Research Article

Formulation Development of Antimicrobial Nail Lacquer by Transungual Delivery System for the Treatment of Paronychia

[1]Muthukumar M[*], [2]Prabhu R, [3]Rajeev T, [4]Arunpandiyan J, [5]Thaila R, [6]Jayalakshmi B, [7]Senthilraja M.

[1,3,4,5,6,7] Kasthooribha Gandhi Pharmacy College, Namakkal, Tamilnadu, India.

[2]Madurai Medical College, Madurai, Tamilnadu, India.

***Corresponding author's E-mail:** mmkumar18498@gmail.com

Received: 12-07-2023; **Revised:** 21-09-2023; **Accepted:** 28-09-2023; **Published on:** 15-10-2023.

ABSTRACT

The goal of this present research was to develop an antimicrobial nail lacquer incorporating Quercetin dihydrate to alleviate Paronychia. The focus of this research has been to develop quercetin dihydrate nail lacquer containing various types of polymers and concentrations, as well as various plasticizers, for the treatment of Paronychia. The goal was to optimize which polymers and concentrations gave better release based on in-vitro permeability studies, as well as the impact of plasticizers on film properties like flexibility, gloss, and adhesive property. Drying time, non-volatile content, viscosity, water resistance, drug content, in-vitro drug release study, antimicrobial assay, and other characteristics will be investigated in the manufactured nail lacquer. Formulation F2 was chosen as the best formulation based on all of these factors, including good flow and gloss, optimal drying time and viscosity, adhesiveness, and permeation testing. The best formulation, F2, had a drug penetration rate of 51.93% after 24 hours and a good antimicrobial activity. Based on the findings of the foregoing investigations, the developed medicated nail lacquer formulation appears to be a promising alternative to currently available Paronychia treatments.

Keywords: Nail lacquer, Quercetin dihydrate, Paronychia, Antimicrobials.

INTRODUCTION

Nail illnesses aren't really life-threatening, and they can be excruciatingly painful, cause discomfort in daily activities, and have major physical, psychological, and emotional consequences, lowering people's quality of life.[1] Human nails can be used for more than just protection and decoration; they can also be considered as an alternative pathway for drug delivery, notably in nail illnesses including Onychomycosis, Paronychia, and psoriasis.[2]

Oral treatment is routinely utilized to treat such nail diseases. When a medicine is administered orally or systemically, the potency of the drug is reduced at the site of action. The topical route of administration is utilized to avoid this loss of medication potency.[3] Because of less systemic adverse effects, non-invasiveness, increased patient compliance, localized action (site-specific action), and probably lower treatment costs, topical drug delivery is preferable to oral drug delivery.[4, 5] Ointments, creams, gels, lotions, and powders, which are commonly used in dermatology, are not suited for Transungual administration. Such formulations are easily eliminated after application by washing or rubbing, resulting in non-uniform medication release. New formulations are suggested in place of traditional topical formulations. Medicated nail lacquers are the most suited formulations. The addition of rate-controlling polymers to cosmetic nail lacquers creates medicated nail lacquers. Because a film generates a depot of the drug substance in the affected nail plate, this technique is thought to be effective as nail disease therapy.[6] This allows for fewer applications while still achieving effective therapy due to the active substance's high bioavailability. The active ingredient is stored in a film on the nail plate surface, which allows for optimal and continuous drug diffusion. Continuous diffusion of the active ingredient results in therapeutic levels in the nail tissues, which are required for efficient nail disease treatment.[7]

Pharmaceutically, these Nail lacquers formulations are known as a Transungual drug delivery system since they contain medications to treat topical disorders. "Trans" means "through," and "unguis" means "nails" in the phrase Transungual.[5] Transungual drug delivery system has been defined as a mechanism for delivering a drug into the keratinized nail plate in order to achieve targeted drug delivery for the therapy of nail illnesses. Because of its greater adherence and localized action, which produces little systemic side effects, the Transungual drug delivery technique is regarded to be extremely successful in managing nail disorders.[8]

The inflammation of the folds of tissue surrounding the finger and toe nails is known as Paronychia. Paronychial infections arise when the seal between the proximal nail fold as well as the nail plate is broken, allowing invading organisms to enter through a portal. Paronychia is a local or superficial bacterial, fungal, or viral infection of the nail folds. Staphylococcus aureus, Candida albicans, and Herpes simplex virus are the most common organisms that cause Paronychia. Pain, redness, swelling, thickness of the nail plate, discoloration of the nail, and separation of the nail folds and cuticles are all symptoms of this illness.[9, 10]

In the making of nail lacquer, Quercetin Dihydrate is incorporated. Quercetin is a bioflavonoid that is rich in

polyphenols (Flavonol). Quercetin is a multifunctional chemical with antioxidant, anti-inflammatory, analgesic, antibacterial, antifungal, and antiviral activities. Thus from above -listed pharmacological properties of the Quercetin dihydrate and taken into account the treatment of Paronychia.[11]

In this study, N-acetylcysteine is used as a penetration enhancer in the formulation of nail lacquer. The inclusion of N-acetyl cysteine in this formulation primarily aids in the achievement of the following three goals.[12, 13]

a) It aids in improving medication penetration from the nail plate to the nail bed.

b) It has analgesic properties.

b) N-acetylcysteine has anti-inflammatory properties.

