Formulation And Evaluation of Nail Lacquer for Anti-Fungal Treatment

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ABSTRACT: The nail plate serves as a significant barrier, thereby restricting drug permeation through this anatomical layer. Recognizing this as a formidable challenge, the current investigation concentrates on the development of an antifungal topical nail lacquer utilizing Oxiconazole nitrate. The originality of this research can be articulated through the implementation of a synergistic approach employing permeation enhancers, specifically salicylic acid, thioglycolic acid, and urea, aimed at providing effective therapeutic intervention for topical nail infections such as Onychomycosis. Results: The optimized formulation, designated as F13, underwent compatibility assessments followed by evaluations regarding post-formulation parameters (drying time, water resistance, etc.). The clipping of the nail segment was analyzed for in-vitro drug release and antimicrobial efficacy, succeeded by stability assessments of the refined formulation. The optimized F13 formulation exhibited a thickness of (57±0.04µm), folding endurance of (183±0.57 mm), and tensile strength of (2.62±0.02 Kg/cm2), respectively. The Fourier Transform Infrared (FTIR) and X-ray Diffraction (XRD) analyses indicated no significant interaction between the drug and excipients. The permeation enhancer, in the proportion of salicylic acid: thioglycolic acid: urea in hydrogen peroxide (1:1:1) at a concentration of 5% each, demonstrated an in-vitro drug release rate of 96.03% over a 48-hour period, assessed through both cellophane membrane and bovine hooves membrane methodologies. The antifungal activity revealed a zone of inhibitionmeasuring 11±0.03 mm. Conclusion: The present investigation, which endeavors to employ a combinatorial permeation enhancer (salicylic acid: thioglycolic acid: urea in hydrogen peroxide), demonstrated favorable permeability and antifungal efficacy. The F13 formulation exhibited all anticipated properties and was subsequently compared with the commercially available (Lakme) topical nail lacquer. In light of the aforementioned findings, it may be concluded that in-vivo studies could represent a promising avenue for future research.

KEYWORDS: - Antifungal, Permeation Enhancers, Nail lacquer, Topical.

INTRODUCTION

Onychomycosis represents a fungal pathology of the nails instigated by dermatophytes, non dermatophytes, and yeast organisms that affect both the fingernails and toenails, exhibiting a significant propensity for recurrence .[1,2]Half of adult nail abnormalities are caused by onychomycosis, and major risk factors include decreased peripheral blood flow. circulation, diabetes, slow-growing nails[3], a family history of fungal infections, excessive sweating, a moist workplace, wearing artificial nails, wearing shoes and socks that block airflow, going barefoot in public areas like gyms, shower rooms, and swimming pools, as well as those with AIDS[4]and cancer patients.

which results in alterations in color, increased thickness, and detachment from the nail bed. assists in the differentiation or categorization of the compromised nail as mild, moderate, or severe [5]. The therapeutic protocol for nail infections encompasses systemic administration and topical application, which comprises emulsions, ointments [6], and nail lacquers containing antifungal agents or antimicrobial substances. Nail lacquers have been utilized as cosmetic agents for an extended period, serving both aesthetic and protective functions for the nails, and are now acknowledged as a formulation capable of addressing various fungal nail infections, typically applied via a brush; alternative methods of application include spatulas and sponge tips. Transparent and non-glossy medicated nail lacquer tends to be more favorably received by male patients.

Lacquer, upon application, establishes an occlusive and adhesive coating on the nail plate, which functions as a reservoir for the prolonged release of the therapeutic agent. Consequently, the persistence of the nail lacquer film on the nail plate represents the most critical characteristic of the nail lacquer formulation[7]. The factors influencing the diffusion of active compounds through the nails encompass the physicochemical properties of the nail itself as well as the physicochemical characteristics of the active ingredient, including molecular solute size, hydrophilicity/hydrophobicity, and ionization.

