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REVIEW ARTICLE ON FORMULATION AND EVALUATION OF HERBAL ANTIFUNGAL CREAM

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ABSTRACT
Fungal infections are a global health concern affecting millions of people each year. Antifungal creams, primarily composed of synthetic chemicals, have been widely used to treat various superficial fungal infections. However, growing concerns regarding the side effects of synthetic drugs, coupled with the increasing resistance of fungi to conventional antifungal agents, have led to a resurgence of interest in herbal remedies. Herbal antifungal creams, derived from plant-based compounds, offer a promising alternative with lower toxicity and fewer side effects. This review provides an overview of the medicinal plants, bioactive compounds, mechanisms of action, formulation, and effectiveness of herbal antifungal creams.

KEYWORDS: Preformulation, Compatibility, Extraction, Garlic & Neem oil.

INTRODUCTION

Fungal infections, ranging from superficial infections like athlete's foot, ringworm, and candidiasis to more severe systemic infections, are prevalent worldwide. Conventional antifungal treatments include a variety of synthetic drugs such as azoles (fluconazole, ketoconazole) and polyenes (nystatin, amphotericin B). However, these treatments often come with undesirable side effects like skin irritation, liver toxicity, and the emergence of antifungal resistance. As a result, there is a growing trend towards the use of natural products derived from plants that possess antifungal properties. Herbal antifungal creams, typically a combination of plant extracts, essential oils, and other natural ingredients, offer a safer and potentially more effective alternative. These creams often have fewer adverse effects, promote healing, and may even have additional benefits such as anti-inflammatory or skin-nourishing properties.

Common Herbal Ingredients in Antifungal Creams

Several herbs have been recognized for their antifungal activities, and their extracts are commonly used in the formulation of antifungal creams. Some key plant-based antifungal agents include.

Tea Tree Oil (Melaleuca alternifolia)

Active Compounds: Terpinen-4-ol, 1,8-cineole
Mechanism of Action: Tea tree oil has potent antifungal activity, particularly against Candida species and dermatophytes. The oil disrupts the fungal cell membrane, leading to leakage of intracellular contents. Applications: Commonly used for treating athlete's foot, ringworm, and vaginal candidiasis.

Garlic (Allium sativum)

Active Compounds: Allicin, diallyl disulfide
Mechanism of Action: Garlic has demonstrated broad-spectrum antifungal activity, especially against Candida albicans. Allicin disrupts the cell wall of fungi, inhibiting their growth and replication.

Applications: Garlic is effective in treating skin infections such as ringworm and candidiasis.

Neem (Azadirachta indica)

Active Compounds: Nimbidin, azadirachtin
Mechanism of Action: Neem is widely used in traditional medicine for its antifungal, antibacterial, and anti-inflammatory properties. It inhibits the growth of fungi by interfering with cell membrane integrity and replication. Applications: Used in the treatment of fungal skin infections such as eczema, ringworm, and athlete's foot.

Lavender (Lavandula angustifolia)

Active Compounds: Linalool, linalyl acetate

Mechanism of Action: Lavender oil exhibits antifungal activity against dermatophytes and yeast species. The oil affects fungal cell membranes and inhibits fungal growth.

Applications: Commonly used for treating fungal infections of the skin, including athlete's foot and fungal nail infections.

Eucalyptus (Eucalyptus globulus)
Active Compounds: Eucalyptol, α-pinene
Mechanism of Action: Eucalyptus oil has shown antifungal activity against various fungi, including Candida species. It disrupts the cell membrane integrity of fungi, leading to their death.

Applications: Used in the treatment of fungal infections like ringworm, athlete's foot, and candidiasis.

Oregano (Origanum vulgare)
Active Compounds: Carvacrol, thymol
Mechanism of Action: Oregano oil is known for its broad-spectrum antifungal and antibacterial properties. It inhibits fungal growth by disrupting cell wall synthesis and the fungal cell membrane.

Applications: Effective against fungal infections such as athlete's foot, ringworm, and yeast infections.

SIGNIFICANCE OF HERBAL ANTIFUNGAL CREAM

Fungal infections are evolving diseases in sanatorium institutions. Herbal medicines are also called as botanical medicine or phytomedicines used to alleviate human illness and for the maintenance of general health. These will be use for treating fungal skin infections, as well as other components that can help improve skin issues. Garlic oil and clove oil are the main ingredients used to treat fungal skin infections.

