Enhancing Stability and Antifungal Efficacy of Medicated Nail Lacquer as a Drug Delivery System: Formulation, Characterization, and Evaluation

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Abstract: The objective of this work was to harness the potential of nail lacquer as a drug delivery system to enhance the stability and antifungal efficacy of an antifungal drug. The nail lacquer formulation was thoroughly characterized, encompassing parameters such as drying time, smoothness, gloss, non-volatile oil content, viscosity, drug content, adhesion, diffusion studies, in vitro antifungal activity, and stability studies. The nail lacquer exhibited a drying time of 40 to 77 seconds, uniform smoothness and gloss, non-volatile oil content of 36±0.38 to 46±0.56, viscosity measurements between 135 and 172 centipoise, percentage drug content range of 87.55% to 98.99%, diffusion studies revealed drug release percentages ranging from 50.43% to 92.43% at 24 hours, and in vitro antifungal activity demonstrated zone of inhibition values of 7.010.56 mm and 7.980.16 mm at various concentrations. Stability studies conducted in accordance with ICH guidelines suggest that the nail lacquer formulation is an efficient drug delivery system for onychomycosis treatment. It has excellent stability, controlled release properties, and potent antifungal activity, making it a promising option. Further research is needed to validate its long-term effectiveness, safety, and therapeutic potential.

Keywords: Nail lacquer, Drug delivery system, Antifungal efficacy, Therapeutic potential, Controlled release, etc.

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Introduction: In order to treat ailments, drugs have been given to the human body in a number of methods throughout the past several decades, including orally, topically, parenterally, inhaled, etc. Every medical condition demands a specific and successful course of treatment. In reality, it is believed that the main goal of any therapy is to cure the patient's illness with as little negative impact on their health as possible. A thorough grasp of the pharmacokinetics and pharmacodynamics of the selected medication is also necessary for a successful treatment strategy. In order to provide the best therapy that ensures the patient's safety and a speedy recovery, we thus toil relentlessly every day to enhance our technology and procedures.

In addition to its defensive and cosmetic roles, human nails can also be utilised to carry medications, especially in the case of nail disorders like onychomycosis or psoriasis.

These ailments that harm nails affect many individuals, especially the elderly and those with compromised immune systems. Despite the fact that oral drugs frequently have systemic side effects and drug interactions, the form and makeup of the nail plate greatly hinder drug penetration. The majority of topical medications may also just slightly enter the nail. In order to successfully treat nail illnesses, the active drug must first penetrate the thick, keratinized nail plate before going further into the nail to the nail matrix and nail bed (1). Insufficient investigation into and understanding of the properties of the keratinized nail plate, the nail bed, and the nail matrix led to a reduction in the amount of attention paid to the ungual system. Because of its horny nature, medicine can enter the body through the nail plate. If something is solid enough to make penetration difficult, just a little amount of topical medicine will be able to pass through. As a direct result, the therapeutic emphasis is unsuccessful. The nail plate's appearance might alter if its brightness is decreased. The involvement of the nail bed, a reduction in blood flow, or the physiological or chemical properties of the nail bed are some of the underlying causes of this condition. This might lead to the development of several illnesses. The right therapeutic concentration of medicine may be produced by utilising a nail drug delivery system, enabling the treatment of a multitude of ailments (2).

The effectiveness of topical treatment for nail diseases is seriously threatened by issues with medication distribution to the nail (ungual drug delivery). These problems include formulae that promote increased ungual distribution and a lack of knowledge of the barrier qualities of the nail. Additionally, because the necessary therapy may take four to eight months to complete, patient compliance with these treatments is low.

However, there is a larger possibility of systemic toxicity, particularly in the liver, because current oral formulations usually include significant levels of the active component and

treatments can occasionally be protracted. As a result, the pharmaceutical industry has placed a strong emphasis on developing more effective methods of delivering nail medications (3).