Commonly used dermatological products such ointments, creams, gels, lotions, and powders are inappropriate for Transungual management. These formulations cause nonuniform medicine release since they are easily removed by washing or rubbing after application[8]. Traditional topical formulations are proposed to be replaced by new ones. The best formulations are medicated nail lacquers. Medicated nail lacquers are made by mixing cosmetic nail lacquers with rate-controlling polymers. This method is believed to be successful as nail

disease treatment since a film creates a depot of the medicinal substance in the afflicted nail plate.

Topical administration enhances medication absorption at the target region, avoids first-pass metabolism, and reduces drug interactions; additionally, it offers regulated and extended medication release via depot formulation without any systemic effects [9]. When oral medication is not appropriate for treating severe conditions, such as in youngsters, pregnant and lactating women, and patients with hepatic and renal impairment, nail lacquers are utilized. [10]

Paronychia is the term for the inflammation of the tissue folds that encircle the finger and toe nails. When the seal between the proximal nail and the paronychial fold and the nail plate breaks, creating a channel for invasive organisms to enter. A bacterial, fungal, or viral infection of the nail folds that is limited or superficial is called paronychia. The most frequent causes of paronychia are Staphylococcus aureus, Candida albicans, and Herpes simplex virus. This illness manifests as pain, redness, swelling, nail plate thickness, nail discolouration, and separation of the cuticles and nail folds. [9, 10]

MATERIALS AND METHODS:

Materials: The subsequent materials were employed in the present investigation: Amorolfine, ethylcellulose , glycerin , propylene glycol , salicylic acid , urea , hydrogen peroxide , thioglycolic acid , and ethanol.

Methods of Preparation:

Preparation of Reagents: A phosphate buffer with a pH of 7.4 was synthesized by combining 50 ml of a potassium dihydrogen phosphate solution with 0.2 M sodium hydroxide, subsequently diluting the mixture to a final volume of 200 ml.

Preparation of Stock Solution: The standard stock solution with a concentration of 1mg/ml was formulated by solubilizing 100mg of Amorolfine in 100ml of phosphate buffer. Subsequently, an ultraviolet spectrophotometric analysis was conducted on the stock solution across the wavelength range of 250-400 nm, allowing for the determination of the λmax.

Formulation of Nail Lacquer: The formulation of nail lacquer was developed utilizing a straightforward mixing methodology. All formulations of nail lacquer incorporated a drug concentration of 1%, along with ethyl cellulose (5%), glycerin (5%), propylene glycol (5%), salicylic acid, thioglycolic acid, and urea dissolved in hydrogen peroxide, which acted as a non-volatile solvent. A series of formulations were prepared and designated as F1 through F13. The quantity of Amorolfine remained constant across all formulations. In formulations F1, F2, and F3, the concentrations of salicylic acid were 1%, 3%, and 5%, respectively. Formulations F4, F5, and F6 contained 1%, 3%, and 5% of urea within an H2O2 solution. Formulations F7, F8, and F9 included 1%, 3%, and 5% of thioglycolic acid. Formulation F10 comprised salicylic acid and thioglycolic acid in a 1:1 ratio. Formulation F11 contained salicylic acid and urea in an H2O2 ratio of 1:1. Formulation F12 contained thioglycolic acid and urea in a 1:1 ratio, while formulation F13 incorporated all three permeation enhancers in an equal ratio of 1:1:1.[11]

TABLE 1**: FORMULATION DESIGN OF AMOROLFINE NAIL LACQUER**

Ingredients	F0	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13
Amorolfine(g)	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Ethylcellulose(g)	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Glycerine (mL)	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Propylene glycol (mL)	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Salicylic acid (g)	-	1	3	5	-	-	-	-	-	-	3	3	-	3
Urea :H2O2 (mL)	-	-	-	-	1	3	5	-	-	-	-	3	3	3
Thioglycolic acid (mL)	-	-	-	-	-	-	-	1	3	5	3	-	3	3
Ethanol (mL)	10	10	10	10	10	10	10	10	10	10	100	100	100	100

Evaluation Parameters:

