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Research Article

FORMULATION AND EVALUATION OF ANTIFUNGAL CREAM CONTAINING "CARICA PAPAYA LEAF EXTRACT" FOR THE TREATMENT OF ONYCHOMYCOSIS

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ABSTRACT:

The current study focuses on formulation and evaluation of an antifungal cream derived from Carica papaya leaf extract for the treatment of onychomycosis, a prevalent fungal nail infection. In this study, alcoholic extraction was efficiently isolated the active components from Carica papaya leaves with key components such as flavonoids, alkaloids, saponins, and tannins which confirm the antifungal properties of the extract. The cream was prepared using an emulsifying base such as bees wax and cetosterol alcohol and evaluated for various parameters including pH, viscosity, spreadability, washability, and antifungal efficacy against Candida albicans through zone of inhibition. The results from the study indicated that formulation F3 demonstrated several desirable properties, both in terms of physical characteristics and therapeutic efficacy. The formulation offers a holistic, natural alternative to conventional antifungal treatments, with good physical properties, effective antifungal performance, and minimal side effects.

Key words: Onycomycosis, Antifungal, Candida albicans, Carica papaya, Papaya leaf extract

INTRODUCTION

The anatomy of the human nail plate is quite intricate, and understanding its structure is crucial for comprehending how fungal infections, like onychomycosis, affect the nail. The human nail plate is composed of three layers: the upper, intermediate, and ventral layers. The intermediate layer, which accounts for three-quarters of the nail's thickness, is made of soft keratin. The upper and dorsal layers are much thinner, consisting of only a few layers of cells but containing hard keratin with relatively high sulphur content, primarily in the form of the amino acid cysteine, which constitutes 94% of the nail's weight. The ventral layer is composed of soft hyponychial tissue, where pathological changes may occur.

The human nail plays a crucial role in protecting and enhancing the functionality of our fingers and toes. The human nail isn't just a decorative feature; it plays an integral role in protecting the delicate fingertip tissues, enhancing sensation, aiding in tasks that require precision, and providing structural support for our hands and feet. These functions make the nails essential for a variety of everyday activities, contributing to both functionality and health. When the nails are damaged, as in cases of onychomycosis or injury, it can hinder one's ability to perform these tasks effectively, hence maintaining healthy nails is so important for overall well-being.[1]

The appearance of the nail plate can become abnormal due to several factors, including congenital defects, skin diseases that involve the nail bed, systemic diseases, reduced blood supply, local trauma, tumours in the nail fold or nail bed, or infections. Some common nail diseases include "Green Nail Syndrome" which is an infection caused by Pseudomonas bacteria, "Paronychia" which is an infection caused by Streptococci, Onychomycosis is a common fungal infection caused by dermatophytes such as Trichophyton rubrum and

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Trichophyton mentagrophytes var. interdigitale, followed by Candida species and non-dermatophytic molds. Candida onychomycosis is more common in fingernails and is often accompanied by paronychia.[2]

Onychomycosis, though often considered a cosmetic issue, can have significant physical and psychological impacts. It is a persistent condition, with no known spontaneous resolution. Treatment options include topical, systemic or a combination of therapies:

Topical antifungals are typically ineffective if nail penetration is poor. Common topical treatments include ciclopirox 8% and amorolfine 5% lacquers, which have broad-spectrum activity against yeasts, dermatophytes, and NDMs. Oral antifungals used to treat onychomycosis include griseofulvin, azoles (such as ketoconazole, itraconazole, and fluconazole), and the allylamine terbinafine. These medications have better penetration into nail tissue and can more effectively treat nail onychomychosis. However systemic treatment of the disease can cause GI discomfort, liver toxicity etc[3].

Papaya (scientifically known as Carica papaya) is a large upright herbaceous species characterized by its broad, lobed, and palmate (hand-like) leaves, which typically measure between 50 and 70 cm in circumference. Research indicates that papaya extracts exhibit a range of beneficial properties, including antioxidant, anti-cancer, anti-inflammatory, antifungal, antimicrobial, and antibacterial activities. These effects are attributed to its rich composition of bioactive compounds, such as carbohydrates, proteins, flavonoids, anthraquinones, saponins, cardiac glycosides, tannins, and alkaloids4.

Studies have further demonstrated the antifungal and antimicrobial effect of papaya leaf extracts when prepared with various solvents, including ethyl acetate, acetone, chloroform, petroleum ether, hexane, hot water, ethanol, and methanol. These extracts have shown activity against six microbial strains, notably Escherichia coli, Staphylococcus aureus, and Candida albicans5.

In this context, the herbal formulation of the antifungal cream is designed with Carica papaya leaf extract as the key active ingredient, leveraging its natural antifungal properties to treat the fungal infection on the nails. This approach seeks to minimize the risks associated with conventional treatments while offering an effective solution, particularly for those who prefer natural remedies or for cases where systemic therapy may not be ideal.

