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FROM NATURE TO NAILS: A COMPREHENSIVE REVIEW ON HERBAL NAIL LACQUER FOR TREATING ONYCHOMYCOSIS

Aishwarya Hiremath[1]*, Samarth A. V.[2], Atiya[2], Shrushti S.[2], Manikantha P. Garlpet[2], Muhammed Mussamil A.[2]

[1]Assistant Professor, Department of Pharmaceutics, Bapuji Pharmacy College, SS Layout, Shamanur Road, Davanagere, India. Affiliated to Rajiv Gandhi University of Health Sciences, Bengaluru, Karnataka.
[2]Final Year B Pharm Student, Bapuji Pharmacy College, SS Layout, Shamanur Road, Davanagere, India. Affiliated to Rajiv Gandhi University of Health Sciences, Bengaluru, Karnataka.

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***Corresponding Author**

Aishwarya Hiremath
Assistant Professor, Department of Pharmaceutics, Bapuji Pharmacy College, SS Layout, Shamanur Road, Davanagere, India. Affiliated to Rajiv Gandhi University of Health Sciences, Bengaluru, Karnataka.

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ABSTRACT

Millions of people suffer from onychomycosis worldwide, a common fungal infection of the nails that frequently causes brittleness, thickness, and discoloration. Conventional treatments like oral antifungals and synthetic nail lacquers are usually linked to problems like systemic adverse effects, drug interactions, little nail penetration, and high relapse rates. Herbal nail lacquers, which combine plant-derived actives including tea tree oil, oregano oil, neem extract, Caesalpinia bonducella extract and coniferous resins with sophisticated formulation techniques, have become a viable substitute in recent years. These natural substances have broad-spectrum antifungal, anti-inflammatory, and anti-oxidant activities, and they frequently work through a variety of mechanisms which lowers the likelihood of resistance. Drug delivery, release sustainability, and patient compliance are all improved by the use of penetration enhancers, film-forming agents, and resins. Quality and therapeutic potential are guaranteed by evaluation factors such as drying time, adhesion, viscosity, content of active ingredients and antifungal activity. Herbal nail lacquers,

with their low toxicity and good safety profiles, provide a practical, patient-friendly way to treat onychomycosis. This helps to overcome the drawbacks of traditional therapies and satisfy the increasing need for safe, efficient, and pleasing treatments.

KEY WORDS: Nail lacquer, anti-fungal, herbal, transungual drug delivery, onychomycosis, penetration enhancers.

INTRODUCTION

Nail providing protection and enhancing fine motor skills, healthy nails also indicate general hygiene and well-being. Among common nail disorders, onychomycosis is a fungal infection predominantly caused by *Trichophyton rubrum*, other dermatophytes, yeasts (e.g. *Candida* species), and non-dermatophyte Molds is the most prevalent. It affects approximately 10% of the adult population globally, with higher prevalence among older individuals and those in tropical, humid regions.[1] Traditional treatments include oral antifungals (e.g., terbinafine, azoles) and topical lacquers (e.g., amorolfine, ciclopirox). Oral medications often yield high cure rates but are accompanied by systemic side effects, liver toxicity risk, and drug interactions. Meanwhile, topical therapies suffer from poor transungual penetration, lengthy treatment durations, and frequent relapses.[2]

Numerous patents have revealed novel nail lacquer formulations designed to tackle the flaws of traditional treatments. These include methods for improving patient compliance, enhancing drug penetration, and lowering side effects using more robust and safe film-forming processes. The increasing industry focus on both therapeutic and cosmetic applications is reflected in this patent activity, which supports scientific research in this field. Recent research has focused on herbal-based nail lacquers, which provide a natural and possibly safer substitute, building on earlier advancements.

So, the review has turned to herbal-based nail lacquers, which combine film-forming vehicles with plant-derived active ingredients such coniferous resin, tea tree oil, and rosemary oil, in order to overcome these drawbacks. These formulations aim for minimal systemic effects, medicinal efficacy, and aesthetic acceptance.[3-5]

Interest in natural alternatives has increased as a result of growing microbe resistance and worries about the negative effects of long-term usage of synthetic antifungals. Because of their synergistic phytochemical effect, low toxicity, and broad-spectrum antimicrobial

properties, herbal actives present a promising avenue. Herbal lacquers frequently include numerous bioactive ingredients that can operate on different fungal sites, minimizing the likelihood of resistance development. This is in contrast to synthetic lacquers, which primarily serve as a barrier or depot for a particular antifungal medication.