Amorolfine Preformulation Studies: Calibration Curve Construction: 10, 11 10 mg of the medication was dissolved in phosphate buffer with a pH of 7.4 and To create a stock solution-

I of 100µg/ml, the volume was increased to 100 ml. To create a stock solution-II of 10 µg/ml solution, 10 ml of the solution was extracted and subsequently diluted to 100 ml using phosphate buffer pH 7.4. To create concentrations of 0, 2, 4, 6, 8, and 10µg/ml, aliquots of 0, 2, 4, 6, 8, and 10 ml were extracted from these and further diluted to 10 ml. A UV-visible spectrophotometer was used to measure the absorbance at 204 nm, and the findings were tabulated.

Amorolfine Solubility Determination: 12 The saturated Amorolfine solution's solubility in various solvents was assessed. (ethanol, methanol, and water). The flasks were then shaken for 48 hours using a mechanical shaker. After filtering, 1 ml of the sample was taken out, diluted with the proper medium, and examined at 204 nm using a UV spectrophotometer.

Compatibility Studies of Drug Excipients: Using an FTIR spectrophotometer and the KBr pellet technique, the infrared (IR) spectra were captured in the range of 400–4000 cm-1 in frequency. To determine if the drug and excipients were compatible, the spectra of Amorolfine and physical combinations of Amorolfine with other excipients were evaluated.

Assessment of Nail Lacquer Loaded with Amorolfine:
Not volatile Content: A 10-milliliter sample was collected. The first weight was noted in a petridish. After one hour at 105 °C in the oven, the petridish was taken out, allowed to cool, and then weighed. The weight discrepancy was noted. After noting the average of the three readings, the outcome was published .

Time Spent Drying: A brush was used to apply a layer of the sample to a petridish. The amount of time needed to create a dry-to-touch film was recorded using a stopwatch.

Flow Smoothness: The sample was transferred into a glass plate from a height of 1.5 inches and created to rise vertically after being spread out on a glass plate.

Gloss: After applying a sample of nail lacquer on the nail, the gloss was observed and compared. Using cosmetic nail polish that is advertised.[13]

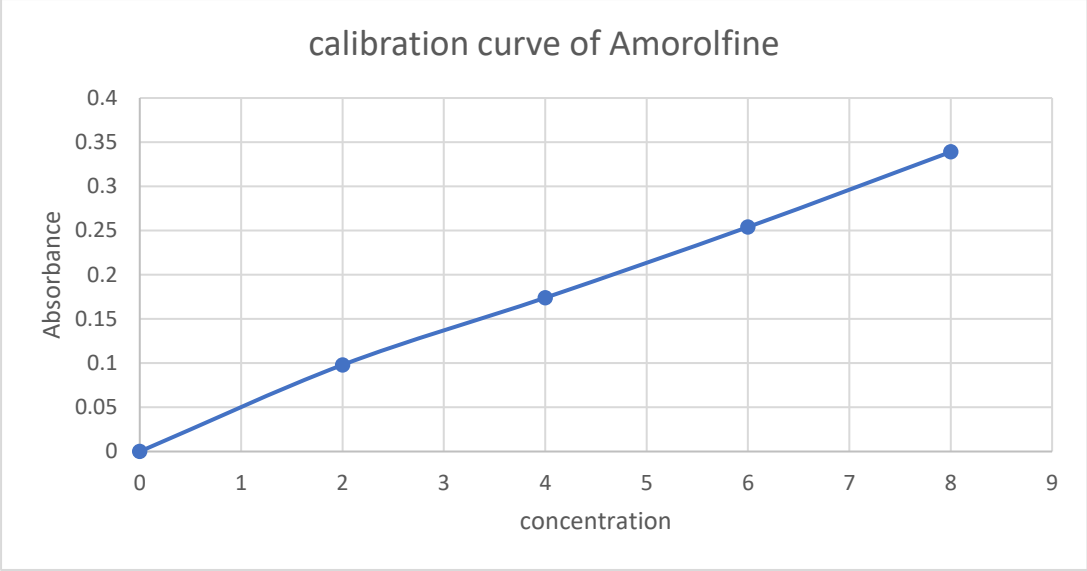
Drug Content Estimation: 50 ml of a pH 7.4 phosphate buffer solution was used to dissolve 100 mg of nail lacquer. Next, The solution underwent a 15-minute ultrasonication. After filtering, 100 milliliters of the resultant solution were prepared using a pH 7.4 phosphate buffer solution. Take 10 ml of the aforementioned solution and add PBS with a pH of 7.4 to make 100 ml. The drug content of the diluted solution was then calculated using spectrophotometry at a wavelength of 223 nm.[14]