Herbal antifungal creams have gained prominence today due to several compelling reasons:
1. Natural Antifungal Properties: Many plants possess inherent antifungal compounds. For instance, essential oils and herbal extracts contain phenolic groups that serve as primary antimicrobial agents, effectively combating various fungal pathogens.
2. Reduced Side Effects: Herbal treatments are often associated with fewer adverse effects compared to synthetic antifungal agents. This makes them a preferred choice for individuals seeking treatments with minimal toxicity.
3. Immunomodulatory Benefits: Traditional medicinal systems, such as Traditional Chinese Medicine (TCM), utilize herbal preparations that not only exhibit antifungal activity but also modulate the immune system. This dual action can enhance the body's natural defenses against fungal infections.
4. Addressing Antifungal Resistance: The overuse of synthetic antifungal agents has led to the emergence of resistant fungal strains. Herbal antifungal creams offer alternative mechanisms of action, which can be effective against resistant pathogens.
5. Holistic Approach: Herbal antifungal creams often incorporate multiple plant extracts, providing a broad spectrum of activity and addressing various aspects of skin health, including hydration and repair.

Mechanis of action

Garlic (Allium sativum) exhibits antifungal properties primarily due to its bioactive compounds, notably allicin and ajoene. These compounds disrupt fungal growth through several mechanisms:
1. Allicin
Membrane Disruption: Allicin interacts with the lipid components of fungal cell membranes, increasing permeability and leading to cell leakage. This disruption compromises the integrity of the fungal cell, resulting in cell death.
Enzyme Inhibition: Allicin inhibits key enzymes involved in fungal metabolism by reacting with thiol groups (-SH) in proteins. This inhibition impairs essential cellular processes, hindering fungal growth and replication.
2. Ajoene
Growth Inhibition: Ajoene, a sulfur-containing compound derived from allicin, has been shown to inhibit the growth of fungi such as Candida albicans. While the precise mechanism is not fully understood, ajoene's antifungal activity contributes to the overall efficacy of garlic-based treatments.

In summary, the antifungal efficacy of garlic-based creams is attributed to the synergistic actions of allicin and ajoene, which compromise fungal cell integrity and inhibit vital metabolic processes, leading to the elimination of fungal pathogens.

A majority of the world's population still relies on herbal medicines to meet its health needs and are often used to provide first-line and basic health services. 1, 2 the demand for plant based medicine is increasing in both developing and developed countries, due to their nontoxicity, less side effects and easy availability at affordable prizes.3, 4.

Creams are biphasic topical preparations usually applied to the skin and mucous membranes such as the rectum or vagina. They are semi solid emulsions containing oil-inwater (O/W) or water-in-oil (W/O) type preparations. Oilin-water (O/W) emulsions are used mostly because they contain water washable bases, whereas water-in oil (W/O) emulsions are emollient and cleansing agents.

The use of cosmetics not only used for developing an attractive external appearance, but also achieving longevity of good health by reducing skin disorders. The herbs used in cosmetic preparation also have properties like antioxidant, anti-inflammatory, antiseptic, emollient, anti kerolytic activity and antibacterial activity. Cosmetic

products are used to protect the skin from exogenous and endogenous harmful agents and enhance the beauty and attractiveness of skin.

Increase in immunosuppressive diseases and conditions have been influencing the epidemiological pattern of mycoses in hospitalized patients the epidemiology of invasive fungal infections is currently at a crucial stage.[1]

Fungal infection caused by Candida has become more prevalent than Escherichia coli and Pseudomonas.sp., Aspergillus sp. and other sp.[2]

There are many host factors that predispose patients to fungal infections. These include: immobility; mucositis; use of antibiotics; radiation therapy or certain immunosuppressive agents; intensive care unit (ICU).[3]

Candida albicans is the most common species in the genus which has been implicated in Candidiasis. The infections range from superficial skin to systemic diseases.

Treatment with herbs is an ancient method for curing diseases. Since the vedic time humans have used medicinal plant material to cure any disease or to give a satisfactory treatment against that disease. Plants are also known for treating the infectious and non infectious skin disorders. The antimicrobial effect of some plants is attributed to the number of phytoconstituents like flavonoid, tannins, triterpenes etc.[5]

The purpose of the current study is also based on the medicinal property of a plant i.e. Garlic (Allium sativum) and clove oil (Eugenia caryophyllus) Garlic oil shows a wide range antimicrobial activity. Alliin is the main chemical constituent in garlic oil which shows antimicrobial activity. This oil consists of sulfur containing six compounds such as i. allicin, ii. alliin, iii. ajoene, iv. diallyl disulfide, v. dithiin and vi. Sallylcysteine. These large amounts of sulfur compounds give the smell and taste to the garlic. Diallyl disulfide is an important component in garlic and being a powerful antibiotic and antifungal compound.[6] Clove oil is reported to have very strong antifungal activity against a lot of fungal species.[7]