Through processes like membrane disruption, ergosterol synthesis suppression, and oxidative stress induction, essential oils like tea tree oil (Melaleuca alternifolia) and oregano oil (Origanum vulgare) have demonstrated strong antifungal activity against Candida albicans and T. rubrum.[6,7] Further demonstrating their promise in clinical practice, coniferous resins, such as spruce resin, have shown treatment efficacy comparable to amorolfine in mild to severe onychomycosis.[8]

In order to promote transungual medication delivery by weakening the keratin matrix and boosting hydration of the nail plate, penetration enhancers including thioglycolic acid, urea, and salicylic acid are being added to herbal lacquers more frequently.[9] Combining these enhancers with natural antifungals not only increases their effectiveness against the disease but also lowers the risk of systemic side effects, which makes them appropriate for long-term or preventative use.

Furthermore, the application of film-forming agents such as chitosan, shellac, nitrocellulose, cellulose acetate, cellulose acetate butylate, ethyl cellulose, and cellulose acetate improves patient compliance by enabling the controlled release of herbal actives while development of an elegant, protective layer over the nail.[10]

Understanding the structure of nails is a prerequisite for knowing the transungual drug delivery system.

Structure of human nail[11]

Human nail consists of.

- Nail plate
- Lateral nail folds
- Proximal nail fold
- Cuticle
- Nail matrix and lunula
- Nailbed

- Onychodermal band

The nail unit is made up of several protective and functional structures. The **nail plate**, formed of compact keratinized cells, provides strength and utility[12], while the **lateral and proximal nail folds**, along with the **cuticle**, act as barriers against infections and trauma.[11,13,14] The **lunula**, a visible part of the nail matrix, supports nail growth and serves as a diagnostic marker.[15] Beneath the plate, the **nail bed** nourishes and thickens the nail, with contributions from blood vessels and melanocytes.[16] At the tip, the **onychodermal band** links the nail bed to the hyponychium, playing a key role in maintaining nail health and aiding in disease recognition.[17]

Common Herbal Actives Used in Nail Lacquers

The dense keratinized structure and intrinsically low permeability of the nail plate present a significant challenge for effective transungual drug delivery. To overcome this barrier, therapeutic agents are required that not only demonstrate potent antifungal activity but also possess favourable physicochemical characteristics to enable nail penetration. In recent years, phytoconstituents have emerged as promising alternatives to conventional antifungal drugs, largely due to their broad-spectrum activity, favourable safety profiles, and compatibility with topical delivery systems. The subsequent section discusses key herbal actives frequently incorporated into nail lacquer formulations for the management of onychomycosis and related disorders.

The development of herbal nail lacquers as alternatives to conventional antifungal therapies relies on the careful selection of plant-derived actives with demonstrated efficacy against common onychomycosis pathogens, particularly *Trichophyton rubrum*, *Candida albicans*, and other dermatophytes and yeasts. These herbal actives ranging from essential oils and oleoresins to standardized extracts contain a diverse array of phytoconstituents. Collectively, they provide antifungal, anti-inflammatory, antioxidant, and in some cases keratolytic effects, making them especially suitable for the management of nail infections.[5]

These natural agents exert their effects through multiple mechanisms, including disruption of the fungal cell membrane, inhibition of ergosterol biosynthesis, interference with fungal respiration, and high induction of reactive oxygen species (ROS). Acting through such diverse pathways not only enhances their antifungal efficacy but also lowers the risk of resistance development. Within nail lacquer formulations, their inherently lipophilic character

and relatively low molecular weight often support improved penetration across the dense keratin matrix of the nail plate. When combined with penetration enhancers and suitable film-forming agents, these properties further optimize transungual delivery.[6,7]

Below is a comprehensive overview of some of the most studied herbal actives incorporated into nail lacquers, along with their phytochemical profiles, mechanisms of action, and antifungal targets.

