



A COMPREHENSIVE REVIEW ON NAIL LACQUER IN TREATMENT OF NAIL DISEASES

Smita Ravindra Mankar*, Vikrant P. Wankhade, Nandkumar Damaranche and Sarang Dalvi

Vidyabharti College of Pharmacy Amravati, (Maharashtra-444602).

***Corresponding Author: Smita Ravindra Mankar**

Vidyabharti College of Pharmacy Amravati, (Maharashtra-444602).

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ABSTRACT

The purpose of written review paper on anti-fungal nail lacquer which is used in treatment of Onychomycosis skin fungal disorder was focus on the disease causes and treatment by nail lacquer, onychomycosis causes by the pathogens include dermatophytes, candida, and non-dermatophytes. Improvement clinical efficacy and also proper the patients compliance. Nail Lacquer preparation by simple mixing non-volatile, gloss, smoothness to flow, drug diffusion studies drug content estimation, Nail lacquer is used on fingernails, toenails of the human beings. Which is protect the nail but, nail plate but most of significantin maximize the beauty, gloss, impart colour. Nail lacquer is mostly applicable for those drug which have poor bioavailability in oral formulation this techniques is used in maximize the topical bioavailability of drug across the nail.

KEYWORD: Nail Disease, Nail Lacquer, Onychomycosis.

INTRODUCTION^[1]

Over the years, the importance of nail permeability to topical therapeutics has been realized, primarily in relation to the treatment of onychomycosis; a fungal infection of fingernails and toenails which affects approximately 19% of the world population and is responsible for approximately 50% of all nail disorders.

Topical therapy is highly desirable because of its non-invasiveness, ability to target drugs to the site of action, minimizing systemic adverse effects and improving patient compliance. Recent advances in ungual delivery technology have led to the introduction of antifungal nail lacquers. Miconazole is a broad spectrum antifungal agent of the broad spectrum antifungal agent class. Its chemical name is (RS)-1-(2-(2, 4-Dichlorobenzyloxy)-2-(2, 4-dichlorophenyl)ethyl) -1H.

It is used in the treatment of superficial and systemic fungal infections caused by Aspergillus, Trichophyton. Interdigitale, Epidermo-phytonflocossum, Trichophytonviolaceum, Mycosporumgypseum, Trichophyton tonsurans and Trichophyton soudanense & Candida species.

The present work investigated the permeability of the antifungal drug, Miconazole through the human nail plate from the nail lacquer formulation with different penetration enhancers. Medicated nail lacquer after application leaves an occlusive film over the nail, which

act as a drug depot from which sustained release of antifungal is provided for entire duration of therapy. Finally the formulations were discussed in respect to their enhancement factors by estimating the zone of inhibition against the dermatophyte, Candida albican.

The success of local topical therapy for onychomycosis depends on the achievement of effective chemical concentrations into/through the human nail plate; therefore, a suitable antifungal drug must be coupled with an appropriate delivery method. The method should maximize the effect of the active principle by aiding its diffusion into the nail bed to levels exceeding the minimum inhibitory concentration (MIC) against local infection by dermatophytes. Thus, a suitable carrier may be needed to enhance drugpenetration throughthe nail barrier.^[2]

1. Nail Disease^[3]

A) Onychomycosis

Onychomycosis is a type of fungal infection affecting nails. It is caused by dermatophytes, yeasts or molds. Our skin, hair and nails are more prone to attack by dermatophyte fungi and responsible for up to 80% fungal infections. Onychomycosis generally affects 10–40% of population. Most likely factors are genetic predisposition towards onychomycosis, diabetes mellitus and damage to the nails or sup-pressed immune system. Aggravating factors are excessive perspiration, poorly fitted footwear and damp feet. Fungal infections cause

thickening, discoloration and splitting of nails leading to irritation and pain. Different fungi infest themselves in different ways causing four peculiar types of onychomycosis

B) Paronychia

This infection causes inflammation of proximal and lateral nail folds. It may be acute or chronic in nature. Acute form is caused by Staphylococcal bacteria which disrupts the cuticle and nail folds causing pain and inflammation. Chronic Paronychia is caused by irritant reaction on exposure to environmental irritants or alkali. The nail fold becomes swollen and provides favorable conditions for proliferation by ubiquitous bacteria which exacerbate the condition.

