



The Role Of Herbal Drugs For The Management Of Fungal Skin Diseases: A Review

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Abstract

The goal of the study was to formulate a cream with a composition for treating fungal skin infections and which enhances skin properties. This formulation belongs to a medicinal cream that has two antifungal active components. It reveals a formula for treating fungal skin infections, as well as other components that can help improve skin issues. For skin infections, the topical approach is the best option. Because of the numerous advantages over traditional routes of drug administration, the development of topical drug delivery systems with systemic effects appears to be advantageous for a variety of medications. Garlic oil and clove oil are the active pharmaceutical ingredients (API) used to treat fungal skin infections. It also includes two types of primary and secondary emulsifiers waxy materials, co-solvents, two preservatives, a buffering agent, a humectants, and water in the cream base. When the active components are combined, they provide a potent antifungal effect. Several experiments were done to assess the physicochemical characteristics of formulated cream, such as visual inspection, pH measurement, extrudability, expandability, skin irritant test, etc. The cream was further analyzed with the use of nutritional agar for antifungal activity. The medicated cream was good in consistency and color; however the smell of the garlic was quite unpleasant, so the odor of the garlic was masked with peppermint oil, which also acting as an additional antifungal agent, in improved version.

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Keywords: Fungal Skin Infections, Tulsi Oil, Garlic Oil, Clove Oil, Peppermint Oil And Neem, Antifungal Cream

1. INTRODUCTION

The last few decades have witnessed an increase in fungal infection. Fungal infections are evolving diseases in sanatorium institutions. 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. *C. albicans*, *C. tropicalis*, *C. glabrata* and *C. parapsilosis* are part of the normal flora of humans and can be isolated from oral cavity, vaginal and other parts of body sites from normal healthy people.^[4]

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 phyto constituents 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. a liin, 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 eugenol 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].

1.1. Advantages of herbal system of medicines

- Lower risk of side effects
- Widespread availability
- Effectives with chronic medicine
- Low cost effectiveness make them all the more alluring
- Natural detoxification process of the body is effectively enhanced by herbal medicine.

1.2. Disadvantages of herbal system of medicines Bulk dosing.

- Poor stability in higher acidic pH, liver metabolism etc.
- Large molecular size limiting the absorption via passive diffusion.
- High amount of raw material is required for processing the medicine.
- Isolation and purification of individual components from whole herbal extract lead to partial or total loss of therapeutic activity.

These limitation lead to reduced bioavailability and hence, low therapeutic index of plant active constituents. Often, the natural synergy is gone which is due to chemically related constituents present in herbal extract. Hence considerable attention has been given to development of novel drug delivery system for herbal drug.^[5]

1.3. Physiology of normal skin

The skin is composed of three layers,

Epidermis (50–100 µm)

Dermis (1–2 mm)

Hypodermis (1–2 mm)

1.4. Fungi

“Fungi are a kingdom of usually multicellular eukaryotic organism that are heterotrops and have important role in nutrient cycling in an ecosystem”.

1.5. Characteristics of fungi

Some fungi are single-celled, while others are multicellular. single-celled fungi are called yeast. some fungi alternate between single celled yeast and multicellular forms depending on what stage of the life cycle they are in. Fungi cells have a nucleus and organelles, like plant and animal cells do. The cell walls of fungi contain chitin, which is hard substance also found in the exoskeletons of insects and arthropods such as crustaceans. They do not contain cellulose, which commonly makes up plant cell walls. Multicellular fungi have many hyphae, which are braching filaments. Hyphae have tubular shape and are split into cell-like compartments by walls that are known as septa. These cells can have more than one nucleus, and nuclei and other organelles can move in between them. A fungus network of hyphae is called a mycelium.^[8]

1.6. Types of Fungi

- Chytridiomycota
- Zygomycota
- Glomeromycota
- Ascomycota

1.6.1. Chytridiomycota: Chytrids, the organisms found in Chytridiomycota, are usually asexual, and produce spores that no around using flagella, small tail like appendages. It can cause fungal infection in frogs by burrowing under their skin.

1.6.2. Zygomycota: These are mainly terrestrial. They cause problem by growing on human few soures. Ex:Rhizopus stolonifer a bread mold.

1.6.3. Glomeromycota: They are found in soil. The fungi obtain sugar from plant and in return, dissolves, minerals in the soil to provide the plant with nutrients. This fungi also reproduce asexually.