MATERIALS AND METHOD

Selection of plant:

The plant used in the formulation of antifungal cream was selected on the basis of literature survey. Collection of plant material:

The Papaya leaves used in formulation were collected from the local area of Belagavi and authenticated by ICMR-National Institute of Traditional Medicine Belagavi.

Drying of papaya leaf

The air-dried leaves of papaya (Carica papaya) were ground into a coarse powder using a mixer grinder and subsequently passed through a 60# sieve to ensure uniform particle size. The resulting dried leaf powder was stored in an air-tight container to preserve its integrity and prevent contamination until it was used for further extraction processes.

Extraction by Maceration

A total of 100 g of pre-dried papaya (Carica papaya) leaf powder was macerated in 500 mL of 95% ethanol in a beaker covered with aluminum foil to minimize evaporation and contamination. The mixture was allowed to stand for 72 hours with periodic shaking to facilitate thorough extraction of bioactive compounds. Upon completion of the maceration process, the mixture was filtered through muslin cloth to separate the solid residue. The filtrate was subsequently evaporated using a rotary vacuum evaporator to remove excess solvent, followed by further concentration on a water bath to obtain the final papaya leaf extract.6,7

Phyto-chemical screening for papaya leaf extract

The phytochemical screening of the plant extract was carried out using qualitative methods to identify the presence of bioactive compounds. The extract was systematically tested for key phytochemicals, including alkaloids, flavonoids, tannins, saponins, and other secondary metabolites.8,9

PREPARATION OF CREAM BASE

A 100 g batch of emulsifying cream base was prepared by melting 30 g of emulsifying wax (beeswax) in a water bath maintained at 70 ± 0.5 °C. To the melted wax, 58.8 ml of liquid paraffin, 0.1 g of methyl paraben, and 1.5 g of borax were added, ensuring thorough mixing. Subsequently, melted bees wax in varying concentrations was incorporated into the mixture. The preparation was then removed from the water bath and stirred continuously until it cooled and achieved a uniform consistency.10,11

FORMULATION OF ANTIFUNGAL CREAM:

Carica papaya leaf ethanol extract creams were formulated according to the composition provided in Table 1. A 30 g portion of the emulsifying cream base was weighed into a demitasse dish and melted in a water bath maintained at 70 ± 0.5 °C. The required quantity of the ethanolic extract was added to the molten cream base and continuously stirred to ensure uniform dispersion. Warm distilled water was gradually added in portions to

the mixture while stirring until a homogeneous blend was achieved. The cream was then allowed to cool before being transferred into labeled cream jars, designated as F1, F2, and F3.12,13

EVALUATION OF CREAM

Physical appearance

Visual examination of the cream was conducted to assess its color, odor and texture. After being transferred to containers, all prepared creams were inspected to evaluate their homogeneity.14

pH measurement

The pH value of the formulated cream was determined by weighing 1 g of the sample and dissolving it in 100 ml of distilled water. The pH measurement for each formulation was conducted individually using a digital pH meter.

Spreadability test

To measure the spreadability of the cream, 1 g of the sample was placed as a 1 cm diameter circle on a glass slide. A second glass slide was carefully placed on top of it, and a 250 g weight was applied for 5 minutes. The increase in the cream's diameter was observed, and the time required to separate the two glass slides was recorded. Three measurements were taken for each formulation, and the average values were calculated. The spreadability was determined using the following formula

$$S = M. L/T$$

The following was used to calculate the spreadability;

S = Spreadability,
M = Weight on the glass slide
L = Length moved the glass slide
T = Time taken to separate the slides.

Washability test

The washability test was carried out by applying the small quantum of cream on the nail of cutlet and also washed under the handling water.

Viscosity determination

The sample was placed in the teacup of a Brookfield Viscometer and allowed to rotate at spindle number 12. The measurements were taken independently at rotational speeds of 20 rpm and 30 rpm. For each speed, the readings were recorded, and the process was repeated three times. The average of the three readings at each speed was calculated to ensure consistency and accuracy.15

Antifungal studies

The antifungal activity was evaluated using the slice prolixity system. Sabouraud's Dextrose Agar (SDA) plates were inoculated with a 72-hour culture of Candida albicans. Sabouraud's Dextrose Broth cultures were prepared in test tubes. Using a sterile cotton swab, the surface of the SDA plates was evenly swabbed to prepare a uniform field culture. Once the agar surface had dried (approximately 5 minutes), wells were aseptically created using a sterile cork borer. The wells were then impregnated with three formulations of the nail cream under study. A standard fluconazole disk was included on the same plate as a reference control. The plates were incubated at 28°C for 24–48 hours. After incubation, the zones of inhibition were measured using a scale to the nearest millimeter for each formulation. (14)

Test of stability

The stability assessment of the final product was carried out by keeping it under a constant temperature (room temperature) for 1 to 3 months. Further the physical instabilities such as changes in color, odor and constituency of the formulation and any signs of bacterial or fungal growths were checked.

