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Herbal Anti-fungal Cream: A Natural Approach to Onychomycosis Treatment

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Abstract: Onychomycosis is a frequent fungal infection of the nails that is difficult to cure and is not well controlled by standard medications, therapeutic options are limited. Herbal remedies have drawn interest as a result of this due to their potential as complementary therapies. The composition and effectiveness of a novel herbal anti-fungal cream that combines the powerful anti-fungal qualities of clove oil, turmeric, and pure peppermint are examined in this abstract. The strong anti-fungal properties of clove oil's high eugenol content are enhanced by curcumin, an anti-inflammatory and anti-microbial compound found in turmeric. Pure peppermint contributes antifungal and calming qualities as well as a pleasant element. The combination of these components offers a viable way to cure onychomycosis, possibly more effectively than conventional therapies because it is all-natural.

Keywords: Onychomycosis, anti-fungal, nail, herbal remedies.

I. INTRODUCTION

A fungal infection of the nails known as onychomycosis affects millions of people worldwide and poses a persistent and difficult clinical condition. Traditional therapies, like oral drugs and topical antifungal creams, frequently have poor effectiveness and carry the risk of side effects or drug interactions.

A growing number of people are interested in investigating complementary and alternative therapies, especially those that come from natural sources, in light of these difficulties. Traditional medical systems have traditionally employed herbal treatments due to their perceived safety and effectiveness.

Because of their strong anti-fungal and anti-microbial qualities, clove oil, turmeric, and pure peppermint have become highly promising options for the treatment of onychomycosis.

The component recognized for its broad-spectrum antibacterial activity, eugenol, is abundant in clove oil, which is extracted from the buds of Syzygium aromaticum.

One of the ginger family's rhizomatous herbaceous perennials, turmeric includes curcumin, a polyphenolic chemical that has been shown to have anti-inflammatory and anti-fungal effects. Mentha piperita is the source of pure peppermint, which is extracted and contains menthol and other bioactive ingredients with calming and antifungal properties.

By going over possible mechanisms of action, this research aims to further our knowledge of natural methods of treating onychomycosis.

By investigating the potential of herbal remedies as a therapeutic tool and encouraging more research into their application to the treatment of onychomycosis, our goal is to provide patients suffering from this common fungal infection with safe, efficient, and easily accessible treatment options. [(1-2).]

A. Onychomycosis

Fingernails and toenails that have onychomycosis, a fungal disease, get thicker, darker, and split from the nail bed. Even if 10% of people worldwide are affected, adults are more likely to encounter it. Onychomycosis is 1.9–2.8 times more common in diabetics than in the general population, and 15%–40% of HIV-positive persons have the disease.

Proximal sublingual onychomycosis, which often spreads from the proximal nail folds, and distal subungual onychomycosis, which affects the nail plate, bed, and hyponychium, are the two main types of onychomycosis that are currently recognized to exist. Clinical variations include the less common superficial white variety and the endonyx type, which does not include hyperkeratosis or onycholysis. [(3-4).]

Fig.1- Types of Onychomycosis [5].

1) Symptoms

The majority of fungal nail infections are harmless. However, some people could find their nails uncomfortable or bothersome. Infections with nail fungi can cause thick, brittle, cracked, or discoloured nails. Additionally, the nail may separate from the nail bed. Athletes' foot, ringworm on the foot, or tinea pedis are common names for fungal skin infections that frequently coexist with fungal toenail infections. [6].

2) Epidemiology

In post-industrialized countries, almost 10% of people suffer with onychomycosis. The prevalences reported in studies conducted in Finland (n = 800) and Canada (n = 2001; n = 15,000) ranged from 6.5% to 9.1%. Although at first thought to be unimportant, there have allegedly been more cases in subsequent years. The frequency was 2.18% in 1979 US research (n = 20,000), and it increased to 1038 by 1997. An increase from 3.5% in 1997–1998 to 4.7% in 2003 was seen in an Indonesian study. The Achilles study conducted surveys with people in East Asia (n = 43,914) and Europe (n = 22,760), and the results showed significant prevalences of 26% and 22%, respectively. [7-8].

