include heat shock proteins, calcineurin, lysine acetyltransferase, lysine deacetylase, protein kinase C, and fungal sphingolipids.[52]

Antifungal adjuvants can enhance or extend the efficacy of existing antifungal regimens and limit resistance. Some of these encouraging adjuvants could eventually be the standard of care in antifungal-adjuvant combination therapy. The potential adjuvants include drugs with widely variable mechanisms of action, like cyclosporin A, deferasirox, FK506, tamoxifen, and sertraline.[53]

Antifungal drug discovery has been bolstered by the Orphan Drug Act (1983) and, more recently, the Generating Antibiotic Incentives Now (GAIN) Act (2012). These policies incentivize pharmaceutical companies and researchers to pursue new leads and expand the existing collection of antifungals. The increasing prevalence of drug-resistant fungal diseases presents a significant challenge to the discovery of antifungal drugs. Yet, there are several promising new drugs and class pipelines, theoretical fungal vaccines, and opportunities to generate compounds that inhibit resistance.[54][55][56]

The caveat to all of these potentially promising leads in new drugs and drug classes is the time it takes from discovery to dispensing a new medication, estimated to be roughly 12 years.[57] Unfortunately, this cycle leads to the need for ancillary and interim solutions, which include judicious prescribing to limit resistance, combinatorial therapy, and antifungal adjuvant therapies.

Several antifungal agents are available on the market in different topical preparations (e. g., creams, ointments, and powders for the purpose of local dermatological therapy). One of these antifungal agents is chlorphenesin (CHL), which has both anti-fungal and antibacterial properties. It is applied locally in mild uncomplicated dermatophyte and other cutaneous infections.[58]

Fungal infections (also called mycoses) represent the invasion of tissues by one or more species of fungi which may cause superficial, localized, deeper tissue infections to serious lung, blood (septicemia) or systemic diseases. Some fungi are pathogenic, causing disease whether the immune system is healthy or not.[59]

Topical treatment of fungal infections has several superiorities including, targeting the site of infection, reduction of the risk of systemic side effects, enhancement of the efficacy of treatment and, high patient compliance. Different type of topical effective antifungal compounds has been used in the treatment of a variety of dermatological skin infections. Currently, these antifungal drugs are commercially available in conventional dosage forms such as creams, gels, lotions and sprays.[60,61]

The most common therapeutic options are systemic and topical antifungal agents; however, oral antifungals are associated with adverse effects that can cause patients to discontinue treatment, which may be complicated by the presence of comorbid conditions.[62]

Antifungal drugs should reach effective therapeutic levels in viable epidermis after dermal administration. The greatest challenge for dermal delivery is stratum corneum, in order to improve its permeability, new formulation approaches have been investigated.[63,64]

Cream

Creams are defined as semisolid, externally applied emulsions of the water-in-oil (w/o) or oil-in-water (o/w) type. Oil-in-water and water-in-oil are the two stages that make up cream. The best solution for addressing skin issues is to use cosmetic items. By reducing skin issues, cosmetics are utilized not only to enhance one's appearance but also to promote health. A cream is a topical preparation that is often applied topically to the skin. Additionally, creams for mucus membrane application such as those of the vagina or rectum are utilized. Creams could be categorized as pharmaceutical goods since unmedicated creams are frequently used for a range of skin problems, including dermatoses, and even cosmetic creams are based on methods created by pharmacies.[65]

The Fingertip unit idea might be useful in determining the quantity of topical cream needed to cover various locations. Creams are dosage forms that are semisolid and include one or more medication ingredients that have been dissolved or spread in an appropriate base. Historically, this term has been used to describe semisolids with a somewhat fluid viscosity that are prepared as oil-in-water (such as Fluocinolone Acetonide Cream) or water-in-oil (such as Cold Cream) emulsions.[66]

Advantages of Topical Drug Delivery Systems

- Avoidance of first pass metabolism.
- Convenient and easy to apply.
- Avoid risk.
- Inconveniences of intravenous therapy and of the varied conditions of absorption like Ph changes presence of enzymes gastric emptying time etc.
- Achievement of efficacy with lower total daily dosage of drug by continuous drug input.
- Avoid fluctuation of drug levels integrand interpatient variations.