Quercetin contains anti-inflammatory, analgesic, and anti-microbial properties, which make it useful in medicine. N-acetyl cysteine, which is used in the manufacture of Quercetin nail lacquer, has both penetrating and anti-inflammatory and analgesic qualities. Because N-acetyl cysteine will have the same benefits as Quercetin, including it in the formulation creates a synergistic effect and a more effective therapeutic impact.

Figure 1: Overview of the research conducted.

MATERIALS AND METHODS

Materials

Quercetin Dihydrate was procured from Central Drug House (PVT) Ltd, New Delhi. Eudragit RL100 and Ethyl cellulose obtained as gift sample from Apex Laboratories PVT. Ltd, Chennai. N-acetyl cysteine, Salicylic acid and castor oil was purchased from Sisco research laboratories, Chennai. PEG 400 and Ethanol was purchased from universal scientific Appliances, Madurai.

Methodology

Method of preparation

Quercetin Dihydrate nail lacquer was prepared by simple mixing method by using magnetic stirrer. The formulation trials were done as per formula [F1-F12] given in table 1. Quercetin Dihydrate was dissolved in required amount of ethanol using a magnetic stirrer at a constant speed. The polymer was dissolved in ethanol. The dissolved drug was added into the polymeric solution. Finally, plasticizer, permeation enhancer, keratolytic agent were added in the desired amount and mixed properly using magnetic stirrer. The prepared nail lacquer was transferred to a narrow mouthed, plastic screw capped glass bottle.

Table 1: Formulation of Nail lacquer [F1-F12]

Ingredients	Formulation code											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Quercetin Dihydrate % w/v	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Eudragit RL 100 %w/v	5	10	15	5	10	15	-	-	-	-	-	-
Ethyl cellulose %w/v	-	-	-	-	-	-	5	10	15	5	10	15
N-Acetylcysteine %w/v	1	1	1	1	1	1	1	1	1	1	1	1
Salicylic acid %w/v	1	1	1	1	1	1	1	1	1	1	1	1
Castor oil %v/v	10	10	10	-	-	-	10	10	10	-	-	-
PEG 400 %v/v	-	-	-	10	10	10	-	-	-	10	10	10
Ethanol [upto 50ml]	50	50	50	50	50	50	50	50	50	50	50	50

Formulation Development

Nail lacquer formulation was developed by taking into account various polymers [Eudragit RL100 & Ethyl cellulose] and different concentration [5-15%] along with various plasticizers [Castor oil & PEG 400]. Optimization of formulation was done by preparing twelve different formulations.

Initial trials were taken with Eudragit RL 100 polymer. As seen from table 1, formulation F1-F3 were prepared containing 5-15% of Eudragit RL 100 with Castor oil as a plasticizer. Formulation F4-F6 were prepared containing 5-15% of Eudragit RL 100 with PEG 400 as a plasticizer. Further trials focused on another polymer [Ethyl cellulose: 5-15%] along with two different plasticizer [Castor oil in F7-F9 and PEG 400 in F10-F12].

The aim was to optimize which polymer and its concentration is suitable for the Quercetin Dihydrate nail lacquer based on the drug permeability studies and also optimize the effect of plasticizer on film properties such as gloss and adhesive property.

Characterization of nail lacquer[14, 15, 16, 17]

Evaluation of the developed nail lacquer was carried out as per Bureau of Indian Standards, IS 9245:1994

1. Drying time:

The prepared Nail lacquer was uniformly spreaded on a petri dish with the help of a brush. The time taken to form a dry to touch film was noted by using stopwatch. The film was considered sufficiently dried when no amount of sample was adhered to finger on touching (non stickiness).

2. Smoothness to flow:

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

3. Glossiness:

The glossiness of the prepared formulation was determined by visual inspection.

4. Nonvolatile content:

First taken initial weight of petri dish (M_1) and then Place 1gm (M) of each sample was taken into Petri dishes and spread evenly. Then weight of each Petri dish with sample was recorded. The Petri dish was kept in the hot air oven for 1 hr at 105 ± 2 ◦C. After 1 hour the Petri dish was cooled down and weighed again (M_2). The percent non-volatile content was calculated by determining the weight difference.

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

5. Water resistance test:

To determine the resistance of the formulation into water the 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 was weighed and then placed in a beaker filled with distilled water. After 24 h, 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 (%).