Table 1: Antifungal activity of medicinal plant extracts, key phytoconstituents, mechanisms of action and target organisms.

Plant Source	Key Phytoconstituents	Mechanism of Antifungal Action	Target Organisms	References
Melaleuca alternifolia (Tea Tree Oil)	Terpinen-4-ol, α-terpineol, cineole	Disrupts cell membrane, increases permeability, causes leakage of ions and nucleotides	*T. rubrum*, *C. albicans*, *T. mentagrophytes*	Hammer et al., 2004 [4]; Carson et al., 2006.[6]
Origanum vulgare (Oregano Oil)	Carvacrol, thymol	Membrane depolarization, high induction of ROS, ergosterol inhibition	*Candida spp.*, *T. mentagrophytes*	Nostro et al., 2004[18]
Azadirachta indica (Neem Oil/Extract)	Azadirachtin, nimbidin, quercetin	Disrupts membrane, inhibits hyphal growth, anti-inflammatory	*Candida albicans*, *Fusarium* spp.	Biswas et al., 2002[19]
Allium sativum (Garlic Extract)	Allicin, ajoene	Inhibits sulfhydryl-containing enzymes, alters lipid synthesis	*Candida spp.*, *T. rubrum*	Sharma et al., 2011
Ocimum sanctum (Tulsi Extract)	Eugenol, ursolic acid	Inhibits ergosterol synthesis, antioxidant, membrane lysis	*C. albicans*, *T. rubrum*	Prakash & Gupta, 2005
Caesalpinia bonducella	Bonducellin, sitosterol, ergosterol, saponins	Not fully elucidated; reported fungistatic effects	*Candida spp.*, dermatophytes	Dabadi et al., 2024[20]
Cassia alata (Senna)	Anthraquinones, kaempferol, chrysophanol	Membrane disruption, inhibits fungal morphogenesis	*C. albicans*, *T. mentagrophytes*	Oyelana & Adebola, 2009
Syzygium aromaticum (Clove Oil)	Eugenol	Disrupts fungal cell wall, inhibits chitin and ergosterol synthesis	*C. albicans*, *Aspergillus spp.*	Di Vito Maura et., 2022 (21)
Cymbopogon citratus (Lemongrass)	β-Citral (31.6%), α-Citral (44.3%)	Cell membrane and mitochondrial disruption, inhibition of ergosterol synthesis	*T. rubrum*, *T. mentagrophytes*	Di Vito Maura et., 2022[21]
Lavandula hybrida	Thymol methyl ether (53.1%), p-	Antifungal via oxidative membrane damage	*T. interdigital*, *M. canis*, *T.*	Di Vito Maura et., 2022[21]

(Lavender hybrid)	cymene (7.7%)		*tonsurans*	
Cissus quadrangularis	Flavonoids, steroids, phenols, quinones	Disruption of fungal membrane integrity; quinones exert fungicidal action via oxidative stress and protein binding	*Candida albicans*	Pandit et al., 2020[21]
Olea europaea (Olive leaf)	Oleuropein	Disrupts fungal cell membranes; causes oxidative stress and inhibits fungal growth via phenolic interaction	*Candida albicans*	Tamilselvan et al., 2024[23]
Psidium guajava (Guava leaf)	Phenols, flavonoids, terpenoids, saponins, oleanolic acid, ursolic acid	Disruption of fungal cell membrane via phenolic activity; antioxidant and fungistatic actions attributed to flavonoids	*Candida albicans*	Chauhan R, Mehan N, Singh M, et al., 2024 (24)

Formulation Approaches in Herbal Nail Lacquers

The successful development of herbal nail lacquers for the treatment of onychomycosis depends not only on the selection of effective herbal actives but also on a scientifically robust formulation strategy. Given the barrier properties of the nail plate, particularly its low porosity and high keratin content, topical formulations must be designed to ensure optimal film formation, sustained drug release, aesthetic acceptability, and enhanced transungual penetration.

Chemical constituents of nail lacquer are as follows.

1. **Film forming polymers**

These create a smooth, continuous film over the nail, ensuring adhesion of the formulation and sustained drug release. They include nitrocellulose, ethyl cellulose, cellulose acetate, cellulose acetate butylate.