Structure and composition of Skin

The skin makes up almost 15% of an adult's total body weight, making it the biggest organ in the body. In addition to preventing the body from losing too much water and helping with thermoregulation, it carries out a number of essential tasks, including providing defense against external physical, chemical, and biological threats. Mucous membranes line the exterior of the body, forming a continuous layer of skin.[67,68]

The skin and its derived tissues make up the integumentary system. The epidermis, dermis, and subcutaneous tissue are the three layers that make up the skin. The outermost layer, the epidermis, is made up of a particular kind of cells called keratinocytes, which are responsible for producing the protective protein keratin, which is a long, thread-like strand. Collagen is essentially a fibrillar structural protein that makes up the middle layer, or dermis.[69]

The subcutaneous tissue, or panniculus, on which the dermis is located, is made up of tiny lobes of fat cells called lipocytes. Depending on the precise position within the body's anatomy, these layers' thicknesses vary significantly. The epidermal layer on the eyelid, for instance, is the thinnest at less than 0.1 mm, while the thickest epidermal layer, reaching around 1.5 mm, is found on the palms and soles of feet. In comparison to the epidermis that covers it, the dermis is 30– 40 times thicker on the back.[70]

In 2018, the WHO reported microbial diseases as the second leading cause of death worldwide, after cardiovascular diseases. While primarily viral or bacterial, opportunistic fungal infections are rising in both humans and animals globally. The increasing prevalence of fungal infections poses a major healthcare challenge, driven by a growing immunocompromised population due to immunosuppressive therapies and aggressive chemotherapy. Prolonged use of antifungal drugs as prophylaxis in high-risk patients has fueled the rise of (multi)drug-resistant fungi. Globally, over 150 million severe fungal infections occur annually, causing 1.7 million deaths, making these diseases escalating global health threat.[71]

Medicinal plants and herbal extracts are valuable in modern medicine due to their natural bioactive compounds. Their secondary metabolites offer diverse structures with significant therapeutic potential.

Medicinal plants provide valuable bioactive compounds with therapeutic potential through their diverse secondary metabolites. Rising antibiotic resistance highlights the need to scientifically evaluate medicinal plants for developing new antimicrobial drugs against resistant pathogens.[72]

Herbal medicine has treated skin conditions for millennia. Growing concerns over synthetic drug side effects, the green movement, and demand for natural remedies have revived herbal use. Their effectiveness and lower toxicity compared to conventional drugs make them increasingly attractive.

Creams are semi-solid topical preparations, either water-based or oil-based, designed for skin application to deliver targeted treatment for skin conditions.

As the body's largest organ, the skin serves as the primary defence against environmental stressors like dust, UV radiation, pathogens, and chemicals, which can lead to infections and aging. It also reflects aging and overall internal health. The practice of using plants or plant parts to treat wounds or illnesses is called herbal medicine, botanical medicine, or herbalism. This includes the use of seeds, leaves, stems, bark, roots, flowers, and extracts to create treatments such as topical applications, pills, capsules, teas, and tinctures. Many pharmaceutical drugs today are derived from these traditional remedies. This approach appeals to medical professionals due to its lower cost and generally safer use. Medicinal plants are crucial for addressing serious illnesses globally, especially in developing countries where they are essential for basic healthcare needs. The medicinal value of these plants comes from chemically active compounds and secondary metabolites, like carbohydrates, alkaloids, glycosides, tannins, flavonoids, and phenolic compounds. Rising antibiotic resistance has made it increasingly important to explore plant-based natural products and secondary metabolites for new antimicrobial activities and unique mechanisms of action. Natural remedies for infectious diseases are effective and minimize the harmful side effects often seen with synthetic antimicrobials. Therefore, it's vital to study plant metabolites to confirm their traditional medicinal uses and identify active ingredients through chemical analysis. Polyherbal compositions involve combining two or more plants. Ayurveda, through "Sarangdhar Samhita," discusses the concept of mutualism that underpins polyherbal remedies. While single-plant formulations contain active phytoconstituents, their quantities are often insufficient for therapeutic effects. Research has demonstrated that combining plants with varying potencies results in better outcomes due to synergistic effects, which can be pharmacokinetic or pharmacodynamic. Creams are semisolid emulsions for external application, classified as water-in-oil (w/o) or oil-in-water (o/w).[73]

2. Formulation and evaluation of antifungal cream using different plant extract

1. Formulation and Evaluation of Herbal Antifungal Cream[74]

Fungal diseases become a major medical problem. Fungal disease is difficult to manage because they tend to be chronic, hard to diagnosis. The fungal infection is a common condition caused by fungi. The herbal antifungal cream was formulated by using various herbs such as neem and aloe vera. Herbal medicine is one of the oldest and most universal system of health care system. The herbal antifungal cream is very helpful, and it is fewer side effects. All herbal ingredients are easily available in market. The herbal antifungal cream is used to treat fungal infection which most commonly affect our skin, hair and nails. Herbal antifungal cream is used to treat fungal skin infection such as athletes foot, ringworm and jock itch. This herbal antifungal cream represents a natural and safe to use, and this herbal antifungal cream is beneficial in reduction of fungal infection.