3) Nail anatomy and Physical Characteristics

The nail unit consists of anatomical structures such the hyponychium, which serves as a barrier of protection at the free edge of the nail plate. The nail unit is mostly composed of the nail matrix, with a small amount of input from the nail bed. The nail plate is 0.5–1.0 mm thick and consists of dorsal, intermediate, and ventral layers. Hard keratin makes up the majority of this plate. Where it originated in the matrix is indicated by the lunula. While fingernails grow at a pace of 3 mm per month, depending on circumstances including gender, temperature, pregnancy, and mild traumas, toenails develop at a rate of about 1 mm per month. Levodopa, antifungal drugs, calcium/vitamin D, and other treatments can speed up nail development, which may help treat onychomycosis. Nevertheless, inadequate medication penetration through the nail plate reduces the effectiveness of traditional topical antifungal treatments. Tineapedis was not often seen in Europe prior to the arrival of T. rubrum because of increased population mobility brought on by many world wars and significant migration. Due to its proliferation, the US saw its first clinical instance of tineapedis after World War I, and in 1928 it saw the first case of onychomycosis. Tineapedis and onychomycosis have been more common in the 20th century due to factors such as population mobility, occlusive footwear use, increased fitness activities, World War II, and Vietnam War. As the most prevalent dermatophyte in the world, T. rubrum has surpassed T. mentagrophytes; around 70% of Americans have dermatophytic fungi on their plantar surfaces. [9-11].

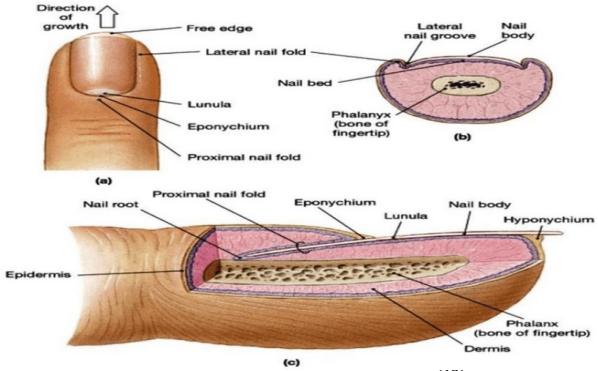

Fig. 2- Anatomy of Finger [12].

B. Morphology and Clinical Presentation

Based on the manner and location of fungal invasion of the nail plate, onychomycosis is classified into five types: total dystrophic onychomycosis, proximal subungual, endonyx, distal and lateral subungual, and superficial white.

1) Distolateral Onychomycosis

The most prevalent type, called distolateral subungual onychomycosis, begins frequently at the hyponychium and moves through the lateral groove or the distal-lateral edges from the distal to the proximal nail matrix. The infection is typically caused by Trichophyton spp., although it can also be caused by Scytalidium spp., Candida spp., and other non-dermatophytes. Paronychia, subungual hyperkeratosis, onycholysis, and thicker nails are some of its symptoms. The nail plate may get discolored a yellow color due to the presence of pathogenic bacteria and fungus in the subungual region. [13].

2) Proximal Subungual Onychomycosis

Even though it is less common, proximal subungual onychomycosis is more common among AIDS patients and others with weakened immune systems, and it frequently acts as a preliminary clinical indicator of HIV infection. This type is frequently linked to T. rubrum, C. albicans, Fusarium spp., Aspergillus spp., and Scopulariopsis brevicaulis. Under the nail cuticle, fungi infiltrate the nail, causing infection in the proximal nail plate and spreading laterally throughout the nail.

3) Superficial white Onychomycosis

Onychomycosis superficialis affects the dorsal aspect of the nail plate, resulting in regions of opaque white nail plate discoloration. The principal pathogens are Trichophytonmentagrophytes and T. rubrum, while non-dermatophyte molds such as Aspergillus spp., Fusarium spp., and Acremonium spp. have also been discovered. The upper layers of the nail's keratin are home to the majority of fungal components.

4) Endonyx onychomycosis

A newly discovered variation of the disease known as endonyx onychomycosis is typified by fungal invasion of the nail plate's deeper layers in addition to its surface. There are no inflammatory alterations, lifting, or thickening of the nails like in other forms. The main culprits are T. violaceum and T. soudanense. Lamellar cracking, coarse pitting, and milky white patches inside the afflicted nail plates are characteristics of this fungal nail infection.

5) Total dystrophic onychomycosis:

The final stage of chronic onychomycosis is called total dystrophic onychomycosis, and it is frequently marked by almost total disintegration of the infected nail plate. Complete dystrophic onychomycosis is recognized to have two subtypes: main and secondary. Individuals with primary full dystrophic onychomycosis are typically those who have persistent mucocutaneous candidiasis. [14].