C. Psoriasis

Psoriasis is a skin disorder with signs of patches of raised, red skin causing irritation and pain. Nail matrix shows signs of pitting and appearance of large transverse furrows, while nail bed shows a characteristic yellow-red nail discoloration similar to drop of blood or oil under the nail plate which gradually lead to thickening of the skin under the nail. The hardness and elasticity of nail plate is lost leading to loosening and crumbling of the nail.

D. Yellow Nail Syndrome

Yellow nail syndrome is characterized by slow-growing, excessively curved and thickened yellow nails which are associated with peripheral lymphoedema and exudative pleural effusions. Abnormalities include nail pits, transverse furrows, crumbling nail plate and roughened nail.

Amorolfine nail lacquer contains the active substance amorolfine (as amorolfine hydrochloride), which belongs to a group of medicines known as antifungal. It kills a wide variety of fungi that can cause nail infections. Amorolfine nail lacquer is used to treat fungal infections of the nails. Amorolfine 5% w/v medicated nail lacquer contains 5.574gms of amorolfine hydrochloride per 100 ml equivalent to 5 gm (5%w/v) of amorolfine base. Its fungicidal and fungicidal efficacy is based on the alteration of fungal cell membrane targeted primarily on ergosterol biosynthesis. The ergosterol content is reduced and at the same time unusual sterically nonpolar sterols accumulate. Amorolfine is a broad spectrum antimicrobial. It is highly active against current or casual agents of onychomycosis.

E. Nail Plate Overgrowth (Onychogryphosis)

It occurs commonly in elderly people due to their inability or neglect for grooming or cutting of nails. It causes nail plate to thicken and attain a curved structure which appears 'claw shaped'. The thickened nails may pinch the skin causing pain. Excessive trauma may cause subungual hemorrhage, especially in the presence of diabetes mellitus or peripheral vascular disease.

Subtype^[4]

There are seven subtype clinical patterns of onychomycosis.

1. DLSO – distal and lateral subungual onychomycosis
2. SO – superficial onychomycosis (white or black)
3. EO – endonyx onychomycosis
4. PSO – proximal subungual onychomycosis
5. MPO – mixed pattern onychomycosis
6. TDO – total dystrophic onychomycosis
7. Secondary onychomycosis-another subtype represents the end stage of the progression of all the above subtypes.

3. Diagnosis of Onychomycosis

a) Electrochemotherapy for Nail Disorders: This therapy is developed as an active method to deliver the drugs across the nail plate which in turn is believed to increase the success rate of topical monotherapy and decrease the duration of treatment of nail disorders. Currently, the electrically mediated techniques for drug delivery across the nail plate are investigated. Recently the Iontophoresis trans-nail delivery method studied. Iontophoresis was found to enhance the transport of drugs across the nail plate significantly. Similar to transdermal Iontophoresis, the predominant mechanisms contributing to enhanced transport of drugs in the case of trans nail Iontophoresis are electrophoresis and electro osmosis.^[5]

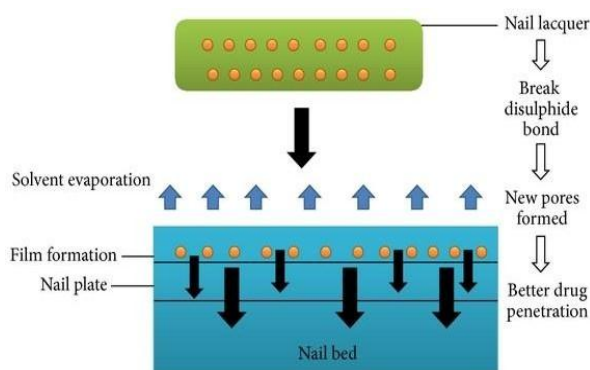
b) Mesosclerotherapy technology: Mesosclerotherapy technology creates a micro-conduit through the skin or nail within a specified depth range. Fully open pathways can be painlessly cut through the stratum corneum of the skin or through the nail. Micro conduits, 300-500 microns in diameter, are produced within seconds and without sensation. These pathways are used to deliver drugs across the skin (in vivo human experiments have shown full anaesthesia occurs within 3 minutes through micro conduits). Such micro conduits also permit access for sub dermal analyte extraction (including blood for glucose testing). They reduce the skin electrical impedance to less than 1000 ohms for bio potential measurements. In nails, micro conduits reduce the painful pressure of subungual hematoma (black toe) and could serve as a prophylactic to prevent such pressure build-up in runner's nails.^[5]

4. Penetration Through Nails

The penetration of drug into nail is quite difficult due to various factors such as the molecular size of the drug, hydrophilicity, pH, solute charge. Consequently researches are currently being undertaken to design novel in vitro methods to assess the ability of compounds to penetrate the nail plate.^[5]