The stability of the final product was evaluated by storing it at a constant room temperature for a period of 3 months. During this time, the formulation was regularly monitored for physical instabilities, including changes in color, odor, and consistency. Additionally, the samples were inspected for any signs of bacterial or fungal growth. 15

RESULTS AND DISCUSSION

EVALUATION OF PAPAYA ANTIFUNGAL CREAM

Physical Appearance

The color, odor, and unity of the set Cream were all visually assessed, and the issues were reported in Table No. 3.

pH measurement

The pH of produced formula ranges between 5.5 – 7.0. The pH of the produced cream expression was determined to be applicable for avoiding skin annoyance when applied to the skin. The results were shown in Table No. 4. The F1, F2 & F3 shows the good pH for skin or nail.

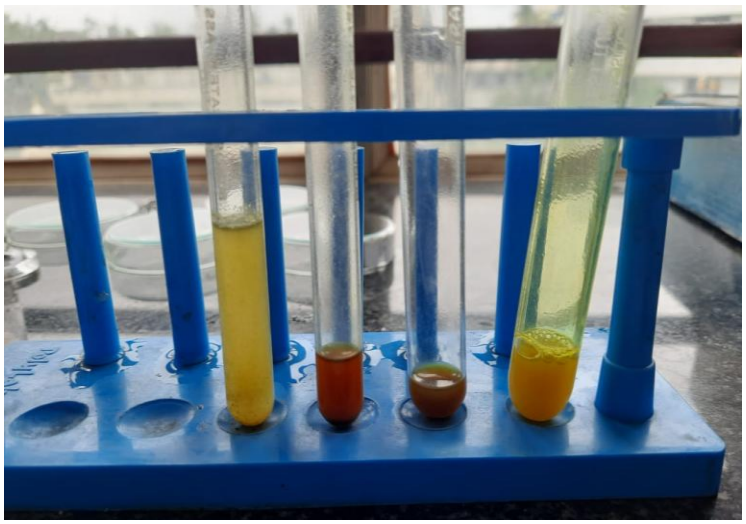

Figure No. 4: Photochemical screening Tests

Figure No.5: Antifungal activity on agar plate

Spreadability test

Spreadability reflects the ease with which the cream covers the surface, with better spreadability being associated with shorter separation times between two slides during testing. The results, summarized in Table No 4, revealed that formulation F3 exhibited superior spreadability compared to F1 and F2. This improvement can be attributed to the higher concentration of beeswax in F3, which enhances the cream's consistency and spreading characteristics. Consequently, F3 achieves moderate spreadability, ensuring effective adherence to the nail and surrounding skin.

Washability test

All the formulations were easily washed off with running water, indicating that the creams are of the water-in-oil (W/O) type.

Viscosity determination

The viscosity of the prepared cream was measured using a Brookfield viscometer, and the results are presented in Table No 4. Among the formulations, F3 demonstrated a moderate increase in viscosity compared to F1 and F2. This higher viscosity enables F3 formulation to stay effectively in place on the nail plate and surrounding skin, minimizing the risk of running off. Consequently, F3 ensures better adhesion to the affected area, which is crucial for effective treatment.

Antifungal studies

The antifungal activity of phrasings F1, F2, and F3 was evaluated by measuring the zone of inhibition against Candida albicans and Aspergillus niger using the well diffusion method. Among the three phrasings, F3 exhibited the strongest antifungal activity, outperforming F1, F2, and even the standard Miconazole. This enhanced activity can be attributed to the higher concentration of beeswax in F3, which improves the efficacy of the papaya leaf excerpt. The increased beeswax concentration in F3 supports better release and stability of the active ingredients, thus boosting its antifungal effects against the tested fungal strains. In comparison, F1 and F2, with lower beeswax content, showed comparatively weaker activity.

The antifungal activity of the best formulation F3 was assessed using agar well diffusion method by measuring the zone of inhibition against Candida albicans and Aspergillus niger. The enhanced antifungal activity of F3 can be attributed to its higher concentration of beeswax, which plays a crucial role in improving the efficacy of the papaya leaf extract. The increased beeswax concentration in F3 enhances the release and stability of the active ingredients, thereby boosting its antifungal effects against the tested fungal strains. Figure No 5 and Table No 5 reveals antifungal activity on agar plate using Miconazole as standard.