C. Herbs for onychomycosis Treatment

One of the oldest and most popular forms of medicine, herbal therapy, has recently benefited from improvements in medication delivery to effectively treat human illnesses. According to data from the World Health Organization (WHO), 80% of people worldwide today receive their primary care from herbal medicine. More and more countries are looking into alternative forms of healthcare, such as herbal cures for self-medication. Scientific facts, clinical experience, understanding of medical science, and traditional knowledge are all integrated in modern herbal therapy. People are gradually turning to alternative medicine. [15].

1) Advantages of Herbal System of Medicines

a) Less chance of adverse effects.
b) Broad accessibility.
c) Performance in long-term care.
d) Their low cost of operation makes them even more enticing.
e) Herbal medicine effectively promotes the body's natural detoxification process.
f) Herbal medications have fewer adverse effects and are gentler.

2) *Disadvantages of Herbal System of Medicines*

g) Bulk dosing.
h) Instable in more acidic pH, metabolism in the liver, etc.
i) A large molecule size that prevents passive diffusion absorption.
j) A large quantity of raw materials are needed to process the medication.
k) The medicinal efficacy of a whole herbal extract may be partially or completely lost when specific components are separated and purified.

II. HERBS USED IN THE FORMULATION OF ANTI-FUNGAL CREAM:

A. Clove Oil

1) *Synonym:* Clove buds, Clove flowers.
2) *Biological Source:* Dried flower buds from Eugenia caryophyllus Thumb are used to make cloves.
3) *Family: Myrtaceae.*

Fig.3- Clove buds [16].

Strong antifungal qualities are found in clove essential oil, which is frequently used in cooking and herbal remedies. Because of its potent scent, it can be utilized in aromatherapy, cosmetic purposes, and even dentistry as a natural anaesthetic. Its efficacy against Aspergillus parasitica and Candida albicans, among other fungal pathogens, has been demonstrated by studies; nevertheless, nothing is known about its antifungal action when applied as a vapor. The purpose of this study is to examine clove essential oil and vapor as potential antifungal agents against dermatophytic fungus. [17].

4) *Chemical Constituents of Clove Oil:* Originating from Syzygiumaromaticum, clove essential oil (CEO) has a wide range of chemicals, the most common of which is eugenol, which can make up as much as 30% to 95% of the oil. β-caryophyllene, α-ilangene, δ-cadinene, methyl eugenol, anetol, chavicol, vanillin, benzyl alcohol, cinnamic aldehyde, benzyl salicylate, and calamenene are some of the other ingredients. The chemical makeup of CEO differs based on the oil's origin and the cloves' stage of maturity, among other things. For example, bud oil contains more eugenyl acetate than leaf oil. The Polish Pharmacopoeia states that eugenol (75–88%), β-caryophyllene (5–14%), and eugenol acetate (4–15%) are the usual ingredients of CEO. [18-19].
5) *Antifungal Activity of Clove Oil:* The therapeutic potential of clove oil has been demonstrated in earlier research, especially in relation to its antifungal qualities against a variety of fungus, including Candida albicans. Although smaller quantities (50% and 20%) were effective against Candida albicans, 100% pure clove oil showed strong antifungal activity against every tested fungus in this experiment. Notably, the oil demonstrated a wide range of antifungal efficacy against various dermatophyte species. [21-22].

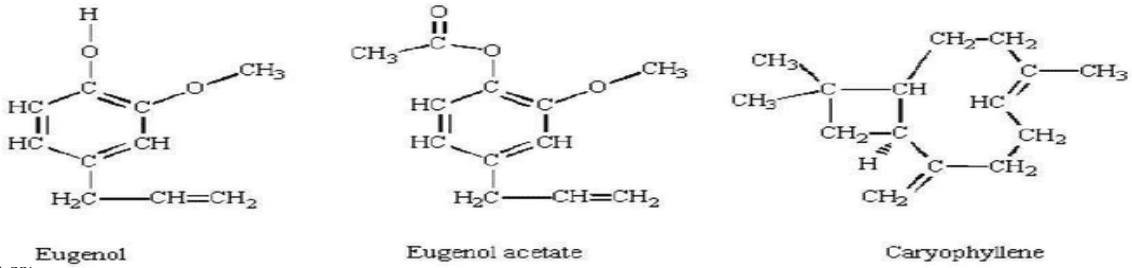

Fig .4- Chemical constituents in clove oil.