2. Formulation and evaluation of antifungal cream of chlorphenesin[75]

Objective: The main aim of our research was to develop an Antifungal cream formulation consisting of Chlorphenesin for the treatment of Fungal infections. Topical route is the most suitable route for skin infections.

Methods: The development of topical drug delivery systems designed to have systemic effects appears to be beneficial for a number of drugs on account of several advantages over conventional dosage forms(or) routes of drug administration. An Antifungal cream formulation consisting of Chlorphenesin was prepared.

Results: The formulation was subjected to *in vitro* diffusion studies. Microbiological studies were performed to find out the safety of materials used in the formulation.

Conclusion: The developed cream consisting of Cholrphnesin was found to be safe and effective for the treatment of fungal infection.

3. Formulation, Evaluation of Antifungal Cream Form Pongamia Pinnata[76]

Background: The aim of this present research work is to formulate and evaluate anti scabies cream. Scabies has been scourged among human beings for thousands of years. It's worldwide occurrence with epidemics during war, famine and overcrowding which is responsible for an estimated 300 million peoples currently infested. It is also greatest impact on children. Scabies refers to various skin infections produced by female mites and their eggs deposited in epidermis of the host. Long- term scabies disease can lead to complications such as septicaemia, acute post- streptococcus glomerulonephritis, heart disease, and secondary infections. Timely treatment to the affected patients is required to control the disease and get rid of the causative agent. Method: The cream formulation was designed by using pongamia pinnata

leaves, neem oil, steric acid, potassium hydroxide, sodium carbonate, white soft paraffin, methyl alcohol, glycerine, methyl paraffin and required amount of rose oil or distilled water The. skin pH, (6.8-7) was maintained by drop wise addition of try-ethanolamine. The prepared cream was evaluated for physical appearance, pH, skin irritation to observed side effect. It was inferred from the result that cream formulation were good in appearance and homogeneity. The overall result of the research the prepared cream formulation shows significant anti- fungal activity. Result: The antifungal cream is assessed utilizing a variety of chemical and physiological assays. Information on numerous formulation parameters is provided by these tests. the tests' findings were documented. Numerous secondary metabolites were examined, such as phytosterols, alkaloids, glycosides, flavonoids, saponins, tannins, and phenolic substances. Conclusion: The oil phase of the cream base consisted of stearic acid, potassium hydroxide, sodium carbonate, white soft paraffin and rose oil. The aqueous phase consists of methanol extract of Pongamia pinnata, glycerine, distilled water and methylparaben. Three batches namely F1, F2 and F3 was prepared with varying concentrations. The characterization of the formulated cream was carried out by standard methods such as homogeneity test, pH test, irritancy test and removal test.

4. Formulation and Evaluation of Polyherbal Anti-fungal Cream[77]

Study investigates the formulation and assessment of a polyherbal antifungal cream comprising garlic oil, cinnamon oil, and anise oil, addressing the escalating issue of fungal infections, particularly those resistant to conventional treatments. Infectious diseases remain a significant global health concern, with fungal infections contributing to substantial morbidity and mortality rates. This research aims to leverage the antifungal properties of herbal extracts to develop an effective topical treatment for fungal infections. The polyherbal cream was prepared using a fusion method involving the combination of the cream base with the active herbal oils. The prepared formulations were subjected to a series of evaluations, including physical characteristics, pH measurement, viscosity assessment, spreadability test, homogeneity, irritancy test, washability, and antifungal activity. The pH and viscosity measurements of the cream were found to be within the acceptable range for topical applications, ensuring compatibility with the skin and being suitable for application and retention on the skin. The spreadability test indicated that the cream spreads easily, enhancing its usability. Homogeneity tests showed a uniform distribution of the active ingredients within the cream. Irritancy tests revealed no adverse reactions, indicating the formulation's safety for topical use. The antifungal activity was assessed against *Candida albicans*, demonstrating significant inhibition zones that were proportional to the concentration of the herbal oils in the cream. These findings highlight the potential of polyherbal cream as a natural alternative to synthetic antifungal agents, offering an effective and safe treatment option with minimal side effects. The study underscores the importance of further exploration into plant-based formulations to address the growing challenge of drug-resistant fungal infections.

