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Review Article

Formulation and Evaluation of Polyherbal Antifungal Cream Using *Azadirachta indica* & *Piper Betel L.* leaves Extract

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ABSTRACT

Fungal illnesses develop into serious health issues. Since fungal diseases are often persistent and challenging to diagnose, they are challenging to treat. A common ailment brought on by fungi is fungal infection. Several herbs, including neem and aloe vera, were used in the formulation of the herbal antifungal lotion. One of the oldest and most widely used medical systems is herbal medicine. There are less negative effects and the herbal antifungal lotion is quite beneficial. The market has easy access to all natural ingredients. The herbal antifungal cream is used to treat fungal infection which most commonly affect our skin, hair and nails. Jockey itch, ringworm, and athletes' foot are examples of fungal skin infections that are treated using herbal antifungal lotion. Reducing fungal infections is one of the benefits of using this natural and safe herbal antifungal cream.

INTRODUCTION

Herbal cosmetics nourish and improve skin and hair by using natural components made from plants, herbs, and minerals. These items are well-liked by people looking for kinder substitutes because they frequently don't include artificial chemicals. Because of their calming, hydrating, and antioxidant qualities, ingredients including aloe vera, tea tree oil, lavender, and rosehip are frequently included in herbal cosmetics. Ayurveda and traditional Chinese medicine are two examples of the many herbal cosmetics that also use traditional cures from other cultures. Compared to

their synthetic counterparts, these products are thought to be safer and less likely to result in negative reactions or skin irritations. Because they are made from renewable resources and may biodegrade, they are also frequently environmentally favorable. But it's important to remember that while though herbal cosmetics can be beneficial, each person will react differently, so it's important to choose products carefully and see a dermatologist if you have any particular skin concerns.[1] *Azadirachta indica*, the scientific name for neem, is a multipurpose tree indigenous to the Indian subcontinent. It is very important from a cultural, medical, and agricultural

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standpoint. For generations, neem has been utilized in traditional medicine. Its extracts include substances that have antiviral, antifungal, antibacterial, and anti-inflammatory qualities. Derived from its seeds, neem oil is applied topically to treat psoriasis, dermatitis, and acne. Because of its antibacterial properties, it is frequently utilized in dental care products. There are several neem-based goods on the market, such as herbal supplements, soaps, shampoos, lotions, and toothpaste. These goods take advantage of neem's antibacterial and skin-beneficial qualities.[2,3]



Azadirachta indica (Neem)

Scientific Name – Azadirachta indica

Biological Source- It consist of fresh and dried leaves of Azadirachta Indica Family – Meliaceae

Chemical Constituent- flavonoids, Alkaloids, Azadirone, nimbin, Nimbidin, terpenoids, steroids, tannic acid

Uses – Antifungal , Antibacterial, Anti-inflammatory, Skin Disorder, Skin Disease.

Taxonomical Classification-

Kingdom: Plantae

Division: Magnoliophyta

Class: Magnoliopsida

Order: Sapindales

Family: Meliaceae

Genus: Azadirachta

In Malaysia, betel leaves are used to treat dental issues, headaches, arthritis, and joint discomfort. In Indonesia, they are used for vaginal douching. In India and Thailand, they are used as a gargle mouthwash. Betel leaf juice is used to treat skin conditions in Sri Lanka. Its boiling leaves may also be used as an astringent, tonic, or cough remedy. The antibacterial and antifungal qualities of betel leaves have led to their traditional uses. Betel vine, or Piper betle (L), is a member of the Piperaceae family. The betel vine's leaf is its most utilized and researched component. In many nations, chewing betel leaves is a common habit that is thought to help prevent bad breath, strengthen gums, preserve teeth, and stimulate the digestive system.[4,5] God created the piper betel, a perennial and evergreen plant, and gave it the shape of his own heart. Anthropologists have discovered betel remains in Northwest Thailand's spirit caves that date back to between 5500 and 7000 BC, long before organized and systematic agriculture was adopted. The blackened teeth of a human skeleton from Palawan, the Philippines, date back to 2600 BC, while similar discoveries have been made in Timor, Indonesia, dating back to 3000 BC. It was included in the Palli-language Mahawamsa, the oldest historical book of Sri Lanka. Due to years of chewing, certain betel chewers in Thailand, Myanmar, and Indonesia have been discovered to have black teeth. It is unknown how long ago these two distinct stimulants were first combined, although archeological evidence suggests that betel leaves and areca nuts have been chewed together since very ancient times. As a result, it could be challenging to pinpoint the exact moment that the paan chewing custom began. But the fact that it is mentioned in Kalidas's Raghuvamsa and the Vatsyayana's Kamsutra alone shows how old this practice is. The fact that receiving paan bida was regarded as a tremendous honor further demonstrates the social standing of paan.[6]

Scientific Name - Piper Betel

Biological Source - It consist of fresh leaves of piper betel L.