6. Determination of Viscosity:

The viscosity of the formulated nail lacquer was calculated by using Brookfield Viscometer (model LVF), in room temperature by using the spindle no.63 at 20 rpm.

7. In-vitro Film adhesion test:

With the help of lacquer brush, a uniform film was formed on a glass plate and dried for 24 h at room temperature. The film was divided into equal areas of 1 mm by cutting with scalpel (0.37 mm blade thickness) both in parallel and perpendicular direction. Then, pressure-sensitive adhesive cellophane tape was placed on the film and finger was used to smoothen the firm, leaving aside a free piece of tape (unadhered). After few minutes, at 60̊ C angle, film of NL was pulled manually by grasping the free end of the unadhered tape. Total number of squares of the film that adhered on the tape was determined and Percentage peel off was determined by the below formula.

$$\% \text{ peel off} = \frac{\text{Initial squares of film} - \text{Final squares of film}}{\text{Iniial squares of film}} \times 100$$

8. Estimation of % drug content:

Nail lacquer equivalent to 1mg was dissolved in 50 ml phosphate buffer solution of pH 7.4. Then the solution was sonicated for 15 mints. The resulting solution was filtered, made up to 100 ml with phosphate buffer solution of pH 7.4. Then the diluted solution was estimated spectrophotometrically at a wavelength of 367 nm and determined the % drug content.

9. In vitro transungual permeation study:

Preparation of Hooves:

Porcine hooves were used as a membrane for *in vitro* transungual permeation studies because human nails are hard to obtain in large quantities. Porcine hooves thickness and overall resemblance to human nails structure were the reasons for its utilization for *in vitro* studies. Hooves were washed, cleaned and was hydrated in pH 7.4 phosphate buffer solution (PBS) for 24 h. A blade was used to remove the soft tissue of the hooves. They were then divided into thin slices and stored for further use. Thickness and diameter of porcine hooves were 0.8 mm ± 0.5 and 25 mm ± 0.8 respectively as determined utilizing micrometer.

Transungual permeation study

Franz diffusion cell was used to carry out *in vitro* experiment. Hoof was placed between receptor and donor compartment of Franz diffusion cell (16 mL volume of receptor). Then the test vehicle (Nail lacquer) equivalent

1mg was applied evenly on the surface of the nail membrane. In order to simulate nail plate conditions, mixture of pH 7.4 phosphate buffer was filled in receptor compartment. The Franz diffusion cell was placed on the Franz diffusion assembly. Assembly was continuously stirred for 24 h at 37 ◦C. 10 mL of sample was withdrawn at intervals of time i.e. at 30min, 1,3, 5, 7, 10, 13, 16, 20 and 24 hrs which was replaced with fresh medium. Samples were analyzed using a UV spectrophotometer at 367 nm.

Selection of best formulation and evaluation

The selection of best formulation among twelve prepared formulations [F1-F12] depends upon their comparison of their Physical characteristics and in-vitro drug permeation study.

1. Comparing Physical Characterization of best formulation with Market product:

The best formulation was compared with marketed formulation by comparing the following physical characteristics such as Drying time, Smoothness to Flow, Glossiness, Nonvolatile content, Water resistance test, Blush test, Viscosity.

2. Microbiological study of best formulation:

a) In vitro antibacterial study:

An agar-well diffusion method was used for determination of antibacterial activity of prepared nail lacquer. The samples were dissolved in PBS, pH 7.4. The cultured bacteria (*Staphylococcus aureus*) were suspended in sterile water and diluted to 10 colony found per unit (CFU)/ml. The suspension (100 µl) was spread onto the surface of nutrient agar medium. Wells (4.6 mm in diameter) were cut with a sterile borer and formulations were added into them. PBS solution was used as negative control. Control sample gentamicin against bacteria were dissolved in PBS buffer pH 7.4 and serially diluted to get concentration of 2-100 µg/ml. Incubation of the inoculated plates was done at 37 °C for 24 h. The diameter of inhibition zone (DIZ) was evaluated and thereby antibacterial activity also.

b) *In vitro antifungal study*:

The antifungal activity of prepared nail lacquer was done by agar-well diffusion method, in which the *Candida albicans* was inoculated with molten potato dextrose agar at 45 °C and allowed to set in a petri dish. Wells (4.6 mm in diameter) were cut in a similar way as for the antibacterial activity and formulations were added into them. PBS was used to prepare the negative control. Control sample fluconazole against fungi) were dissolved in PBS buffer pH 7.4 and serially diluted to get concentration of 2-100 ug/ml. The plates were incubated at 28 °C for 3 days. The diameter of inhibition zone was evaluated.

3. *Ex-vivo* release kinetics:

Determination of the release pattern of the prepared nail lacquer formulation, the data of ex-vivo release was considered & it is treated by several mathematical models which are zero order, first order, higuchi & korsmeyer-peppas model. In which the R (correlation coefficient), n (diffusion exponent) and K (release constant) values getting from curve fitting of release data were determined a model which is suitable for the nail formulation.