(Eugenol, Eugenol acetate, caryophyllene) [20]

B. Turmeric

1) *Synonyms:* Saffron Indian; haldi (Hindi); Curcuma; Rhizoma cur-cumae.
2) *Biological Source:* The dried rhizome of Curcuma longa Linn. (syn.C.domesticaValeton) is known as turmeric.
3) *Family: Zingiberaceae.*

Fig.5- Turmeric powder [23]

Curcumin, the primary ingredient in turmeric, has demonstrated potential in the fight against the fungi that cause nail infections. It can be used to inhibit the growth of two dermatophytes that are frequently seen in nails, Trichophyton rubrum and Trichophyton mentagrophytes. It is believed that curcumin's anti-fungal action damages the integrity of fungal cell walls and obstructs vital fungal metabolic processes, which inhibits fungal growth and lessens the severity of infection. Turmeric's anti-inflammatory qualities can help reduce onychomycosis-related pain and inflammation and speed up the healing process for the afflicted nails as a whole. [24-25].

4) *Chemical Constituents of Turmeric:* Curcumin, a polyphenolic compound extracted from the rhizome of the Curcuma longa L. plant, often known as turmeric, has garnered significant attention in scientific investigations because of its numerous biological features. Asian medicine has always used turmeric, a well-known natural source of curcumin. This suggests that turmeric has a wide range of possible medical uses. [26-27].

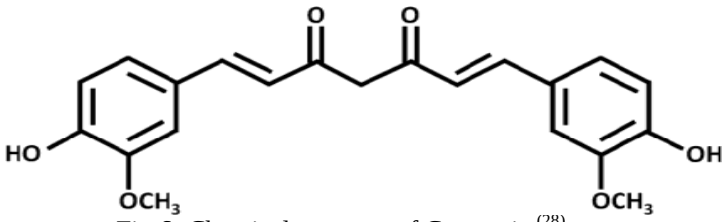

Fig.6- Chemical structure of Curcumin [28].

5) *Antifungal activity of Turmeric:* Due to its widespread use in culinary goods, turmeric's antifungal qualities have drawn attention. According to studies, adding turmeric powder to plant tissue culture successfully prevents fungal contamination. Turmeric methanol extracts are also promising; they exhibit antifungal efficacy against pathogens such as Candida albicans and Cryptococcus neoformans. [29].

C. Pure Peppermint

1) *Synonym:* Mentha nigricans Mill, Mentha officinalis Hull, pudina, pepper mint.
2) *Biological Source:* The fresh leaves of Mentha piperita peppermint are steam-distilled to get pure peppermint.
3) *Family: Lamiaceae.*

Fig.7- Pure peppermint [30].

Pure peppermint's antifungal properties in relation to onychomycosis can be linked to its primary ingredients, specifically menthol and menthone. The potential of these substances to prevent the growth of different fungi, including those that cause nail infections, has been investigated. The antifungal qualities of pure peppermint may also be attributed to the various terpenes and menthol derivatives it contains. These ingredients cooperate when applied topically to ailing nails to inhibit the growth of fungi and encourage recovery. Though encouraging, more studies are required to ascertain whether pure peppermint is particularly beneficial in treating onychomycosis. [31].

4) *Chemical Constituents of Pure Peppermint:* A prevalent ingredient in pure peppermint, menthol shows promise as an antifungal agent that could help cure nail infections like onychomycosis. While there isn't much study specifically on using menthol to treat nail infections, studies have shown that it can stop a variety of fungi from growing. The antibacterial action of menthol may aid in the overall treatment of nail infections by battling the fungi that cause them. Furthermore, the cooling and calming properties of menthol can help with nail infection symptoms like itching and soreness. [33].

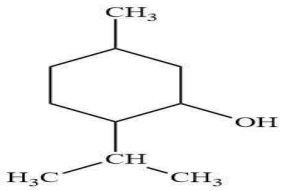

Fig.8- Chemical structure of Menthol [32].

5) *Antifungal Properties of Pure Peppermint:* Studies on the antifungal characteristics of menthol, a major ingredient in pure peppermint, suggest that it may be useful in the treatment of fungal infections such as onychomycosis. Research has looked into menthol's capacity to stop the growth of a number of fungi, including Candida species and dermatophytes, which are frequently linked to nail infections. Menthol disrupts fungal cell membranes and interferes with fungal enzyme systems, among other processes, to produce its antifungal effects. Furthermore, the cooling effect and analgesic qualities of menthol may help alleviate the discomfort linked to fungal nail infections. [34].