1.6.4. Ascomycota: These are the pathogens of plant and animals, including humans in which they are responsible for infection like Athelete's Foot, Ringworm, and ergotism, which causes vomiting, convulsions, hallucination.and sometimes even death.[8]

1.7. Fungal Infection

Definition: - an inflammatory condition caused by a fungus. mycosis. zymosis - (medicine) the development and spread of an infectious disease (especially one caused by a fungus) blastomycosis - any of several infections of the skin or mucous membrane caused by Blastomycosis.

1.7.1. Type of fungal infection

1.7.2. Superficial: Affect skin mucous membrane. e.g. tinea versicolor dermatophytes: Fungi that affect keratin layer of skin, hair, nail. e.g. tinea pedis, ring worm infection Candidiasis: Yeast- like, oral thrush, vulvo-vaginitis, nail infections.

1.7.3. Deep infections: Affect internal organs as: lung, heart, brain leading to pneumonia, endocarditis, meningitis.[10]

1.7.4. Symptoms

- Skin changes, including red and possibly cracking or peeling skin.
- Itching.

1.7.5. Causes of fungal skin infection: Imbalance of bacteria is due to following reasons:

- Due to use of antibiotics.
- Hormone imbalance
- Poor eating habbits

1.8. Treatment Antifungal drugs

- Measures to prevent moisture
- Fungal infections are typically treated with antifungal drugs, usually with antifungal drugs that are applied directly to the affected area (called topical drugs). Topical drugs may include creams, gels, lotions, solutions, or shampoos. Antifungal drugs may also be taken bymouth.
- In addition to drugs, people may use measures to keep the affected areas dry, such as applying powders or wearing open-toed shoes.
- For some infections, doctors give corticosteroids to relieve inflammation and itching.

1.9. Cream Definition- "Cream is semisolid preparation of a medication for topical use (on the skin) that contains a water base. Essentially, it is a preapation of oil (often lanolin or petrolatum) in water. "An ointment is preparation for topical use". [9]

1.9.1. Advantages of Cream

- Able to calm inflammation
- Promote skin tone
- Keep wrinkles and acne away
- Increase cell metabolism and blood circulation
- Easily water washable. Easy to wipe away.
- Less greasy compared to ointment.
- Easy to spread on the skin's surface (i.e. easy to apply).
- Suitable for sensitive, dry, and fair skin.
- Suitable for acute lesions

1.9.2. Disadvantages of Cream

- Stability is not as good as ointment
- They are less hygroscopic than other semi-solid preparation, so risk of contamination is high than other.
- Less viscous than other semi-solid preparation.

2. PHYTOCHEMISTRY OF HERBAL DRUG

2.1. Tulsi Oil



Synonyms: Sacred basil, Kali-Tulsi, Veranda

Biological source: Tulsi consists of the fresh and dried leaves of *Ocimum* species like *Ocimum sanctum* L. and *Ocimum basilicum* L.

Family: Lamiaceae.

2.2. Garlic Oil:



Synonyms: Allium; lissan (Hindi).

Biological Source: Garlic is obtained from ripe bulb of *Allium sativum* Linn.

Family: Liliaceae.

Chemical Constituents: Allicin, Alliin, volatile and fatty oils, mucilage and albumin

2.3. Clove Oil:



Synonyms: Caryophylli; Clove buds and Clove flower, Lavang (Hindi).

Biological Source: Clove is obtained from dried flower and buds of *Eugenia caryophyllus* tree.

Family- Myrtaceae

Chemical Constituents: Clove contains Volatile oil (16-21%):- Phenol group mainly in the form of Eugenol (80-88%), acetyl eugenol (10- 15%); α and β -Caryophyllene. Also present Pyrogallol tannins, methyl furfural and dimethyl furfural.

2.4. Peppermint oil



Synonyms: Mentha

Biological source: Mentha oil is obtained by steam distillation of flowering tops of *Mentha piperita* Linn.

Family: Labiatae.

Chemical Constituents: Not less than 50% total menthol including 5-9% esters calculated as menthyl acetate; menthyl isovalerate, menthone, inactive pinene, L-limonene, cadinene, phellandrene, some acetaldehyde, isovaleric aldehyde, amyl alcohol, dimethyl sulfide.

2.5. Neem Oil



Synonyms: Margosa, Nimtree or Indian lilac,

Biological source: Neem consists of the fresh or dried leaves and seed oil of *Azadirachta indica* J. Juss (*Melia Indica* or *M. azadirachta* Linn.).

Family: Meliaceae.