❖ **Zero order release kinetics:**

To study the zero order release kinetics the release data was fitted into the following equation;

$$dQ / dt = Ko$$

Where 'Q' is the amount of drug release, 'Ko' is the zero order release rate constant and't' is the release time. The graph is plotted percentage cumulative drug release (%CDR) verses time.

❖ **First order release kinetics:**

To study the first order release kinetics the release rate data are fitted into the following equation;

$$dQ / dt = K_1 Q$$

Where, 'Q' is the fraction of drug release, 'K_1' is the first order release rate constant and 't' is the release time. The graph is plotted log %CDR remaining verses time.

❖ **Higuchi Release Model**

To study the Higuchi release model the release rate data are fitted into the following equation.

$$Q = K_H t^{½}$$

Where, 'Q' is the fraction of drug release, 'K_H' is the release rate constant and 't' is the release time. The graph plotted % CDR verses square root of time.

❖ **Kosmeyers and Peppas Kinetics:**

To study Kosmeyers and Peppas release kinetics the release rate data are fitted into following equation:

$$Mt / M\infty = K_{KP} t^n$$

Where, Mt/M∞ is the 'fraction of drug release, 'K_{KP}' is the release rate constant and 't' is the release time and 'n' is the diffusion exponent related to mechanism of drug release. The graph is plotted log %CDR verses time.

RESULTS AND DISCUSSIONS

The prepared nail lacquer were subjected to preliminary tests included drying time, smoothness to flow and gloss. Also prepared Nail lacquer will be evaluated for various parameters like Drying time, Non volatile content, Viscosity, Water resistance, Drug content, In-vitro drug release study, Antimicrobial assay etc.

Drying time

The ideal drying time, according to Bureau of Indian Standards IS 9245: 1994, was six minutes. For formulas F1-F12, the drying time was determined to range between 57 and 95 seconds. It was revealed that as the polymer concentration increases the drying time increases respectively shown in table 2.

Smoothness to flow

Formulations F1-F6 were found to have good flow properties due to the use of Eudragit RL 100 as a polymer, which creates optimal viscous nail lacquer, whereas formulations F7-F12 generate high viscous nail lacquer due to the use of Ethyl cellulose as a polymer.. Viscosity is fair by using eudragit RL 100 as polymer than ethyl cellulose. The results of flow property are presented in table 2.

Glossiness

Due to the use of castor oil as a plasticizer and eudragit RL 100 as a polymer, formulations F1-F3 have good glossiness, whereas formulations F4-F6 possess satisfactory glossiness due to the use of PEG 400 as a plasticizer. Formulations F7-F12, on the other hand, have a fair glossiness and will generate a dull film due to its use ethyl cellulose like a polymer. The glossiness results are shown in table 2.

Non-volatile content

In order to have adequate coverage on nail plate, non-volatile content should be 20% or more. Non-volatile content depends upon the concentration of polymers used and was found to be directly proportional to the concentration of polymer. The non-volatile content of different formulation F1-F12 was calculated and results are shown in table 2.

Table 2: Drying time, Smoothness to flow, Gloss and % Non-volatile content of formulations [F1-F12]

Formulations	PARAMETERS			
	Drying Time [Seconds]	Smoothness To flow	Gloss	% Non Volatile Content
F1	57	Good	Good	25
F2	63	Good	Good	35
F3	79	Good	Good	48
F4	66	Good	Satisfactory	23
F5	68	Good	Satisfactory	40
F6	85	Good	Satisfactory	45
F7	69	Fair	Fair	26
F8	65	Fair	Fair	33
F9	80	Fair	Fair	53
F10	77	Fair	Fair	24
F11	89	Fair	Fair	37
F12	95	Fair	Fair	51

Water resistance test

As per Bureau of Indian Standards IS 9245: 1994, % weight loss was less than 10%. From the water resistant test, it is evident that as the water resistant capacity of the formulations was increased with increase in concentration of polymers. The results are summarized in table 3.

Viscosity

The viscosity of all the formulations ranged from 133- 270 cps. Viscosity in the range of 140-160 cps resulted in good adherence and glossy formulations. Viscosity outside this range produces clouding and decreasing gloss which will not be cosmetically acceptable. The viscosities of all developed formulations are summarized in table 3.

In vitro film adhesion

The peel off percentage of the film should be less than 10%, according to Bureau of Indian Standards IS 9245: 1994. In comparison to all other formulations [F4-F12], the formulations with Eudragit RL 100 [F1-F3] created with castor oil as the plasticizer had the best adhesiveness of the film on the nail. Despite the fact that eudragit RL 100 is utilised as a polymer for F4-F6 with PEG 400 as a plasticizer, it has no adhesive properties. Similarly to F4-F6, formulations containing ethyl cellulose [F10-F12] as a polymer and PEG 400 as a plasticizer generate poor adhesiveness. However, formulations containing ethyl cellulose like a polymer and castor oil like a plasticizer [F7-F9] provide fair but not the best adhesiveness. The results revealed that, the formulations containing castor oil as a plasticizer have good adhesiveness, compared to that of PEG 400. Also Eudragit RL 100 containing formulations produce better results. The results are shown in table 3.