The essential ingredient liable for its antifungal activity is ugenol from the clove. Eugenol is the major volatile compound of extracted oil from clove buds (S. aromaticum L). It is reported that clove oil possesses tough antifungal activity against C. albicans, C. neoformans.[8]

Aim of this present work is to prepare various cream formulations with herbal antifungal extract of garlic oil, clove oil and peppermint oil by using emulsification method. And evaluate the cream properties like various organoleptic property, viscosity, spreadability, tube extrudability, and microbiological study, to check the antimicrobial property.

MECHANISMS OF ACTION OF HERBAL ANTIFUNGAL CREAMS

Herbal antifungal creams function through several mechanisms that make them effective in treating fungal infections.

Disruption of Cell Membranes

Many herbal compounds, such as those found in tea tree oil and neem, disrupt the integrity of the fungal cell membrane. The active compounds interact with the lipid bilayer, increasing membrane permeability, leading to the leakage of cellular contents and ultimately cell death.

Inhibition of Cell Wall Synthesis

Some herbal compounds inhibit enzymes involved in the synthesis of the fungal cell wall. For example, compounds in garlic and oregano prevent the formation of critical fungal cell wall components, weakening the cell and causing it to collapse.

Modulation of Enzyme Activity

Herbal extracts may also inhibit key enzymes that are involved in fungal metabolism. For instance, compounds in lavender oil have been shown to interfere with fungal enzymatic activities, reducing fungal growth.

Anti-inflammatory and Healing Properties

Many herbal ingredients, such as neem and lavender, not only have antifungal properties but also possess anti-inflammatory and skin-healing characteristics. This can help reduce skin irritation, redness, and swelling associated with fungal infections, promoting faster healing.

FORMULATION OF HERBAL ANTIFUNGAL CREAMS

The formulation of herbal antifungal creams involves the careful selection of herbal extracts, excipients, and preservatives to ensure efficacy, stability, and safety. Key components of an herbal antifungal cream include.

Herbal Extracts

The concentration of active ingredients from herbal extracts must be optimized to ensure the desired antifungal activity. Standardized extracts are preferred to ensure consistency in therapeutic outcomes.

Base Cream (Vehicle)

A suitable cream base is selected to ensure easy application and effective penetration of the active herbal ingredients into the skin. Common base materials include emulsifying waxes, oils (e.g., coconut oil, olive oil), and water-based components like glycerin.

Preservatives

Herbal creams are susceptible to microbial contamination. Therefore, preservatives such as

phenoxyethanol or ethylhexylglycerin are often included to prevent bacterial and fungal growth in the cream.

pH and Stability
The pH of the cream is adjusted to match the skin's natural pH (typically around 4.5–5.5). Stability studies are conducted to assess the shelf-life and effectiveness of the cream under various environmental conditions (e.g., temperature, humidity).

Clinical Efficacy and Safety of Herbal Antifungal Creams
Several clinical studies have demonstrated the efficacy of herbal antifungal creams in treating superficial fungal infections. For instance: Tea Tree Oil has shown effectiveness against dermatophytes like Trichophyton rubrum and Candida albicans.

Neem has been used successfully in the treatment of various skin infections, including fungal infections.

Garlic has been found to be highly effective against Candida species, both in vitro and in clinical trials.

Herbal antifungal creams are generally considered safe, with few side effects. However, allergic reactions or skin sensitivities may occur, particularly in individuals with sensitive skin. Patch testing is recommended before widespread use.

PROCESS OF FORMULATING HERBAL ANTIFUNGAL CREAM
The preparation of a herbal antifungal cream involves several key steps that include selecting the right herbs, creating an appropriate base, ensuring proper extraction methods, and testing the final formulation for its effectiveness and stability. Here's a detailed breakdown of the process

1. Selection of Herbal Ingredients
The first step in formulating an herbal antifungal cream is selecting the herbal ingredients with proven antifungal activity. Common herbs used for their antifungal properties include:
Tea Tree Oil (Melaleuca alternifolia)
Neem (Azadirachta indica)
Garlic (Allium sativum)
Lavender (Lavandula angustifolia)
Oregano (Origanum vulgare)
Each of these herbs contains active compounds (e.g., terpenes, allicin, phenolic compounds) known for their ability to inhibit fungal growth.