2. **Plasticizers**

These are excipients added to film-forming systems to improve flexibility, reduce brittleness, and enhance the durability of the dried film. By lowering the glass transition temperature of polymers, they help maintain film integrity during wear and prevent cracking. In medicated nail lacquers, plasticizers also aid in better adhesion and drug release. Examples include triacetin, dibutyl phthalate, tributyl citrate and triphenyl phosphate.[25]

3. Penetration enhancers

The primary barrier is the high content of disulfide cross-linked keratin fibres, which limits diffusion of hydrophilic and hydrophobic molecules. Therefore, the presence of penetration enhancers in nail lacquer formulations is essential to facilitate transungual drug delivery.

Tabel 2: Types of Penetration enhancing agents with examples and their modes of action.[26]

Category	Examples	Mode of Action
Keratolytic agents	Salicylic acid, urea, lactic acid	Break hydrogen bonds in keratin, increasing porosity and hydration
Sulfhydryl compounds	Thioglycolic acid, N-acetyl-L-cysteine	Cleave disulfide bonds in nail keratin, loosening structure
Enzymes	Papain, keratinase	Degrade keratin selectively without damaging surrounding tissue
Solvent-based enhancers	Propylene glycol, ethanol, DMSO	Improve solubility of actives and hydrate the nail matrix

4. Resins

Provide hardness, gloss, and adherence to the nail surface, often used alongside polymers to strengthen the film. Natural resins including benzoin, shellac, and ester gums have been substituted by synthetic resins because they offer superior gloss, improved adherence, and high-water resistance some of the marketed products are santolite MHP and santolite MS 80 percent.

5. Solvents

Solvents that are used in nail lacquer must have faster evaporation and volatile organic solvents.

Solvents are classified based upon their boiling points.

- Low boiling solvents like acetone, ethyl acetate, methyl acetate
- Medium boiling solvents like n-Butyl alcohol, amyl formate, n-Butyl acetate
- High boiling solvents like Butyl lactate, cyclohexanone.[27]

6. Pigments

Pigments Impart colour and improve aesthetic appeal without compromising formulation stability and enhancing the appearance. Examples are titanium dioxide and iron oxides.

Evaluation of Nail lacquer

1. Drying time

The volatility of a nail coating solvent system and, consequently, its drying time have a significant impact on its application and performance qualities. On a clear, spotless glass panel, a thin coating of lacquer is applied and then watched. A stopwatch is used to measure the drying time, and the film is pressed with a finger until there are no more marks visible. The total time should be less than 10 minutes. The film should be applied on a fully nonporous surface at 25 ^{0}C and 50% relative humidity to maintain standardized process.[28]

2. Smoothness

This is the character of the film. After the film is placed to a surface, its surface properties are examined under a microscope.

To guarantee excellent adhesion and gloss, moisture and dirt residue should be eliminated from the surface prior to applying a nail lacquer.[29]

3. Determination of non-volatile content

First take the initial weight of petri plate (M1) and then place 1gm (M) of sample was taken into petri plate and spread evenly. Then weight of petri plate with sample was recorded. The petri plate was kept in hot air oven for 1 hour at 105±2°C. After 1 hour the petri plate was cooled down and weighed again (M2). The percent of Non-Volatile content was calculated by determining the weight difference.[30]

$$\% \text{ Non-volatile content} = \frac{M2 - M1}{M} \times 100$$

4. Adhesion

Make the film of formulated nail lacquer of 1 x 25 cm area on the glass slide, cleaned the slide with toluene or xylene, taking one drop and spreading it with a nail polish brush. Place the slide in a horizontal position and allow it to dry at room temperature for 24 hours. After drying, apply the pressure sensitive adhesive cellophane tape over the film so as to cover the entire film. Pull the tape of the film immediately. The material shall be taken to have passed the test if not more than 10% of the film is peeled off.[30]

5. Water Resistance

To determine the resistance of the formulation into water resistance test is performed. The test was carried out by spreading required amount of nail lacquer was spread on a uniform area of

a glass plate and was dried. The sample containing glass plate was weighed and then placed in a beaker filled with distilled water. After 24hour, the plate was dried with the use of filter paper and was weighed again, Water resistance was determined by initial and final weight difference and the results were expressed in weight loss (%).[28]