Percentage drug content

Percentage drug contents for the entire developed nail lacquers were obtained to be satisfy and in between 96.07-99.39% which is shown in table 3**.** Largest % of drug contents was obtained to be 99.39 % (F3) and the smallest % of drug content was 96.07% (F1)

***In-vitro* Transungual permeation**

The *in-vitro* Transungual permeation studies of all the formulations were carried out using procine hooves in PBS pH 7.4 for 24hrs. The formulations F1-F6 consist of Eudragit RL 100 in varying Concentrations. It was found that increase in concentration of Eudragit RL 100 consequently increases

the % drug permeation. Conversely, the release quercetin dihydrate decreased when concentration of ethyl cellulose in nail lacquer was increased. But the ethyl cellulose containing formulations [F7-F12] was found to be highly viscous and sticky with lack of good gloss and smooth flow. So ethyl cellulose was determined to be not applicable for quercetin dihydrate nail lacquer formulations. The results are shown in figure 2 & 3.

Table 3: Water resistance, Viscosity, Film adhesion, % Drug content and % Drug permeation of formulations [F1-F12]

Formulations	Parameters				
	Water resistance test [% Weight loss]	Viscosity [Cps]	Film adhesion [% peel off]	% Drug content	% Drug permeation [At 24hrs]
F1	12	57	5	96.07	43.57
F2	7	63	0	98.17	51.93
F3	4	79	0	99.39	76.40
F4	10	66	50	98.19	45.37
F5	8	68	60	98.94	54.09
F6	3	85	60	99.17	82.03
F7	13	69	25	99.29	59.67
F8	10	65	15	99.01	47.72
F9	4	80	20	99.07	35.35
F10	12	77	70	99.25	62.03
F11	8	89	60	99.03	48.25
F12	5	95	70	99.19	36.14

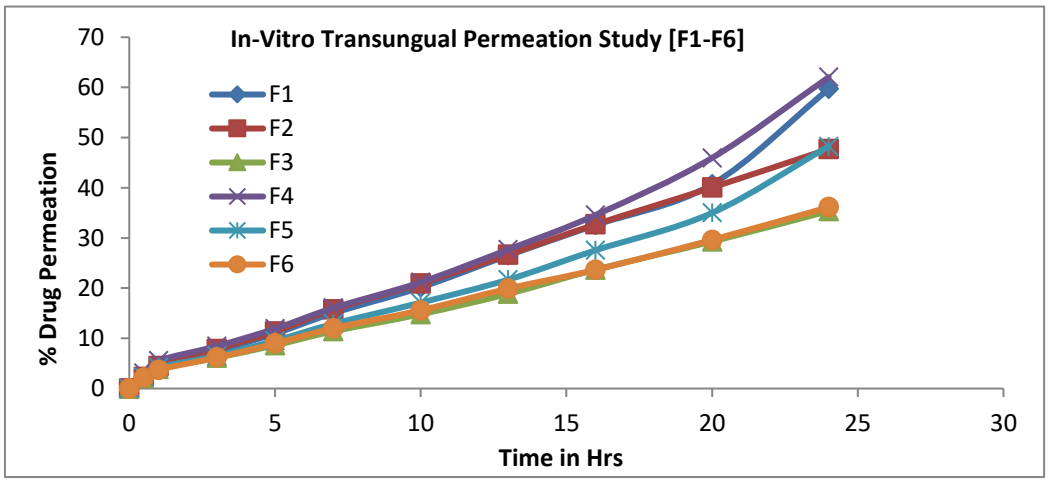

Figure 2: In-vitro Transungual Permeation Study [F1-F6]