2. Preparation and Extraction of Herbal Active Ingredients
To prepare a cream with the antifungal properties of these plants, their active ingredients need to be extracted. The methods of extraction vary based on the plant and the compounds are targeting.

Essential Oil Extraction (e.g., Tea Tree Oil, Lavender Oil)
Method: Steam distillation or cold-pressing for oil-based herbs.
Purpose: Essential oils are rich in the bioactive compounds that possess antifungal properties.

Tincture or Decoction (e.g., Neem, Garlic)
Method: Using solvents such as ethanol or glycerin for tinctures or water for decoctions. A decoction involves boiling plant materials (like neem leaves or garlic) to extract soluble compounds.
Purpose: These methods help extract water-soluble and alcohol-soluble active compounds from herbs.

3. Formulation of the Cream Base: The cream base serves as a vehicle for delivering the herbal active ingredients to the skin. The formulation should be smooth, non-greasy, and easy to apply, while ensuring that the herbal ingredients remain stable and active. The base is typically composed of the following components.

Emollients: These are oils and fats that help soften and smooth the skin. Examples include shea butter, coconut oil, or olive oil.

Emulsifiers: Used to combine oil and water phases, allowing the cream to maintain a uniform consistency. Common emulsifiers include cetyl alcohol, glycerin, or polysorbate 60.

Water Phase: Water is often used as the primary solvent to dissolve water-soluble active compounds. It also serves as the medium for blending the oil phase.

Thickening Agents: These give the cream its texture. Examples include xanthan gum, guar gum, or carbomer.

Preservatives: To ensure the cream remains free from microbial contamination, preservatives like phenoxyethanol or ethylhexylglycerin are added.

4. Manufacturing Process: The manufacturing of herbal antifungal cream generally follows a cold process or hot process. Here's a basic outline of the steps involved.

Step 1: Preparation of Oil and Water Phases: Oil Phase: Combine the selected oils (e.g., coconut oil, olive oil) with emulsifiers and heating agents (e.g., cetyl alcohol). Heat gently to around 60–70°C to melt the solid components and allow them to mix thoroughly. Water Phase: In a separate container, heat the aqueous phase (typically water and glycerin) to the same temperature (60–70°C) to dissolve any water-soluble ingredients, like herbal extracts or thickening agents.

Step 2: Emulsification
Slowly add the water phase into the oil phase while continuously stirring. This creates an emulsion, which should be mixed until a smooth, homogenous cream

consistency is achieved. If using a high-shear mixer, this step can be faster and more efficient.

Step 3: Cooling and Addition of Active Herbal Ingredients
Once the emulsion is formed, allow the mixture to cool to around 30–40°C.

Herbal Extracts and Essential Oils (such as tea tree oil or neem oil) are added at this stage. These volatile ingredients are sensitive to heat and may degrade if added while the cream is too hot.

Step 4: Mixing and Homogenization
After adding the herbal extracts, thoroughly mix the cream to ensure uniform distribution of the active compounds. This is particularly important for the essential oils, which can separate from the cream if not mixed properly.

Step 5: pH Adjustment
The pH of the cream should be adjusted to match the skin's natural pH, typically between 4.5 and 5.5. This can be done by adding citric acid or sodium hydroxide solution.

Step 6: Packaging
The final cream should be packaged in air-tight containers that protect it from light and contamination. Packaging options include jars, tubes, or airless pumps. Ensure that the packaging is moisture-resistant to maintain the stability of the cream.

EVALUATION PROCESS FOR HERBAL CREAM
Quality control (QC) testing for cream formulations, including herbal antifungal creams, is crucial to ensure product safety, efficacy, stability, and consistency. Here are the key QC test parameters for creams, along with the associated tests and limits:

Appearance
Test: Visual Inspection
Description: The cream should have a uniform, smooth texture, and the color should be consistent. There should be no signs of separation, discoloration, or other defects.
Limit: No visible separation, discoloration, or particulate matter.

pH
Test: pH Measurement
Description: The pH of the cream should be within the skin's natural pH range (typically 4.5–5.5). This helps avoid skin irritation.
Limit: pH should be between 4.5 and 5.5.

Viscosity
Test: Brookfield Viscometer or Rheometer
Description: Viscosity measures the cream's flow properties, which are crucial for its spreadability and texture. A cream that is too runny or too thick may not apply effectively.
Limit: The viscosity should be suitable for the intended use (e.g., not too thin or thick, as per the product specification). Typically, a cream should have a viscosity range of 20,000–50,000 cP.