Material and Method

Material

Flucytosine purchased from BLD Pharmatech Pvt Ltd, Telangana (India). Eudragit RS100 and 2- Hydroxy-beta-Cyclodextrin purchased from Central drug house (P) Ltd, New Delhi (India). Propylene glycol and Ethyl cellulose purchased from Thomas Baker (Chemicals) Pvt, Ltd, Mumbai, (India). Salicylic acid purchased from All the chemicals were used analytical grades.

Method

Formulation of Nail Lacquer

Selection of solvent

By using the unassisted eye in ambient light to visually assess the drug's solubility in several solvents, the solvent for the production of nail lacquer was chosen. The solvents used in this experiment were ethanol, propylene glycol, Eudragit RS 100, and 2-hydroxy beta-cyclodextrine. Weighed doses of the drug (50 mg) were separately dissolved in various solvents (5 mL each) at room temperature and placed in 10 mL glass vials. The solubility of the drug in each solvent was then evaluated visually in well-lit settings after dissolution.

Selection of Stabilizers:

Stabilizers are selected on the basis of drug polymer compatibility test.

Method of preparation of nail lacquer

Formulation tests were carried out in accordance with the formula in Table No. 1. The required quantity of flucytosine and Eudragit RS 100 was dissolved in ethanol using a magnetic stirrer at a constant speed. The aforementioned clear solution had a 100ml volume and was made by entirely combining propylene glycol, salicylic acid, and the required amount of 2-H-CD. A glass container with a narrow mouth and a plastic screw top was filled with the prepared nail polish.

Table 1: Formulation of Nail Lacquer

Sl. No	Ingredients %	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
1	Flucytosine	2	2	2	2	2	2	2	2	2	2
2	Eudragit Rs 100	6	6	6	6	6	6	6	6	6	6

3	Salicylic acid	5	-	10	15	20	15	10	15	15	15
4	2-H-β-CD	-	2.5	5	7.5	10	10	10	10	10	10
5	Ethyl cellulose	-	-	-	-	-	-	0.25	0.50	0.75	1.00
6	Propylene glycol	10	10	10	10	10	10	10	10	10	10
7	Ethanol	100	100	100	100	100	100	100	100	100	100

Evaluation of Nail Lacquer (3,4)

Non-volatile content

In a petri plate, 10 ml of the material was collected, and the starting weights were noted. The dish was baked for one hour at 105°C, removed, cooled, and weighed. The weight discrepancy was noted. A three-fold average of the measurements was noticed.

Drying time

The drying time of a sample film was measured by applying it with a brush on a petri plate and timing how long it took to dry.

Smoothness to flow

The sample was stretched out on a glass plate, raised vertically to a height of 1.5 inches, and then the smoothness of the film was measured.

Gloss

When put to the nail and contrasted with cosmetic nail lacquer that is easily accessible on the market, the shine of a nail lacquer sample could be visible.

Viscosity

The Brookfield Viscometer, model LVF, with spindle No. 61 operating at 3 revolutions per minute was used to determine the viscosity of the sample while it was at room temperature.

Drug content estimation(5)

200mg of nail polish were dissolved in 50 ml of phosphate buffer solution, which has a pH of 7.4. After that the fluids received 15 min of ultrasonic treatment. 100ml of pH 7.4 PBS should be mixed with a pH 7.4 phosphate buffer solution that is created by filtering the completed product. The amount of medicine present in the diluted solution was then determined by spectrophotometric analysis at a wavelength of 285 nm.

Diffusion studies across artificial membrane(3) (4) (6)

Using a Franz diffusion cell and a 0.8-mm cellophane artificial membrane, diffusion experiments were conducted. The receptor compartment was filled with solvent, and the membrane was immersed in the solvent solution for 24 hours. The membrane's surface was equally coated with 200 milligrams of nail polish. To prevent air bubbles from becoming trapped beneath, the prepared membrane was carefully positioned with the cell in it. The entire assembly was held at 37°C and swirled steadily for 24 hours. At intervals of 0.5hours, 1hours, 2hours, 4hours, 8hours, 12hours, and 24hours, a 5 ml aliquot of the drug sample was collected and replaced with new solvent. A double-beam UV spectrophotometer was used to analyse the samples in accordance with the procedure described in the drug content estimation.