In-vitro Drug Release Study: Fifteen newly killed cattle's hooves, devoid of cartilaginous and adherent connective tissue, were bathed in 24 hours of distilled water. A sharp knife was used to remove a membrane that was about 1 mm thick from this hoof. Franz diffusion cells were used to conduct in-vitro penetration tests. The cell was carefully covered by the hoof membrane. The nail membrane's surface received an even application of the medication in the amount of 10 mg. pH 7.4 phosphate buffers were added to the receptor compartment, and for 48 hours, the entire assembly was kept at 37 °C while being constantly stirred. After a predetermined amount of time, the 5 ml aliquot of drug sample was removed and replaced with a new buffer. 48 hours after the spectrophotometer at 204 nm; the absorbance information and, as a result, the drug's percentage release .
A new solvent was used to wash out the remaining medication from the hoof.
The Shimadzu 1800 was used to evaluate the samples.model UV-visible sous times were acquired.[15]

RESULTS AND DISCUSSION:

: STANDARD CURVE DATA FOR AMOROLFINE pH 7.4

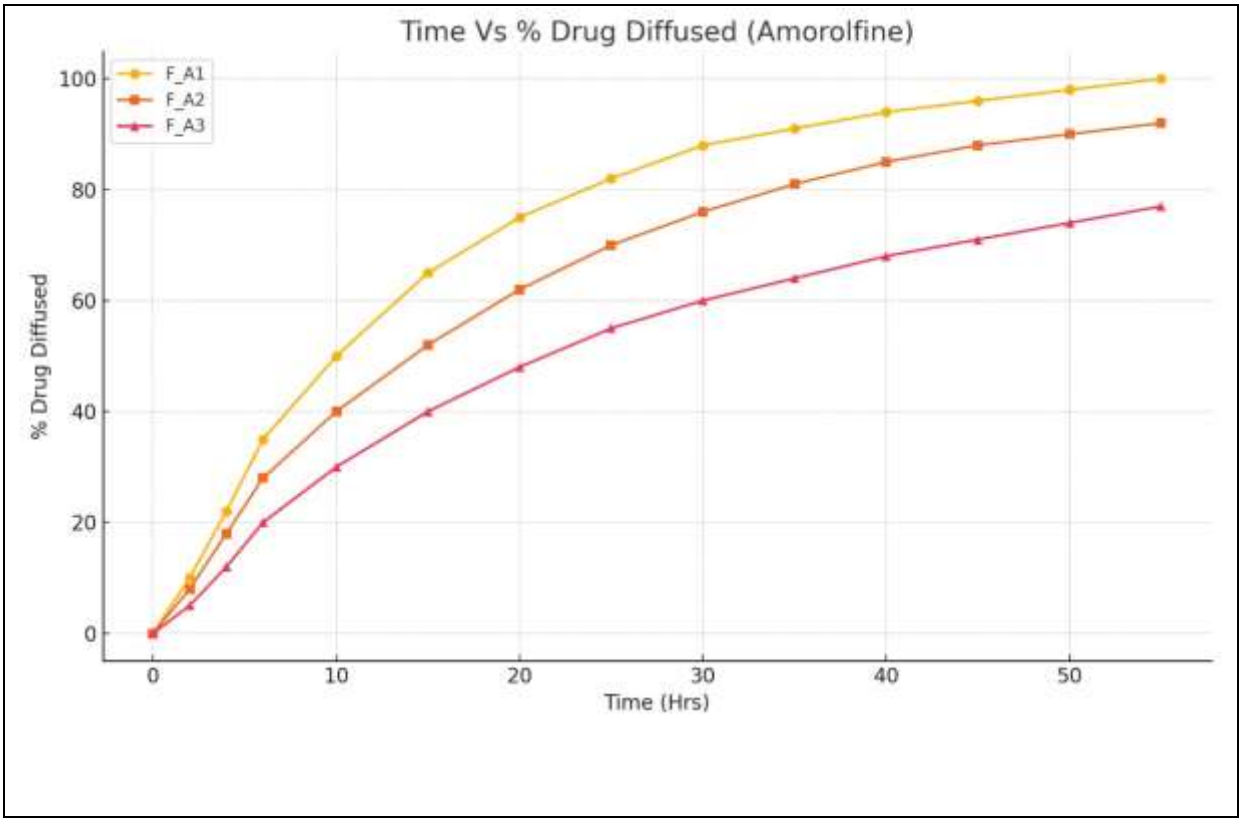
Concentration (µg/ml)	Absorbance
0	**0**
2	**0.098**
4	**0.174**
6	**0.254**
8	**0.339**