Chemical Constituents: The chemical constituents are found in the leaves of neem as nimbin, nimbanene, 6-desacetylnimbinene, nimbandiol, nimbolide, ascorbic acid, n-hexacosanol and amino acid, 7-desacetyl-7-benzoylazadiradione, 7-desacetyl-7-benzoylgedunin, 17-hydroxyazadiradione and nimbiol [3],

3. PREPARATION OF CREAM

3.1. Preparation of oil phase

The oil phase is the internal phase in a cream, which contains all the oil-soluble ingredients. The oil phase is prepared by mixing the ingredients in order of increasing melting points. This ensures a homogeneous mixture, as ingredients with lower melting points can become overheated and lose their properties if added to hot oils or waxes.

3.2. Preparation of Aqueous phase

Water was heated to 65 to 70°C. To this aqueous medium pre weighed all the reagent were added; Then the temperature of the aqueous phase was maintained at 65 to 70°C.

3.3. Development of Cream formulation

Total Oil phase was then slowly pour into the aqueous phase at 65-70°C and mixed for 10 to 15 Minutes. When the temperature of both the medium were at the same temperature, the aqueous phase was slowly added to the oil phase with moderate agitation and was kept stirred until the temperature dropped to 40°C. The o/w emulsion was then cool down to room temperature to changed a thick cream base.

4. EVALUATION PARAMETERS OF HERBAL CREAM

4.1. pH test: The pH meter was calibrated using standard buffer solution. About 0.5g of the cream was weighed and dissolved in 50.0 ml of distilled water and its pH was measured.¹⁸

4.2. Color and odor: Physical parameters like color and odor were examined by visual examination.¹⁸

4.3. Homogeneity: The formulations were tested for the homogeneity by visual appearance and by touch.¹⁹

4.4. Type of emulsion under dye test: The scarlet red dye is mixed with the cream. A drop of the cream was sited on a microscopic slide, then it was enclosed with a cover slip and examined under a microscope. If the disperse globules appear red and the ground is colorless, the cream is O/W type. The reverse condition occurs in W/O type cream i.e. the disperse globules appear colorless in the red ground.²⁰

4.5. Viscosity: Viscosity measurements of the formulations were determined using rotational-type viscometer (Brookfield DVII, Germany TA spindle, 25±1°C). Measurements were taken in 3 replications in 100 rpm (n: 3). Viscosity values were recorded in centipoise (cP).²⁰

4.6. Type of smear: After application of cream, the type of film or smear formed on the skin was checked.²²

4.7. Irritancy test: Mark an area (1sq.cm) on the left hand dorsal surface. The cream was applied to the specified area and time was noted. Irritancy, erythema, edema, was checked if any for regular intervals up to 24 hrs and reported.²⁰

4.8. Accelerated stability testing: Accelerated stability testing of prepared formulations was conducted for 2 most stable formulations at room temperature, studied for 7 days. They were formulation number 3 and 4 at 40°C ± 1°C for 20 days. The formulations were kept both at room and elevated temperature and observed on 0th, 5th, 10th, 15th and 20 th day for the different parameters.²²

4.9. Evaluation of antifungal activity

Inoculum quantification was performed by quantitative plating on SAB to determine viable CFU per milliliter. The adjusted suspensions were vortexed and diluted 1:100 in distilled water. The diluted (1:100) suspensions were vortexed again, and 0.01-ml aliquots were spread (using a calibrated quantitative loop) onto SAB plates with a glass hockey stick. The plates were incubated at 28 to 30 °C and checked daily to determine the CFU per milliliter. Colonies were counted as soon as possible after growth became visible. For slower growing colonies, the plates were reinsulated for several days. Inoculum quantitation for isolates needed to be performed at 24 h or less because of their rapid confluent growth. Assay of antifungal activity was performed by two methods:

4.9.1. Filter paper disc method: An antibiotic- or extract-impregnated filter paper disk is then placed on the surface of the agar. The disk constituent(s) diffuse from the filter paper into the agar. The concentration of these constituents will be highest next to the disk and will decrease as the distance from the disk increases.

4.9.2. Agar well diffusion method: The agar well diffusion method is a technique used to assess the antimicrobial activity of microbial extracts or plants. It involves creating a well in the medium, then adding the extract solution to the well.²³

5. CONCLUSION

Most of the people are unaware of the uses of the medicinal plants like Garlic Oil, Clove Oil, Neem, Oil Peppermint oil and in case of any fungal infections, they use allopathic medicines to treat it which may cause some side effects. These oils showed effective antifungal activity against different types of fungi. It has many medicinal properties such as healing abilities, antioxidant activity etc. Therefore People instead of using allopathy medicines can move in a natural way to heal fungal infections.

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