The goal of topical therapy for Onychomycosis is drug penetration into deep nail stratum at amounts above the minimal inhibitory concentration (MIC). Effective penetration still remains challenging as the nail is

composed of approximately 25 layers of tightly bound keratinized cells which in comparison to stratum corneum is 100- fold thicker.^[6]



Mechanism of drug penetration via Nail lacquer

Currently, topical onychomycosis treatments are focused on formulations containing agents such as amorolfine, ciclopirox, tioconazole, efinaconazole, and tavaborole. However, condition improvement is usually achieved in less than 30% of the cases, with complete cure rates below 20%. as chemical strategies and physical methods have been studied to circumvent the physiological barriers and improve treatment efficacy.

Different methods developed so far are^[6]

- A. Chemical means
- B. Mechanical means
- C. Physical means

A. Chemical methods to enhance nail penetration

Chemically, drug permeation into the nail plate can be assisted by breaking the physical and chemical bonds responsible for the stability of nail keratin. This would destabilize the keratin, compromise the integrity of the nail barrier and allow penetration of drug molecules.

Wang and Sun (1998), identified the disulphide, peptide, hydrogen and polar bonds in keratin that could potentially be targeted by chemical enhancers such as.

1) Nail softening agents or Keratolytic enhancers

Keratolytic agents such as (papain, urea, and salicylic acid) enhance the permeability of three imidazole antifungal drugs (Miconazole, Ketoconazole, and Itraconazole) Urea and salicylic acid hydrate and soften nail plates. Urea and salicylic acid also damage the surface of nail plates, resulting in a fractured surface. Effects of the physical enhancers were penetrant specific, but the use of a reducing agent followed by an oxidizing agent (Urea, H₂O₂) dramatically improved human nail penetration while reversing the application order of the physical enhancers was only mildly effective. Both nail physical enhancers are likely to function via disruption of keratin disulphide bonds and the associated formation of pores that provide more 'open' drug transport channels.

B. Mechanical means involves

1) Nail abrasion

Nail abrasion thins the nail plate, decreasing the fungal mass of onychomycosis and exposing the infected nail bed.

2) Nail avulsion

Total nail avulsion and partial nail avulsion involve surgical removal of the entire nail plate or partial removal of the affected nail plate, and under local anesthesia. Keratolytic agents such as urea and salicylic acid soften the nail plate for avulsion. Urea or a combination of Urea and Salicylic acid has been used for nonsurgical avulsion.

C. Physical Method : Involves the use of agents that by delipidization or fluidization of the intracellular lipids in the nail plate can help in drug permeation. Some of the approaches have been used to resolve these barriers to drug delivery include.

1. Iontophoresis: Iontophoresis involves delivery of a compound across a membrane using an electric field (electromotive force). Drug diffusion through the hydrated keratin of a nail may be enhanced by iontophoresis.

2) Electroporation

Electroporation is a method in which, with the application of an electric pulse of about 100–1,000 V/cm creates transient aqueous pores in the lipid bilayers making the solute particles permeable through it.

3) Micro needle enhanced delivery systems

Method using arrays of microscopic needles to open pores in the SC directly to the skin capillaries; also has the advantage of being too short to stimulate the pain fibers, thus facilitating drug permeation.

4) Etching "Etching" results from surface-modifying chemical (e.g. Phosphoric acid) exposure, resulting in formation of profuse micro porosities. Presence of micro porosities improves "interpenetration and bonding of a polymeric delivery system and facilitation of inter diffusion of a therapeutic agent."

5. Factors Affecting Drug Transport Across The Nail

• **Molecular size of drug:** The larger the molecular size, the harder it is for drug to diffuse through the keratin network and lower the drug permeation. Mertin and Lippold demonstrated the decreasing permeability coefficients through human nail plate and through bovine hoof membrane with increasing molecular size of a series of alkyl nicotines 31.^[5]

• **Hydrophilicity / lipophilicity of drug:** Walters et al. studied the permeation of a series of homologous alcohols (C₁–C₁₂), diluted in saline, and through avulsed human nail plates. Increasing the chain length from one carbon to eight carbon atoms resulted in a

decrease in permeability coefficient, after which, increasing chain length (>C12) resulted in increased permeability coefficient. The study by Walters et al. concluded that the nail plate is characterized as a hydrophilic gel membrane.^[5]