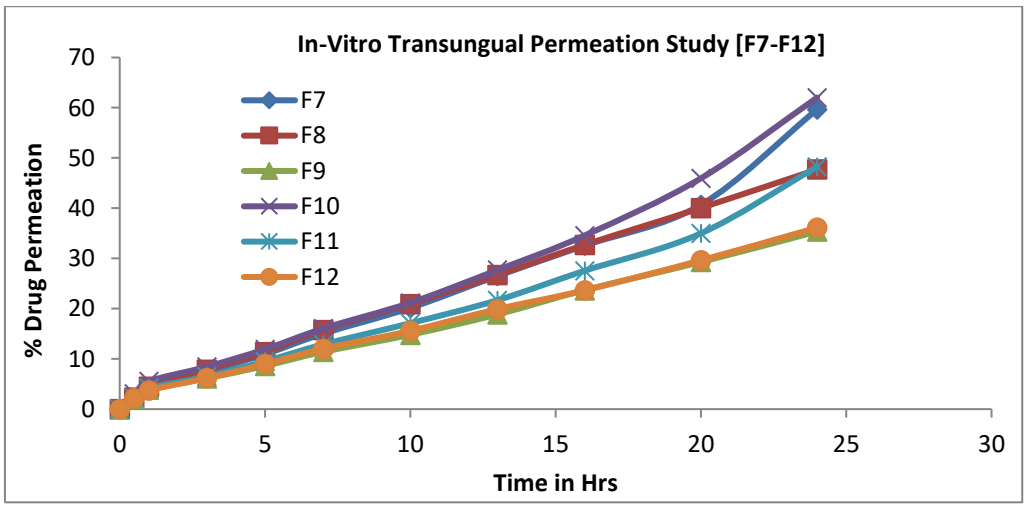

Figure 3: In-vitro Transungual Permeation Study [F7-F12]

Selection of best formulation and evaluation

Among twelve formulations, the best formulation was selected on the basis of Good gloss and flow, Optimum drying time and viscosity, Good adhesiveness of film and sustained drug release.

The formulations using ethyl cellulose as a polymer [F7-F12] give poor results in terms of glossiness, drying time, viscosity, and adhesiveness, based on the preceding data and results. As a result, ethyl cellulose was ruled out for quercetin dihydrate nail lacquer formulations. Due to the use of two distinct plasticizers, castor oil and PEG 400, the formulations [F1-F6] containing Eudragit RL 100 as a polymer give variable results. When compared to F4-F6, the formulations [F1-F3] employing castor oil as a plasticizer offer the greatest results due to their good glossiness, adhesiveness, and flow property, as well as their optimum drying time and viscosity. As a result, the formulations with Eudragit RL 100 as a polymer and castor oil as a plasticizer have been determined to be the best.

According to drug permeation studies, F2 is the best of the three formulations [F1-F3] since it provides the best drug release for 24 hours. Due to the low and high concentrations of Eudragit RL 100, F1 has a delayed release while F3 has an early release. The formulation F2, which contains 10% Eudragit RL 100 and 10% Castor oil, was shown to be the most effective in terms of all nail lacquer criteria.

Evaluation of best formulation

1. Comparing Physical Characters of best formulation with marketed product:

Physical characters of best formulation [F2] compared with marketed product [Amrolmac]. Best formulation showed optimum drying time, good viscosity, good adhesiveness, good gloss and flow property (similar to marketed preparation). The results are summarized in table 4.

Table 4: Comparison of Best formulation [F2] with Marketed product

PARAMETERS	RESULTS	
	Best Formulation [F2]	Marketed product [AMROLMAC]
Drying time	63 seconds	60 seconds
Glossiness	Good	Good
Smoothness to flow	Good	Good
Viscosity	155 Cps	149 Cps
Adhesiveness	Good	Good

2. Microbiological study of best formulation:

In vitro antibacterial study

The zone of inhibition for the best formulation was compared with the zone of inhibition of the gentamicin (positive control). The zone of inhibition for gentamicin (***S)*** was found to be 25 mm and for best formulation (***T)*** 23.5 mm, indicating that the best formulation **[F2]** was sensitive to the microorganism *s. aureus.*

In vitro antifungal study

The zone of inhibition for the best formulation was compared with the zone of inhibition of the fluconazole (positive control). The zone of inhibition for fluconazole (***S)*** was found to be 23 mm and for best formulation (***T)*** 22 mm, indicating that the best formulation **[F2]** was sensitive to the microorganism *c. albicans.*

The Zone of inhibition of for different organisms is shown in figure 4 & 5.