5. Formulation and evaluation of antifungal cream using nelumbo nucifera and azadirachta indica leaves extracts[78]

The main aim of this investigation was to evaluate the antifungal activity of leaves of Nelumbo nucifera (Nelumbonacaea) and Azadirachta indica (Meliacaea). Study involved qualitative estimation of the methanolic and ethanolic extracts of N. nucifera and A. indica. The results showed good antifungal activity against Candida albicans. Further, it was found that F1 formulation has better antifungal action against C. albicans in comparison to F2 formulation. F1 Formulation has given equivalent antifungal effect in comparison to standard formulation. It was revealed that both plant leaves showed significant antifungal activity against C. albicans and may be used as an antifungal agent in the form of cream formulation. Key words: Nelumbo nucifera, Azadirachta indica, Candida albicans, Antifungal activity, Cream.

6. Formulation and evaluation of polyherbal antifungal cream by using neem, guduchi and mint plant extract[79]

Fungal infections pose a significant challenge to public health, necessitating the development of effective and safe antifungal agents. Herbal remedies have garnered attention for their potential antimicrobial properties, including antifungal activity. In this study, we formulated a polyherbal antifungal cream utilizing the synergistic effects of neem (Tinospora cordifolia), guduchi (Tinospora cordifolia), and mint (Mentha spp.). These botanical extracts are renowned for their broad-spectrum antimicrobial activities and have been traditionally used in various medicinal preparations. The cream was prepared using a standardized method and evaluated for its antifungal efficacy against clinically relevant fungal strains using agar diffusion and broth dilution methods. Additionally, physicochemical properties such as pH, viscosity, and stability were assessed to ensure product quality and consistency. Preliminary results demonstrated promising antifungal activity of the polyherbal cream against common fungal pathogens, including Candida albicans and dermatophytes. Furthermore, the cream exhibited favourable physicochemical characteristics suitable for topical application, including a pH conducive to skin health and optimal viscosity for easy Spreadability. Overall, our findings suggest that the polyherbal antifungal cream containing neem, guduchi, and mint holds great potential as a natural alternative for the management of fungal infections. Further studies including clinical trials are warranted to validate its efficacy and safety for clinical use. Keywords: Fungal

infection, antifungal activity, polyherbal cream, polyherbal formulation.

7. Formulation and Evaluation of Herbal Antifungal Cream of Zingiber officinale[80]

The aim of the study was to formulate a cream containing a composition to treat fungal infections of the skin and improve skin properties. This preparation belongs to medicinal creams containing antifungal agents. It reveals a formula for treating skin fungal infections. For skin infections, a topical approach is the best option. Developing a local drug delivery system with systemic action may be advantageous for a variety of drugs, as it offers many advantages over traditional drug administration routes. Ginger extract is an active pharmaceutical ingredient (API) used to treat fungal skin infections. The cream base also contains two primary and secondary emulsifiers, a waxy substance, a co-solvent, two preservatives, a buffer, a humectant, and water. When the active ingredients combine, they exert a powerful antifungal effect. Several experiments were performed to evaluate the physio-chemical properties of formulated creams, including: B. Visual inspection, pH measurement, homogeneity, removal test, skin irritation test, viscosity, spreadability test, saponification value, acid value, etc. The antifungal effect of the cream was further analysed using nutrient agar. The medicated cream had good viscosity and colour. However, the scent of ginger was characteristic.

2. CONCLUSION

Antifungal agents remain essential in the prevention and treatment of fungal infections, ranging from superficial skin infections to severe systemic mycoses. The development of antifungal therapy has progressed significantly, with multiple drug classes such as Amphotericin B, Fluconazole, Itraconazole, Terbinafine, Caspofungin, and newer agents like Ibrexafungerp and Rezafungin expanding treatment options. These drugs target fungal cell membranes, cell walls, nucleic acid synthesis, and mitotic processes, providing diverse mechanisms to combat fungal pathogens.

Despite these advances, antifungal therapy continues to face major challenges, including drug resistance, toxicity, drug–drug interactions, and limited availability of newer agents. Selecting the appropriate antifungal requires careful consideration of the type of infection, causative organism, host immune status, and pharmacokinetic properties of the drug. Early diagnosis, rational drug selection, and close monitoring of therapeutic response are critical for successful outcomes.

Future research should focus on developing safer, more effective antifungal agents with broader spectra and reduced resistance potential. Strengthening antifungal stewardship, improving diagnostic techniques, and enhancing interprofessional collaboration will further optimize patient care and reduce the global burden of fungal infections.

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