In vitro antifungal activity(7)

Using the agar cup-plate technique, Candida albicans' in vitro antifungal activity was evaluated. Nutrient agar plates were prepared and sterilised in an autoclave set to 120 degrees Celsius and 15 pounds of pressure for 15 minutes. Then, 30 mL of nutritious agar medium was inoculated with the fungal strain *C. albicans* (2 mL of inoculum to 100 mL of nutritional agar media). Two sterile petri plates each received the liquid and had three 5 mm diameter wells drilled into them using a sterile borer. Each of the aseptically labelled and transferred optimised and control formulations got 0.2 mL in the cups. As positive and negative controls, respectively, uninoculated medium and media seeded with the test organism but devoid of an antifungal drug were utilised. Before being incubated at 28°C for 48 hours, the prepared Petri plates were maintained at room temperature for two hours to allow the solutions to diffuse into the medium. Each well's zone of inhibition's circumference was measured.

Stability study

The stability of nail lacquers was examined in accordance with ICH guidelines. Samples were kept at a temperature of 25°C and 60% RH for six months and at a temperature of 40°C and 75% RH for one month, respectively. The samples were examined for the presence of non-volatile components, drying time, gloss, smoothness of flow, drug content, and diffusion through a synthetic membrane.

Result and Discussion

Evaluation of nail lacquer

Non-volatile content

Table 2 & Figure 1, below reports the non-volatile composition of all formulations.

Drying time

The drying time for nail polish ranged from 40 to 77 seconds, as shown in Table 2 & Figure 2. The best drying time for nail polish was shown to be between one and two minutes. Every formulation (NL1–NL10) had drying times that were within specification. Formulation NL1, which was created using Eudragit RS 100, had the least amount of TGA. The drying time for the NL6 formulation was 77 seconds longer than for the quickest formulation NL 1 has 40 seconds.

Smoothness to flow and Gloss

Both of these parameters were judged to be adequate. It was discovered that the nail polish spread out and formed a smooth, uniform film when it was placed over the glass plate. The shine of the applied lacquer was equivalent to a cosmetic sample that was being sold, demonstrating the popularity of cosmetics.

Viscosity

The sample was clear and lustrous between 140 and 160 centipoises, and its viscosity varied from 100 to 220 centipoises. Additionally, this viscosity range provided good adhesion and flow properties. Outside of this range, the viscosity causes clouding and decreases shine, both of which are dreadfully unappealing, shown in Table 2 & Figure 3.

Table 2: Non-volatile content, Drying time and Viscosity of various formulation of Nail lacquer

S. No	Formulation code	Non-volatile content (%)	Drying time (sec)	Viscosity (Centipoise)
1	NL1	38±0.48	40	135
2	NL2	40±0.33	57	146
3	NL3	39±0.71	48	148
4	NL4	46±0.56	44	172
5	NL5	43±0.44	41	151
6	NL6	45±0.53	77	167
7	NL7	37±0.69	53	165
8	NL8	42±0.55	42	169
9	NL9	40±0.95	45	150
10	NL10	36±0.38	58	156