Amorolfine's solubility in methanol was determined to be 20 mg/ml; as a result, it was

Amorolfine's solubility in a range of solvent

S.no	Solvents	Solubility (mg/ml)	Inference.
1	Methanol	20.01	Soluble
2	Ethanol	12.15	Sparingly soluble
3	Water	0.008	Very slightly soluble.



Ethyl Cellulose (EC) Concentration Optimization:

Different ethyl cellulose concentrations were used to create nail lacquer films, which were then tested for thickness, folding endurance, and tensile strength. contrasting with the commonly sold formulation. concentration of ethyl cellulose was thought to be an ideal composition to create because it had acceptable folding endurance and tensile strength. nail polish. In order to keep the medication release going, it continued until the 48th hour.

Assessment of Amorolfine-Loaded Nail Polish:

Non-volatile Content: When all of the volatile materials evaporated completely, a small layer of nonvolatile matter was left behind; this ranges from21-22%. The non-volatile content rises in tandem with the polymer concentration.

Drying Time: Research indicates that less than two minutes is the ideal drying time for medicated nail lacquer. The duration of drying for The range of 79-99 seconds was determined for the formulated nail lacquer. The outcome was deemed satisfactory.

Smoothness of Flow: When compared to the standard, the formulas' smoothness of flow was judged to be good, indicating that all the Using a brush, the composition is simple to apply to the nail plate.

Gloss: The nail lacquer's gloss was assessed and contrasted with the benchmark. It was determined to be adequate, and any formulation has the appropriate gloss range.[16]

CONCLUSION:

The medicinal nail lacquer formulation exhibits effective permeability over the nail plate. The assessed mix of enhancers, The different mechanisms by which urea in H2O2, thioglycolic acid, and salicylic acid used in formulation F13 improve Amorolfine penetration and permeation into the nail plate lead to its increased antifungal activity, which is correlated with a drug release rate of 96.03% at 48 hours through both the membrane of the cellophane and the membrane of the cow's hoofs. Unlike traditional antifungal creams or lotions, the applied nail lacquer won't be removed from the nails because the formulated nail lacquer (F13) dries quickly. Consequently, there is no need to apply medications to the nail repeatedly. Because the created nail lacquer is clear, it can be Consequently, the need for frequent nail medication application is eliminated. Given the transparency of the produced nail lacquer, it can be advised for both sexes. Because oral antifungal medications like allylamines and azoles require high dosages, they are linked to numerous adverse effects. These issues can be resolved by creating nail lacquer that contains significantly lower dosages for treatment, which also leads to fewer adverse effects. The potential of ungula medication delivery systems for human application To determine whether ungula drug delivery methods can be used in humans, more clinical and pharmacokinetic research is needed.

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