Table:1- Antifungal cream formulation

Sr.No	Formula	Quantity		
		F1	F2	F3
1.	Clove oil	0.4ml	0.6ml	0.5ml
2.	Turmeric extract	1.5ml	1ml	1ml
3.	Pure peppermint	1gm	1.2gm	1.2gm
4.	Steric acid	5gm	7gm	5gm
5.	Cetyl alcohol	1.8gm	1.5gm	1.5gm
6.	KoH	0.2gm	0.3gm	0.4gm
7.	Propyl paraben	0.04gm	0.04gm	0.04gm
8.	Petroleum jelly	3gm	6gm	5gm
9.	Water	q.s	q.s	q.s

III. METHOD OF PREPARATION

A. *Heat Oil Phase (75°C)*

1) In a jar that can withstand heat, mix stearic acid, petroleum jelly, cetyl alcohol, and clove oil.
2) Using a hot plate or water bath, heat the mixture to 75°C until it is completely melted and combined.

B. *Prepare Aqueous Phase (75°C)*

1) In another heat-resistant container, combine distilled water, KOH, propyl paraben, turmeric extract, and pure peppermint.

2) In order to dissolve the materials and produce a clear solution, heat the mixture to 75°C.

C. Emulsification

1) Incorporate the aqueous phase gradually into the oil phase, continuously stirring in one direction.

2) To blend materials and prevent lumps, use a mortar and pestle.

D. Cooling and Homogenization

1) To encourage emulsification, keep stirring as the mixture cools to room temperature.

2) If necessary, use an ice bath to expedite cooling and guarantee consistency.

E. Quality Check and Adjustments

1) Examine the stability, texture, and consistency of the emulsion.

2) If additional oil or water phase components are needed, adjust the formulation accordingly.

F. Packaging

1) Place the completed emulsion in the proper containers.

2) Make sure to properly label the containers and keep them out of direct sunlight in a cool, dry spot. [35].

IV. CHARACTERIZATION OF HERBAL ANTIFUNGAL CREAM:

A. Physical Evaluation

Physical characteristics like color, smell, and look were assessed.

Fig.9- Antifungal cream

Fig.10- Packaged cream

B. pH Determination

The pH of various gel compositions was determined using pH paper. The 2.0 g of cream were weighed precisely, combined with 20 ml of distilled water, and stored for two hours. We tested and noted the pH. A representation of the pH values is present. The pH of the dispersion was measured using pH paper.

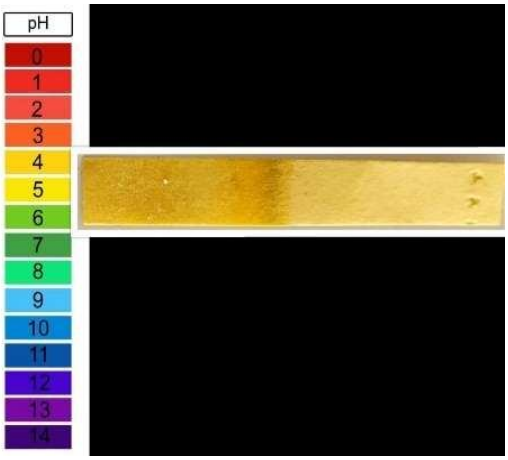

Fig.11- pH determination

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C. Type of Emulsion Under Dye test

Scarlet red dye mixed with cream. On a slide, put a drop of the cream-dye mixture, and then cover it with a cover slip. Examining a particular kind of emulsion under a microscope.

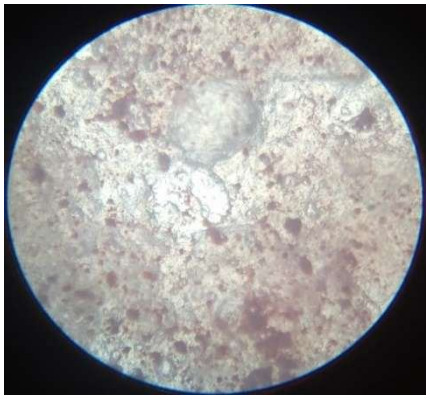

Fig.12- Dye test

D. Stability Study

Herbal antibacterial and antifungal cream was tested in vitro for 28 days at various temperatures at 8, 25, 40, and 45 degrees Celsius, as well as 40 degrees Celsius at 75% relative humidity in stability chambers. Color, liquefaction, phase separation, conductivity, and pH changes were all observed and documented.