Test for stability

The stability of the final product was assessed by storing at room temperature (25°C) for a period of up to 3 months. During this time, no significant changes were observed in the physical appearance, including color, odor, or consistency. Furthermore, there were no signs of bacterial or fungal growth, indicating that the formulation maintained its stability throughout the storage period.

Figure No. 1: Onycomycosis affected nail

Figure No. 2: Marketed products for treatment of onychomycosis

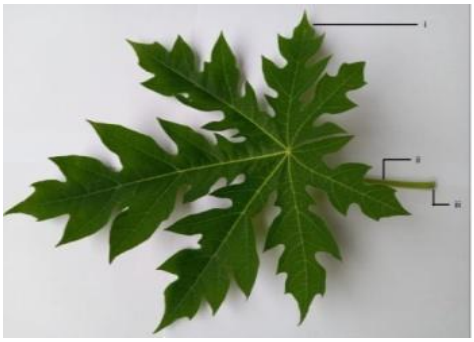

Figure No. 3: Papaya leaf

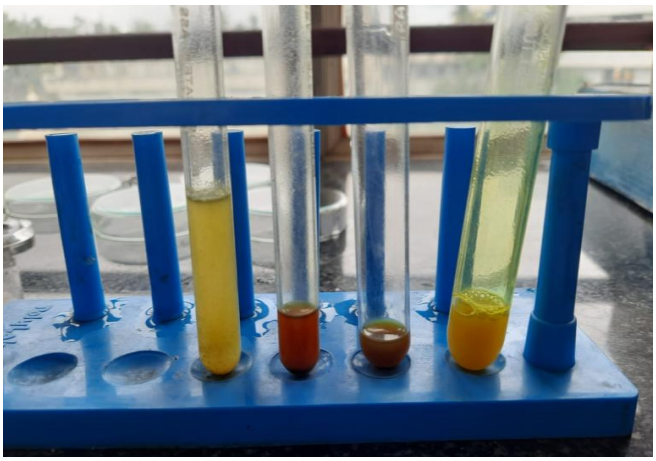

Figure No. 4: Photochemical screening Tests

Figure No.5: Antifungal activity on agar plate

Table No 1: Formulation of Various Antifungal creams containing *Carica Papaya* Extract

SR. NO.	INGREDIENTS	F1	F2	F3
1	Papaya leaf excerpt	0.625gm	0.625gm	0.625gm
2	Bees wax	8gm	9gm	10gm
3	Borax	1.5gm	1.5gm	1.5gm
4	Liquid Paraffin	58.8ml	58.8ml	58.8ml
5	Methyl paraben	0.1gm	0.1gm	0.1gm
6	Cetostearyl alcohol	30gm	30gm	30gm
7	Essence oil	2 drops	2 drops	2 drops
8	Distilled water	Q.S	Q.S	Q.S

Note: Formulation was prepared for 100 gm

Table No 2: Photochemical Screening of *Carica Papaya* leaf extract

Sl no.	Chemical Constituents	Test	Confirmation
1.	Alkaloid	Wagner's Test	+
2.	Flavonoid	Sulphuric acid test	+
3.	Tannin	Nitric acid test	+
4.	Saponin	Saponification test	+

Table No. 3: Physical appearance of formulated cream

Appearance	F1	F2	F3
Color	Greenish brown	Greenish brown	Greenish brown
Odor	Characteristic	Characteristic	Characteristic
Homogeneity	Absence of aggregates	Absence of aggregates	Absence of aggregates

Table No. 4: Measurement of Spreadability, pH and Viscosity of antifungal cream

Formulation code	Spreadability (gm.cm/sec)	pH Measurements	Viscosity (cp)
F1	175	5.86	676.33
F2	179.1	6.12	923
F3	190	6.90	1080.66

Table No. 5: Antifungal activity

Sl. NO.	SAMPLES	ZONE OF INHIBITION (mm)
1	Control	0
2	Standard (Miconazole)	24
3	F3 Formulation	15

CONCLUSION

This study involved the development and characterization of a herbal nail cream containing papaya leaf extract (Carica papaya). The papaya leaf extract was prepared through a hydroalcoholic extraction process using fresh papaya leaves and was analyzed for the presence of phytoconstituents such as alkaloids, flavonoids, saponins, and tannins.

The cream base was formulated using beeswax, borax, liquid paraffin, methylparaben, cetostearyl alcohol, and water. The herbal nail cream was evaluated based on various parameters, including pH, viscosity, spreadability, washability, and antifungal activity against Candida albicans. Stability testing was performed over different time intervals to assess the formulation's durability.

Among the tested formulations, F3, which contained a higher concentration of papaya leaf extract and beeswax, exhibited superior performance. It showed excellent appearance, optimal pH, viscosity, high spreadability, washability, as well as potent antifungal activity. These characteristics identified F3 as the most promising formulation in the study.

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