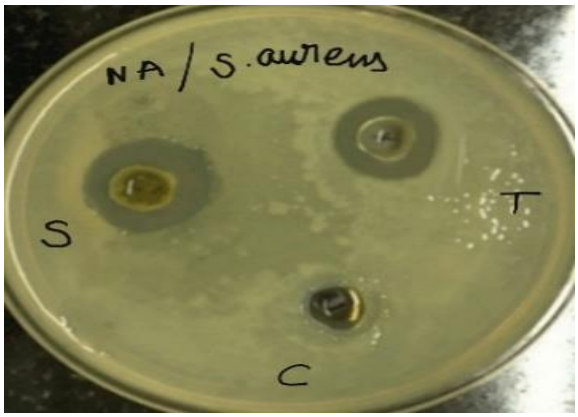

Figure 4: Antibacterial activity of best formulation F2

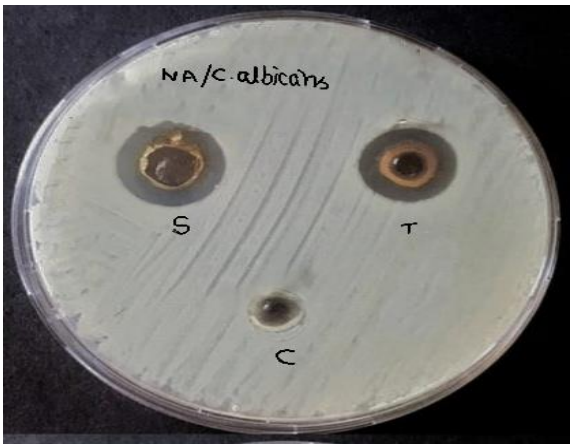

Figure 5: Antifungal activity of best formulation F2

3. Ex-vivo release kinetics of best formulation:

The *in-vitro* release profile of the drug from formulation F2 could be expressed by zero order equation, as the plots shows high linearity **(R^2 = 0.9909)** in comparison to first order **(R^2 = 0.9668)** and Higuchi **(R^2 = 0.9176)**. To confirm release mechanism the data were fitted into Korsmeyer-Peppas model. The diffusion exponent value (n) of best formulation F2 was found to be 0.617. Hence it shows the optimized formulation followed non-fickian diffusion release mechanism. The plots are shown in figure 6.