E. Irritancy Test

A 1cm² region was designated on the left dorsal surface. This designated surface was covered with the cream. Next, for a period of up to 24 hours, irritancy, erythema, and edema were assessed at regular intervals, and the time was recorded and reported.

Fig.13- Before

Fig.14- After

F. Spreadability

Two sets of glass slides were taken. The cream was spread over one slide, and then another slide was placed on top of the cream, sandwiching the cream in a 6.0 cm-long gap between the two slides. A 100-gram weight was placed on the upper slide to generate a thin layer of cream between the two slides. On a platform, two slides were arranged so that they could not be moved in any way and that the only weight that could slide off freely was attached to the top slide. The upper slide was gently secured with a 20-gram weight. The higher slide's movement of 6.0 cm beneath the weight's impact was timed. to disengage from the lower slide and move 6.0 cm. This experiment was repeated three times, and the average time was found. Spreadability was calculated by using the formula:

$S = M * L / T$

where, T is the time (in seconds) needed to separate the slide, L is the length moved on the glass slide, M is the weight attached to the top slide, and S is the spreadability.

G. Saponification Value

A reflux condenser was attached to a 250 mL round-bottom flask containing around 2 g of the material. Next, 25 mL of the ethanolic 0.5 M potassium hydroxide was added, and it was allowed to boil for 30 minutes over a water bath. The sample was given a few minutes to cool. Using phenolphthalein as an indicator, the sample solution was then titrated against 0.5 M hydrochloric acid (HCl). Moreover, blank titration was carried out without sample addition.

Fig.15- Test assembly

Fig.16- Result

H. Acid Value

After weighing out 10 g of the sample in the round-bottom flask, it was dissolved in 50 mL of the neutralized combination of ether and 95% ethanol (1:1 v/v). Subsequently, the material was dissolved by gradually heating and shaking a reflux condenser. After that, the endpoint was found by titrating the sample solution with standardized 0.1M potassium hydroxide. As an indicator, phenolphthalein solution was employed. [35,36].

Fig.17- Test assembly

Fig.18- Result

V. RESULT AND DISCUSSION

Table:2- Characterization of herbal antibacterial, antifungal cream.

Sr.No.	Parameters	Result F1	Result F2	Result F3
1.	Colour and homogenecity	White and homogeneous	White and homogeneous	White and homogeneous
2.	Odour	Characteristics	Characteristics	Characteristics
3.	Consistency	Watery	Watery	Semisolid cream
4.	Spreadability	20.16	19.50	19.06
5.	pH test	6	5	6

6.	Irritancy	No rashes were seen	No rashes were seen	No rashes were seen
7.	Washability	No traces of serum were seen	No traces of serum were seen	No traces of serum were seen
8.	Phase separation	No phase separation was seen	No phase separation was seen	No phase separation was seen
9.	Saponification value	23.2	27.4	26.2
10.	Acid value	6.4	6.4	5.8
11.	Cyclic temperature a)Freezer b)Room temperature	Shows lumps Stable	Shows lumps Stable	Shows lumps Stable

I. Discussion

The evaluation parameters applied to the cream produced a number of noteworthy conclusions. For example, the cream with the label F3 was white in color, had a distinct smell, and was semisolid in consistency, whereas the creams with the labels F1 and F2 were runny. Additionally, all three formulations (F1, F2, and F3) showed good spreadability and a pH of 6. Furthermore, none of the formulations showed any indications of irritation. In addition, all formulations were found to have good washability, with no phase separation observed. Nevertheless, it was shown that F1, F2, and F3 were unstable in freezing conditions but stable at ambient temperature throughout the cyclic temperature research.

VI. CONCLUSION

In conclusion, Clove oil, turmeric, and pure peppermint make up a natural anti-fungal cream that shows promise in treating onychomycosis, a common and difficult-to-treat nail fungal infection. This herbal treatment successfully fights fungal diseases by utilizing the combined antibacterial qualities of its constituents, treating the illness as well as any accompanying symptoms.