- **PH of vehicle and solute charge** The pH of aqueous formulations affect the ionization of weakly acidic/basic drugs, which in turn influences the drug's Hydrophilicity / hydrophobicity, solubility in the drug, formulation, solubility in the nail plate and its interactions with the keratin matrix. It seems that the pH of the formulation has a distinct effect on drug permeation through the nail plate.^[5]

- **Nail plate hydration:** The degree of nail plate hydration is an important factor for denervation of drug penetration. The permeation of ketoconazole through excised human nails under different relative humidity (RH) from 15 to 100% showed a 3-fold improvement in the delivery of the radio labeled drug.^[4]

- **Presence of an intact dorsal layer:** Overlapped cells represent the greatest barrier to the drug penetration across the nail plate. If this layer is partially or totally removed e.g., by debridement or chemical etching with 30-40% phosphoric acid or use of keratinolytic enzymes, then drug permeability increases.^[4]

6. Evaluation of Nail Lacquer^[7]

Nonvolatile content

10 ml of sample was taken in a petri dish and initial weights were recorded. The dish was placed in the oven at 105°C for 1hr, the petri dish was removed, cooled and weighed. The difference in weights was recorded. Average of triplicate readings was noted.

Drying time

A film of sample was applied on a petri dish with the help of a brush. The time to form a dry-to-touch film was noted with the help of stop watch.

Smoothness

to flow The sample was poured from a height of 1.5 inches into a glass plate and spread on a glass plate and made to rise vertically and visually observed for smoothness of film.

Gloss

Sample of nail lacquer was applied over the nail and gloss was visually seen, compared with marketed cosmetic nail lacquer.

Viscosity

Viscosity was determined using Brookfield Viscometer, model LVF at room temperature using spindle No.3 at 20 rpm.

Adhesion

There are no quantitative evaluation tools available to

assess the medicinal nail lacquer at this time. Hence an equipment designed in the Pharmaceuticals Lab has been used to determine the adhesive property of nail lacquer.

Force of Adhesion = Mass x Acceleration due to gravity
= Kilogram. Meter/ second²
= Newton's. Meter/seconds²

Adhesive Strength = Force of Adhesion (N) / Surface area (m²)

MEDICATED NAIL LACQUERS.^[8]

1 Ciclopirox Nail Lacquer 8% for the Treatment of Onychomycosis

Onychomycosis is prevalent in the Canadian population, and risk factors, such as old age and diabetes, are increasing. This condition has traditionally been treated using oral antifungal agents with varying degrees of success. Recently, ciclopirox nail lacquer 8% solution became the first topical agent approved in Canada for onychomycosis. Ciclopirox nail lacquer may be safe and effective for the treatment of onychomycosis, and certain candidates may benefit from therapy. Ciclopirox may be implicated for prophylactic use in order to prevent recurrent infection and may be used in combination with oral agents. Demographic studies suggest that onychomycosis affects between 6.1% and 6.9% of the Canadian population.

2. Amorolfine nail lacquer

- Amorolfine is an antifungal used for fungal infections of the finger and toe nails.
- Amorolfine lacquer is usually applied once or twice a week, after filing and cleaning the nails.
- Amorolfine occasionally causes side-effects including skin irritation such as redness, itching, or a burning sensation.

About amorolfine nail lacquer

Type of medicine Antifungal, Used for Fungal infections of the finger and toe nails, Also called Loceryl®, Curanail®

Fungal infections may be caught from another person, from an animal, from soil, from the floors of showers, or from household objects such as chairs or carpets. The appearance and symptoms of fungal infections vary according to where the infection is. When the nails are infected they become thickened, discoloured and crumble when cut.

3. Curanail 5% w/w Medicated Nail Lacquer

1. Name Of The Medicinal Product Curanail 5%w/v Medicated Nail Lacquer.

2. Qualitative And Quantitative Composition.

Curanail 5% nail lacquer contains 5% w/v amorolfine in the form of hydrochloride.

Amorolfine is chemically

Described as cis-4-[(RS)-3[4-(1,1-Dimethylpropyl)phenyl]-2-methylpropyl]-2,6-

dimethylmorpholine.
Amorolfine hydrochloride HSE 6.40 %w/w.

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CONCLUSION

purpose of the present study was to Nail lacquer in Treatment of Nail Diseases. Fungal nail diseases are the dermatological and allergic disorders. They are harmful to nail but they can be easily prevented by using the proper treatment and use of good medicated nail lacquers. The people may get worried due to change in nail appearance but now days it is very easy to formulate nail lacquers with good effects and less side effects than nail disease.

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