Family- Piperaceae

Chemical Constituent - Leaves contain protein, carbohydrate , minerals and tannins. It contains calcium, phosphorus, iron, iodine, potassium, vitamin B, vitamin C and vitamin A.

Taxonomical Classification –

Kingdom : Plantae

Division: Magnoliophyta

Class: Magnolipsida

Order: Piperales

Family: Piperaceae

Genus: Piper

Species: Betel [6]



Piper Betel L (Betel leaf)

EVALUATION OF CREAM [7,8]

physical apperance:

The visible qualities of a cream, such as its look, feel, consistency, homogeneity, and spreadability, are known as its physical parameters. Color, smell, and general visual presentation are all considered aspects of appearance. The apparent smoothness upon application is indicated by texture. Consistency affects usability by reflecting firmness or softness. Without discernible particles or phase separation, homogeneity guarantees a consistent dispersion of materials. The cream's spreadability is a measure of how quickly it covers

the skin's surface. It is essential to evaluate these factors in order to guarantee product quality, customer pleasure, and effectiveness in providing the desired therapeutic or cosmetic advantages.

physical sepration test:

By putting a cream through stressful situations like centrifugation or temperature changes, the phase separation test assesses its stability. It evaluates if the components of the cream split into separate layers, a sign of instability. The cream is examined for any indications of phase separation, such as obvious layering or separation of the water and oil phases, after stress has been applied. Under the studied conditions, the existence of phase separation suggests instability, whereas its absence shows cream stability. This test is crucial for guaranteeing product quality and providing guidance for formulation and storage decisions.

pH determination:

Using a pH meter or pH indicator strips, one can measure the acidity or alkalinity of an antifungal cream to find its pH. This procedure yields important details regarding the chemical characteristics of the cream, which may impact its stability, effectiveness, and skin compatibility. To guarantee maximum efficacy and skin tolerability, antifungal lotions must be kept at the proper pH. Since this range maintains the preservation of active chemicals and is compatible with the skin's natural pH, it is generally considered the best pH range for topical formulations. Manufacturers can guarantee product quality and improve fungal infection treatment results by precisely measuring the pH of an antifungal cream.

Irritancy test:

An antifungal cream's irritancy test evaluates how likely it is to irritate skin or trigger allergic reactions. To assess the cream's impact on human skin, this test usually uses a patch test or other techniques. Volunteers' skin is treated with a tiny

quantity of the cream under carefully monitored circumstances during the test. After that, the skin is observed for a predetermined amount of time to look for any negative reactions, such as rash, swelling, itching, or redness. Researchers can ascertain the cream's safety profile and evaluate its appropriateness for topical application by performing an irritancy test. This knowledge is essential for making sure antifungal creams are well-tolerated and don't hurt people too much.

Spreadability test:

An antifungal cream's spreadability test determines how quickly and uniformly the cream covers the skin's surface. After that, the cream is covered with a standard weight for a predetermined amount of time. Next, the cream spread's diameter is measured. Better spreadability is indicated by a bigger spread diameter since the cream can cover more ground with less effort. The viscosity, consistency, and composition of the cream are some of the factors that affect its spreadability. Manufacturers can improve formulation to guarantee even application and efficient coverage for antifungal creams by evaluating spreadability, which will improve treatment results and customer satisfaction.

Topical Route:

The best treatment for skin infections is topical. Given the many benefits over traditional drug administration methods, the creation of topical drug delivery systems with systemic effects seems advantageous for a variety of medications.[9]

Cream:

Cream is defined as semisolid emulsions which are oil in water (o/w) or water in oil (w/o) type and these semisolid emulsions are intended for external application[10]

Classification of cream :

All the skin creams can be classified on different basis:

1. According to function, e.g. foundation, massage, cleansing etc.
 2. According to characteristics properties, e.g. cold creams, vanishing creams, etc.
 3. According to the nature or type of emulsion.
- Types of creams according to function, characteristic properties and type of emulsion:
1. Make-up cream (o/w emulsion): a) Vanishing creams. b) Foundation creams.
 2. Cleansing cream, cleansing milk, cleansing lotion (w/o emulsion).
 3. Winter cream (w/o emulsion): a) Cold cream or moisturizing creams.
 4. All-purpose cream and general creams.
 5. Skin protective cream.
 6. Hand and body creams.
 7. Night cream and massage creams. [11]

Advantages:

- ☐ Convenient and simple to use.
- ☐ First-pass metabolism should be avoided.
- ☐ Intravenous therapy is inconvenient, as are the many circumstances of absorption, such as pH changes, the presence of gastric emptying time, and so on.
- ☐ Avoid medication level fluctuations due to inter- and intra-patient changes. [12]

Disadvantages

- Allergic reactions are a possibility.
- Continuous drug input achieves efficacy with a lower total daily dose of medicine.
- Some drugs have a low permeability through the skin

- Can only be used for medications that require very low plasma concentrations to work .[12]

Ideal properties:

- ☐ Easy to apply is one of the best qualities.
- ☐ Easily spread over the skin.
- ☐ It has a pleasant aspect.
- ☐ Skin irritation is reduced.
- ☐ When applied to the skin, it will melt or liquefy. [12]

Antifungal Cream:

Topical drugs called antifungal creams are used to treat fungal skin illnesses such jock itch, ringworm, and athlete's foot. Active chemicals like terbinafine, miconazole, clotrimazole, or ketoconazole are commonly included in these creams; they function by preventing the growth of fungi and curing the infection. When prescribed by a medical practitioner, antifungal creams are administered topically to the afflicted area and are typically used for a predetermined amount of time. When used regularly and as directed, they can successfully eradicate fungal infections and relieve symptoms like itching, redness, and irritation. For safe and efficient use, it is imperative to adhere to the directions on the container or those given by a healthcare professional.

Antifungal Activity of piper betel

examined the hydroxychavicol that was extracted from piper betel leaves for its antifungal properties in vitro. The broth microdilution method was used to determine the minimum fungicidal concentration (MFC) and minimum inhibitory concentration (MIC). With MICs ranging from 15.62 to 500 ug/ml for yeasts, 125 to 500 ug/ml for *Aspergillus* species, and 7.81 to 62.5[13]

Antifungal activity of neem

At the Medical Mycology Laboratory at Universidad de Antioquia in Colombia, dermatophyte fungus were isolated from patients. Classification included biochemical testing in addition to microscopic and macroscopic analysis according to predetermined standards. Among the isolates were three isolates of *Epidermophyton floccosum*, one strain of *Microsporum canis*, and five isolates each of *Trichophyton rubrum* and *Trichophyton mentagrophytes*. The isolates of *T. Mentagrophytes*, *T. Rubrum*, and *E. floccosum* were cultivated for eight days in either boiling rice or Potato-Dextrose-Agar in order to produce a conidial suspension for the inoculum. The conidial suspension was adjusted to a concentration of 1.0 to 3.0×10^3 CFU/mL after a sterile saline solution was added to promote conidial production. In accordance with CLSI recommendations, the M38-A2 broth microdilution method was used to perform the antifungal activity testing. Neem extracts were serially diluted twice in a MeOH:DMSO solvent to create RPMI 1640 medium, which also contained a positive control using a commercial antifungal Terbinafine and a solvent control in Khokrale Pratiksha. There were no additions in the sterile and negative controls. In 96-multiwell microdilution plates, the prepared medium and conidial suspension inoculum were incubated for seven days at 35 °C without being shaken or exposed to light. The quantities of neem extracts that were tested ranged from 0.0019 µg/mL to 7000 µg/mL. Due to a scarcity of *E. floccosum* inoculum, only particular isolates of *T. mentagrophytes* and *T. rubrum* were examined. Every extract and dermatophyte isolate was used in three separate experiments. The lack of turbidity, which denotes total inhibition of fungal growth, was used to calculate the Minimum Inhibition Concentration [14]

composition

Ingredients	Role
Neem leaves	Antifungal



Betel leaves	Antifungal
Alov-vera gel	moisturizer
Tween 20	Emulsifier
Bees wax	Emollient
Borax	Buffer
Glycerin	Lubricant
Silica gel	Adsorbent
Bentonite	Thickening agent
propyl paraben	preservative
Peppermint oil fragrance	

CONCLUSION:

The increasing global awareness of the environmental impact of pharmaceuticals and a growing desire for sustainable, natural solutions have propelled herbal remedies into the spotlight. Herbal antifungal creams, harnessing the power of plant extract, represent a compelling alternative to synthetic medications, offering a balance between efficacy and safety. One of the key strengths lies in the generally well-tolerated nature of herbal formulation, often associated with synthetic counterparts. Scientific advancements in herbal medicine research further substantiate the efficacy of specific plant compounds against fungal pathogens. This intersection of traditional herbal knowledge and modern scientific validation enhances the credibility of herbal antifungal remedies, paving the way for great integration into mainstream health care practices. The future trajectory of herbal antifungal creams is marked by sustainability, safety and efficacy making them a compelling choice in the evolving landscape of antifungal treatments.

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