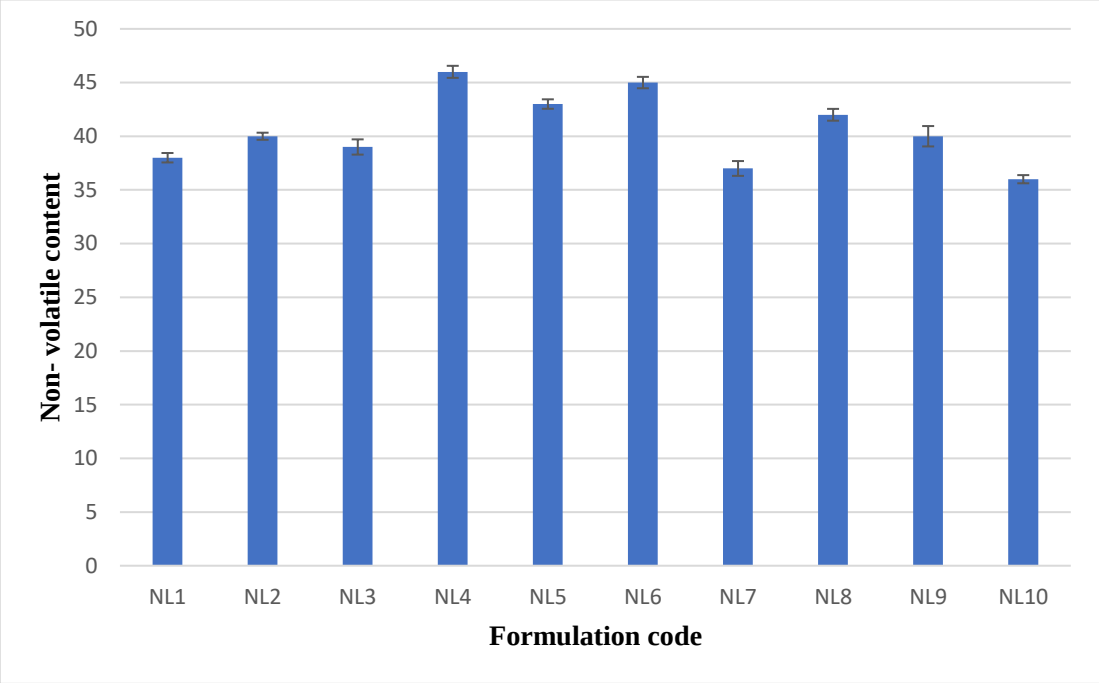

Figure 1: Non-volatile content of various formulations

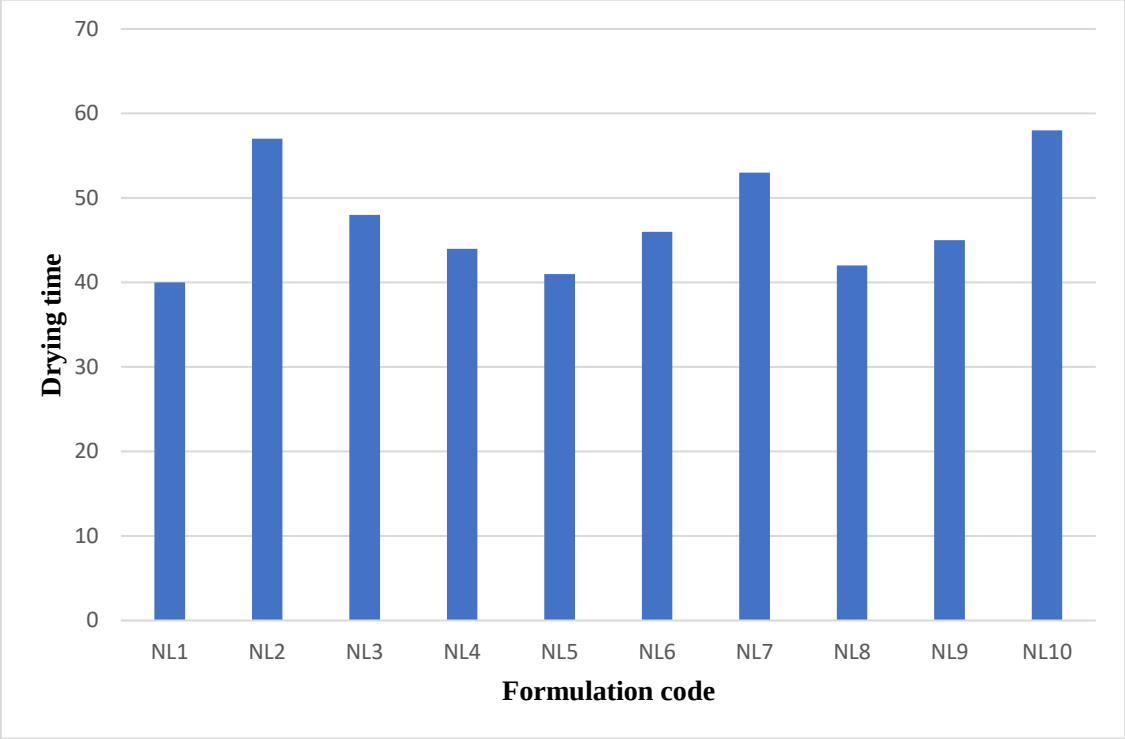

Figure 2: Drying time of various formulations

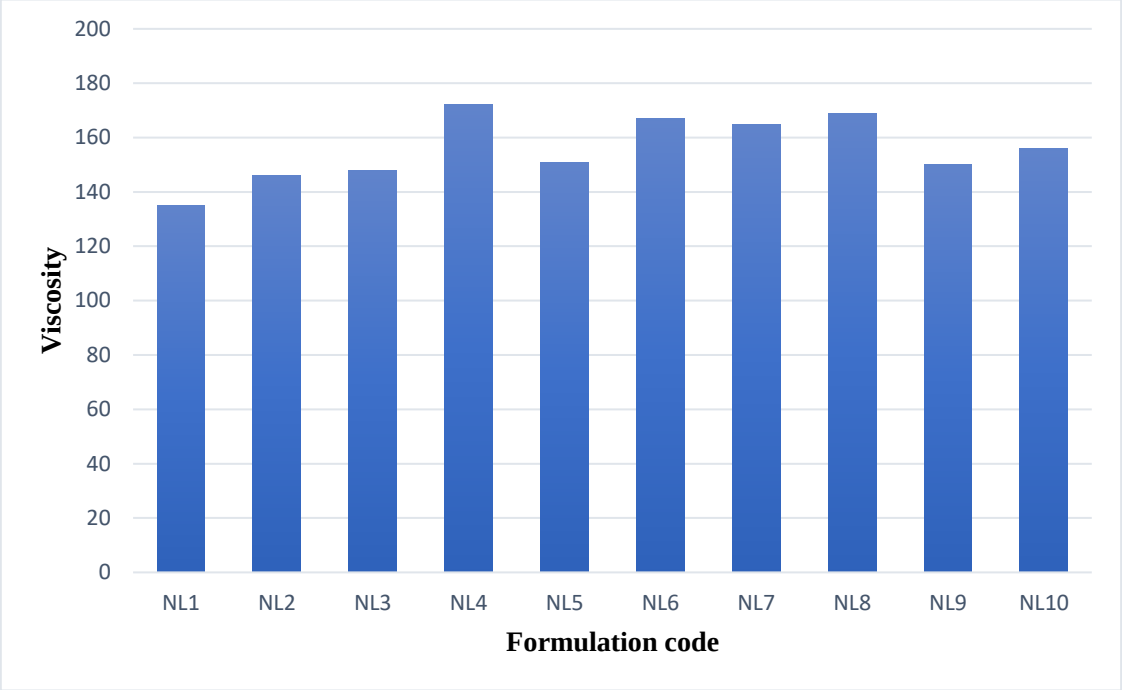

Figure 3: Viscosity of various formulations

Percentage drug content determination

All nail lacquers' percentage drug content was determined to be adequate and ranged from 87.55 to 98.99%, as shown in Table 3 & Figure 4. The lowest percent of drug content was 87.55% (NL3), while the highest percent was found to be 98.99% (NL10). Having a drug content of more than 90% in the formulation verifies that the techniques of formulation and the components chosen are not having an impact on the stability of the medicine. A high medication content also ensures that a successful treatment outcome may be anticipated.