Spreadability
Test: Spreadability Test
Description: The ability of the cream to spread evenly on the skin is important for ease of application. This is tested using a spreadability apparatus that measures how far a fixed amount of cream will spread under a specified force.
Limit: Should spread smoothly and evenly without excessive friction.

Moisture Content
Test: Loss on Drying (LOD) or Karl Fischer Titration
Description: Moisture content is crucial for ensuring the stability and shelf life of the cream. High moisture content can lead to microbial growth, while too little moisture may affect product efficacy.
Limit: Moisture content should typically be <5%.

Microbial Contamination
Test: Microbial Limit Test
Description: This test determines whether the cream is free from harmful microorganisms, including bacteria, fungi, and molds.
Limit: Total Aerobic Microbial Count (TAMC): <100 CFU/g
Total Yeast and Mold Count (TYMC): <10 CFU/g
Absence of pathogenic microorganisms such as Salmonella, Escherichia coli, and Pseudomonas aeruginosa.

Active Ingredient Content
Test: High-Performance Liquid Chromatography (HPLC), UV-Vis Spectrophotometry, or Gravimetric Method
Description: Measures the concentration of active ingredients (such as herbal extracts or essential oils) in the cream.
Limit: The concentration should match the labeled claim within an acceptable margin of error, typically ±5% of the stated amount.

Stability Testing
Test: Stability Studies
Description: Creams are tested for their physical, chemical, and microbiological stability under various conditions (e.g., temperature, humidity, light).
Limit:
Temperature: Room temperature, accelerated testing (e.g., 40°C for 3 months).
Shelf-life: Product should remain stable for at least 6 months under normal storage conditions without any visible separation, discoloration, or loss of activity.

Homogeneity
Test: Uniformity of Content
Description: Ensures that the active ingredients are evenly distributed throughout the cream.
Limit: The active ingredient content should be uniform throughout the product with no significant variation.

Heavy Metal Contamination
Test: Atomic Absorption Spectroscopy (AAS) or Inductively Coupled Plasma Mass Spectrometry (ICP-MS)
Description: Ensures that harmful levels of heavy metals like lead, mercury, cadmium, and arsenic are not present in the cream.
Limit: The levels of heavy metals should be well below the permissible limits, generally:
Lead: <10 ppm
Arsenic: <5 ppm
Cadmium: <1 ppm
Mercury: <1 ppm

Odor
Test: Sensory Evaluation
Description: The odor of the cream should be consistent with its ingredients and should not be unpleasant.
Limit: The cream should have a pleasant or neutral odor, free from any rancid or off-putting smells.

Texture and Consistency
Test: Sensory Evaluation
Description: This test checks the cream's consistency, smoothness, and ease of application.
Limit: The cream should have a smooth texture, and it should apply easily without being too greasy or sticky.

Spreadability Test
Test: Spreadability Apparatus
Description: Measures the extent to which the cream spreads on the skin. It reflects the cream's ease of application.
Limit: It should spread smoothly with an acceptable level of ease under a fixed pressure.
Emulsification Stability
Test: Centrifugation or Freeze-Thaw Cycling

Description: Ensures that the emulsion of the cream remains stable and does not break down into separate phases (oil and water).
Limit: There should be no phase separation after testing.
The quality control (QC) tests for herbal antifungal creams ensure the product is effective, safe, and stable for consumer use. Regular monitoring of these parameters during production is essential to maintain consistency and quality. Additionally, the testing should comply with local regulatory guidelines to ensure the product is safe and effective for the intended use.

CONCLUSION

Guidance received from above various literature study and concluded that the process of making herbal antifungal cream is a delicate balance of selecting the right active herbal ingredients, combining them effectively into a base, and ensuring that the final product is safe, stable, and effective. Proper formulation, extraction methods, quality control, and testing are crucial to producing a high-quality herbal antifungal cream. These creams, when formulated correctly, offer a natural, effective alternative to conventional antifungal treatments, with the added benefit of fewer side effects. Herbal antifungal creams represent a natural, safe, and effective alternative to conventional antifungal treatments. The combination of plant-based active ingredients such as tea tree oil, neem, garlic, and lavender offers broad-spectrum antifungal activity with additional benefits like anti-inflammatory effects. With growing consumer preference for natural products and increasing concerns about the side effects of synthetic drugs, herbal antifungal creams present a promising solution for managing superficial fungal infections. However, further clinical research and standardized formulations are necessary to optimize their therapeutic potential and establish clear guidelines for their use.

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