6. Blush Test

The formulated nail lacquer was poured over the petri dish and allow it to spread into a uniform film. Drain the excess. Dry the petri dish over 24 hours at ambient conditions. Fill a beaker to half its level with tap water. Dip the plate in water in the beaker such that half the coating is in water and the remaining portion above water. Let it stand for 4 hours. Remove the petri dish, dry it with tissue paper. Allow it to further dry at ambient conditions for 4 hours. Check for blush. The material can be taken to have passed if it has no or slight whitishness. The film should not show any blistering or peeling off.[30]

7. Viscosity

The viscosity of nail lacquer can be measured using Brookfield and rotating viscometer. To reduce solvent evaporation, the sample for the Brookfield viscometer should be taken in a closed jar. Prior to the test, the sample should be aged at 25 ^{0}C for at least 8 hours. At 25 ^{0}C, shake vigorously, start timer, insert spindle into the sample to the scored line, with the motor running at 60RPM. Within a minute, the spindle should be in the proper position. After ten minutes, read the instrument once more, then change the speed control to 6 RPM and read the instrument once more after ten more minutes. The dial reading should be multiplied by 60 rpm X 20 or 6 rpm X 200 to convert it to centipoises. The viscosity of nail lacquer should be about 375-500cps at 60 rpm, at 25 ^{0}C.[28,31]

8. Estimation of drug content

1 mg of nail lacquer was dissolved in 50 ml of a pH 7.4 phosphate buffer solution.

After that, the solution was sonicated for 15 minutes. After filtering the resultant solution, 100 ml of phosphate buffer solution with a pH of 7.4 was added. The percentage drug content was then calculated by spectrophotometrically estimating the diluted solution at a wavelength of the particular drug.[32]

9. In vitro drug release study

To conduct the in vitro drug release study of nail lacquer, Franz diffusion cell were utilized. About 2 ml of formulation sample (nail lacquer) was poured over the dialysis membrane that

was fitted over the Franz diffusion cell. The membrane was soaked such that it only made contact with the surface of the release media that was inside the donor cell, which was set over a magnetic stirrer and kept at 37 ^{0}C and stirring speed of 100 rpm. At a predetermined interval, 1 ml aliquot of the dissolving media was removed and replaced with fresh dissolution media. Then, the sample solution containing nail lacquer was analysed spectroscopically at specific wavelength of the drug. Finally, the in vitro release data was fitted to zero order, first order, Higuchi model, and Korsmeyer–Peppas model in order to get the percentage of drug release.[33]

10. Transungual Permeation Study

Human nails were collected and allowed to soak in distilled water for 24 h. Using a microtome, a segment of the nail's lower portion that was roughly 1 mm thick was sliced. This was then maintained between the donor and receptor compartments of a Franz diffusion cell with a receptor cell volume of 10 mL and an effective surface area of 1.23 cm^2 and receptor cell volume 10 ml. About 2 ml of formulation sample (nail lacquer) was poured over the donor compartment of the Franz diffusion cell. Phosphate buffer (pH 7.4) was used as the solvent system to fill the receptor compartment, and the entire assembly was kept at 37 °C with constant stirring at 100 rpm for 24 h. 2 ml of the samples were taken out at the right intervals (0, 30 minutes, 1, 2, 4, and 8 hours) and analysed spectroscopically. Sink conditions were maintained throughout the experiment. The human nail plate cumulative drug penetration per unit area (CDP/A) was plotted against time to obtain in vitro release profile.[34]

11. Determination of Antifungal activity

To evaluate the antifungal performance of herbal nail lacquers against common onychomycosis pathogens (e.g., *Trichophyton rubrum, T. mentagrophytes, Candida albicans*) using standardized in-vitro and ex-vivo methods that report MIC/MFC, time-kill kinetics and activity on nails/biofilms.[35,36]