Our study has shown that the cream is effective in preventing the growth of common fungal species linked to onychomycosis, indicating that it may be a safe and effective therapy alternative. Moreover, clove oil, turmeric, and pure peppermint have anti-inflammatory and calming qualities that help to reduce discomfort and support healthy nails during the therapy process.

This herbal cream can address concerns about side effects and medication resistance while providing a natural substitute for conventional antifungal therapies. It also appeals to those who prefer holistic and plant-based remedies. Furthermore, using it topically offers a practical and non-invasive way to treat onychomycosis, which may improve patient compliance and treatment results.

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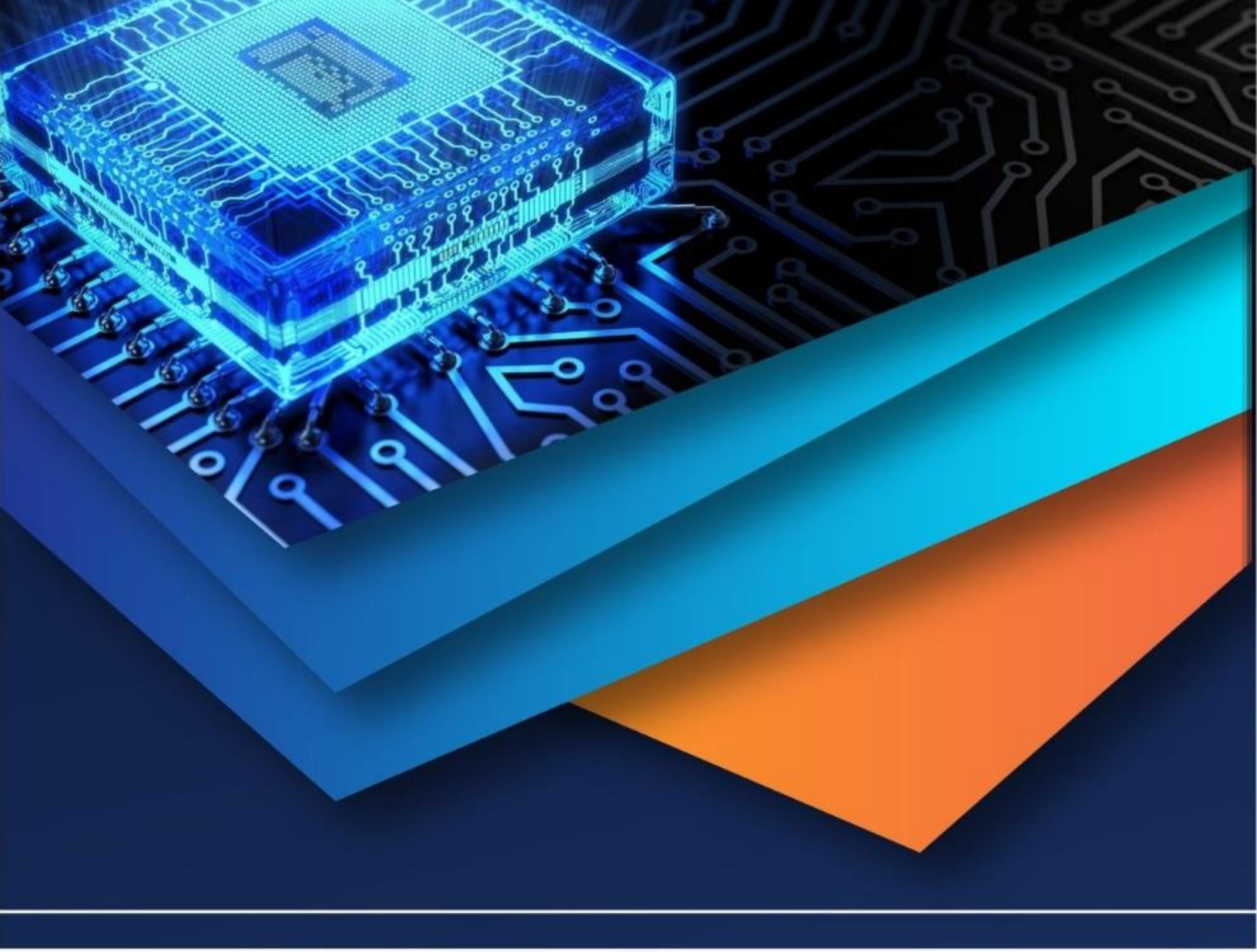

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