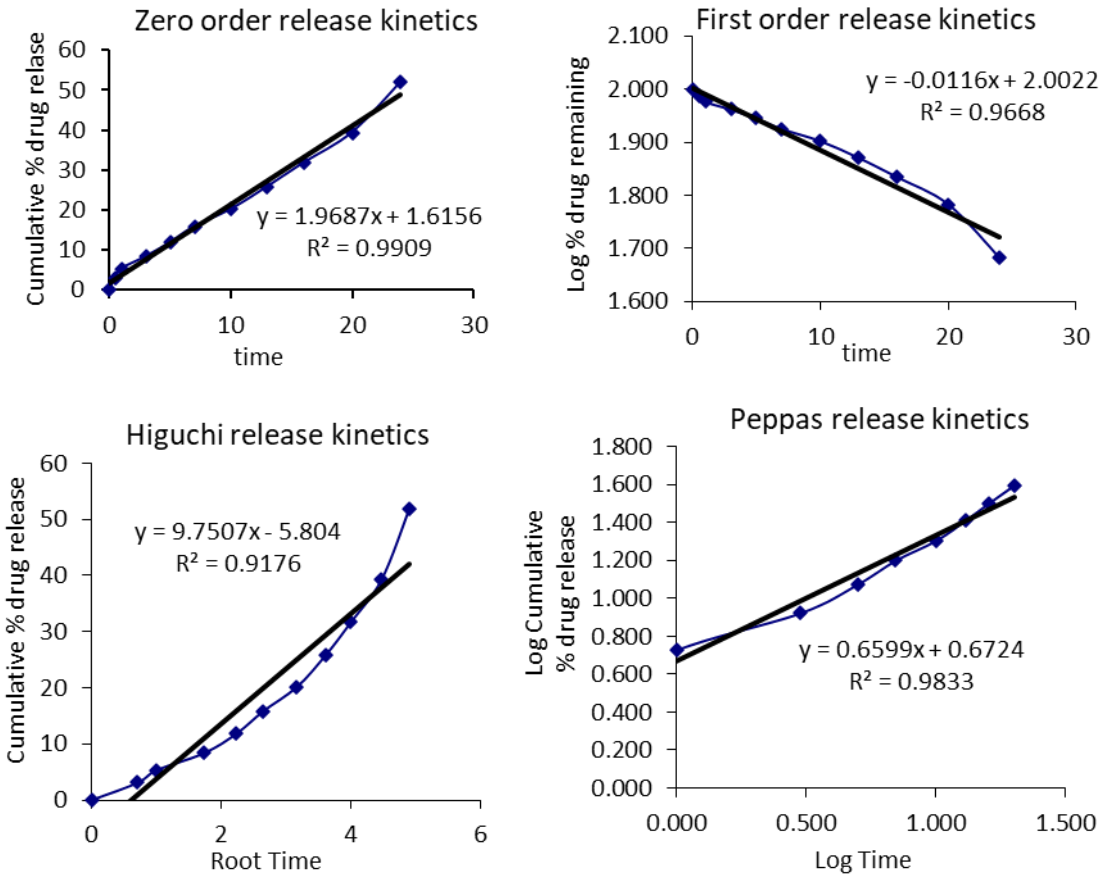

Figure 6: Ex-vivo release kinetic study of best formulation F2

CONCLUSION

The goal of this study was to create a Quercetin dihydrate nail lacquer formulation that included N-acetyl cysteine as a permeation enhancer. The inclusion of N-acetyl cysteine in the formulation of Quercetin nail lacquer not only has penetrating properties but also has anti-inflammatory, analgesic properties. Because N-acetyl cysteine will have the same benefits as Quercetin, including it in the formulation creates an synergistic effect and a more effective therapeutic impact. With the addition of rate-modifying polymers such as Eudragit RL100 and Ethyl cellulose, it was possible to achieve sustained and full drug release for up to 48 hours, making it appropriate for thrice-weekly use. F2 was the best of the twelve formulations, with a drying time of 63 seconds and good glossiness, flowability, and adhesivness. The best formulation F2 gave 51.93% of drug permeation at 24 hrs. The best formulation F2 was subjected for in-vitro antimicrobial study. Microbial study results proved that the formulations are sensitive to the microorganism *Staphylococcus aureus and Candida albicans*. From the above studies, it can be concluded that, the developed medicated nail lacquer formulation can serve as a promising alternative to the available formulations to treat paronychia. Apart from treating the nail infections, the medicated nail lacquers can be also used for beautification of nails with ease of application. This improves patient compliance and acceptability.

REFERENCES

1. Jeremiah M Christi, Chintan Aundhia, Avinash Seth, Nirmal Shah, Dip Kondhia, Snehal Patel. Review on Transungual Drug Delivery System. Indo American journal of pharmaceutical research. 2017 Sep 14; 7(8): 686-706.
2. Mohd Azharuddin, Suresh Bhat H, A.R. Shabaraya, N.G. Prasad Zilu. Preparation and in-vitro evaluation of antifungal nail lacquer. International journal of universal pharmacy and biosciences. 2013 July 10; 2(4): 78-85.
3. Kalvatala Sudhakar. Topical drug delivery of antimicrobial agent using modern technique to treat various nail infection. *Researchgate.* 2021; 51(1): 708-721.
4. Akanksha Goja, Ganesh Kumar Bhatt**,** Nail Lacquer As A Transungual Drug Delivery System. Journal of emerging technology and innovative research. 2019 Feb; 6(2): 177-186.
5. Ashutosh Badola, Satish, Shweta Baluni. A Review: Transungual Drug Delivery A New And Novel System. Asian journal of pharmaceutical science and technology. 2015; 5(4): 227-233.
6. Indre Sveikauskaite, Vitalis Briedis.Effect of Film-Forming Polymers on Release of Naftifine Hydrochloride from Nail Lacquers. International journal of polymer science. 2017 February 16.
7. Alisa elezovic , Amar elezovic, Jasmina hadeiabdic. The influence of plasticizer in nail lacquer formulations of fluconazole permeability through the bovine hoof membrane. Acta poloniae pharmaceutica. 2019 November 4; 77(1): 43-56.

8. Ganesh Kumar,Bharti Lohani ,Preeti Khotiyal. Formuation and evaluation of medicated nail lacquer of butenafine HCL for effective treatment of paronychia. Journal of emerging technology and innovative research. 2018 July; 5(7): 319-343.

9. Pamela G, Rockwell, D.O. Acute and chronic Paronychia. *American family physician. 2001* March 15; 63(6): 1113-1116.

10. Brook I. Paronychia: a mixed infection. Microbiology and management. Journal of hand surgery [British]. 1993; 18 (3): 358-359.

11. Ch. Supriya, Dr. Ch. Sivareddy, Dr. M. Basaveswarao, E. Harshita and P. Yashwanthi. Anti-bacterial, Anti-fungal and Analgesic activity papain conjugated quercetin. European journal of pharmaceutical science. 2017 March 6; 4(4): 280-285.

12. Oliveira Fonseca Goulart et al. N-Acetylcysteine (NAC): Impacts on Human Health. Mdpi. Antioxidants 2021 June 16; 10(6): 967.

13. Ferdinando nicoletti et al. N-Acetylcysteine, a drug that enhances the endogenous activation of group II metabotropic glutamate receptors, inhibits nocieptive transmission in humans. Molecular pain (2015) 11:14.

14. Kanchan Yadav , Dr. Jai Narayan Mishra , Mr. D.K Vishwakarma. Formulation and Development of Antifungal Nail Lacquer Containing Miconazole Nitrate Use in Treatment of Onychomycosis. International journal of scientific and research publications. 2019 April; 9(4): 736-752.

15. Mohd Azharuddin, Suresh Bhat H, A.R. Shabaraya, N.G. Prasad Zilu. Preparation and invitro evaluation antifungal nail lacquer. International journal of universal pharmacy and biosciences.2013 July 10; 2(4): 78-85.

16. Eryvaldo S.T Egito. Polishing the therapy of onychomycosis induced by candida spp; Amphotericin B-loaded nail lacquer. Pharmaceutics MDPI. 2021; 13: 784.

17. Patel namarata ashwinbhai. Formulation development and evaluation of nail lacquer of posaconazole for treatment of onychomycosis. International journal of advance research and innovative ideas in education. 2021; 7(2): 2395-4396.

Source of Support: The author(s) received no financial support for the research, authorship, and/or publication of this article.

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.