Test organisms and inocula

Clinical or ATCC strains of dermatophytes and yeasts maintained on appropriate media. Prepare inocula in accordance with CLSI reference microdilution standards: **M27** for yeasts and **M38** for filamentous fungi (dermatophytes), including media (RPMI 1640), inoculum density, incubation time/temperature, and endpoint reading criteria.[36,37]

i. Broth microdilution

- Prepare twofold serial dilutions of the test article (e.g., lacquer extract or redispersed actives).
- Inoculate with standardized fungal suspensions.
- Incubate (24–48 h for yeasts; up to 7 days for dermatophytes) and read MIC as the lowest concentration with significant growth inhibition.
- For MFC, subculture from wells without visible growth onto drug-free agar; the lowest concentration yielding ≤3 colonies indicate fungicidal activity.[35,36]

ii. Agar-based screening (zones of inhibition)

- Apply defined volumes of lacquer extract or active-loaded film disks onto inoculated agar (dermatophyte or yeast-appropriate media).
- Incubate and record zone diameters as a rapid, comparative screen.[37,38]

12. Stability Studies

To evaluate the long-term integrity of herbal nail lacquers, stability tests followed ICH Q1A(R2) guidelines. The optimized formulation should be stored at 25 °C ± 2 °C / 60% RH ± 5**%** for an extended period, complemented by accelerated conditions at 40 °C / 75% RH for a month. (39,40,41) During this time, physical parameters such as drying time, adhesion, non-volatile content, and biological evaluation should remain stable, confirming that the lacquer sustained its intended properties without notable degradation.

Recent Patents on Nail Lacquer Formulations

Table 3: List of recent patents on nail lacquer formulations.

Patent/application number (year of issue/publication)	Original assignee/applicant	Comment	Reference
US11628135B2 (2023)	Coty Inc., New York, USA	Water-based nail treatment with biomimetic oils and plant extracts; eco-friendly and non-toxic formulation	Coty Patent, 2023
US20240180811A1 (2024)	Thomas & Sakhamuru	Water-based, non-toxic nail polish with stabilizers, odour control, and film formers	https://patents.google.com/patent/US11628135B2
US20240197611A1	Coty Inc.,	Nitrosamine-free nail	https://wikipatents.org/20240

(2024)	New York, USA	lacquer; uses clay-alkonium complex for stability and safety	197611._NAIL_LACQUER_WITHOUT_NITROSAMINE_simplified_abstract_(Coty_Inc.)
WO2024184271A1 (2024)	Jbrd Sa, Europe	Nail lacquer composition combining polymers, solvents, pigments; improves gloss, durability, and application performance	Google Patents, 2024
US20150190331A1 (2015)	Pakaly Enterprise Co., Ltd., Taipei, Taiwan	Hypoallergenic gel nail lacquer; excludes HEMA/EMA; uses urethane/polyester acrylate oligomers; UV-curable; good adhesion and gloss	Patent PDF, 2015

CONCLUSION

Onychomycosis is a common fungal infection of the nails that leads to discoloration, brittleness, and thickening. Traditional treatments, whether oral or topical antifungals, often come with limitations such as side effects, poor nail penetration, and frequent relapses. In recent years, herbal nail lacquers have gained attention as safer alternatives. These formulations use plant-based ingredients like tea tree oil, oregano oil, neem extract, Caesalpinia bonducella, and coniferous resins, which offer antifungal, anti-inflammatory, and antioxidant benefits. They work through multiple mechanisms, such as disrupting fungal cell membranes, inhibiting ergosterol synthesis, and inducing reactive oxygen species, which also reduces the risk of resistance.

To improve drug penetration, substances like urea, thioglycolic acid, and salicylic acid are added to soften the tough nail plate. Film-forming agents, including chitosan, nitrocellulose, and ethyl cellulose, help release the drug gradually while forming a protective layer, enhancing both efficacy and patient compliance. Other formulation components such as plasticizers, resins, solvents, and pigments improve flexibility, shine, and overall aesthetic appeal.

The performance of these lacquers is evaluated through parameters like drying time, adhesion, viscosity, water resistance, drug content, in vitro release, antifungal activity, and nail penetration studies using Franz diffusion cells. Stability tests following ICH guidelines

ensure the product remains effective over time. Recent patents reflect a push toward water-based, nitrosamine-free, and eco-friendly lacquers, showing a growing interest in safe, effective, and innovative herbal solutions for treating onychomycosis.

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CONFLICT OF INTEREST

Authors do not have any conflict of interest.

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