Table 3: Percentage drug content of various formulation of Nail lacquer

Sl. No.	Formulation code	% Drug content
1	NL1	90.35
2	NL2	92.48
3	NL3	87.55
4	NL4	95.76
5	NL5	94.43
6	NL6	91.63
7	NL7	96.45
8	NL8	98.23
9	NL9	97.48
10	NL10	98.99

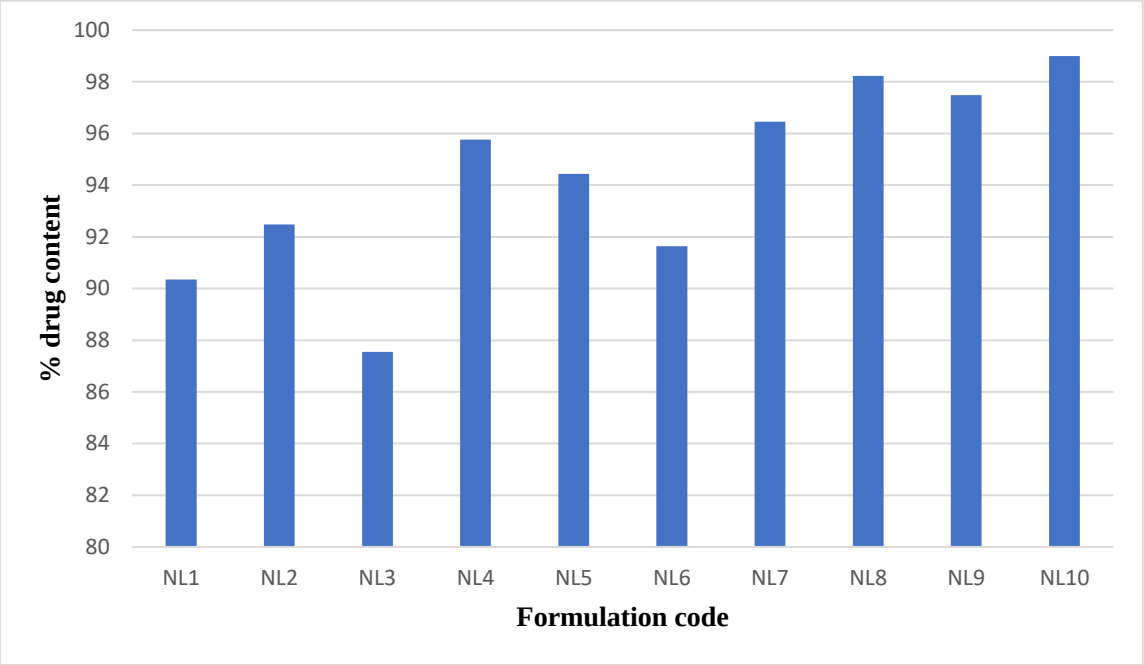

Figure 4: % drug content of various formulations

Diffusion studies across artificial membrane

Using an artificial membrane (cellophane membrane, 0.8 m), diffusion experiments of all the formulations were conducted for 24 hours. All formulations were subjected to the diffusion investigations, which are listed in Table 4.

Table 4: Percentage drug release of various formulation of Nail lacquer

Time (hr)	% Drug Release through artificial membrane									
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
0	0	0	0	0	0	0	0	0	0	0
0.5	10.92	12.94	15.23	16.82	16.94	17.48	18.72	19.23	19.90	20.93
1	13.14	15.35	16.38	19.35	20.34	21.67	22.67	24.76	27.43	29.14
2	21.84	24.97	25.84	26.54	26.85	27.98	28.09	30.21	32.56	36.84
4	34.82	35.86	36.53	37.45	38.18	38.43	38.89	40.43	41.43	45.24
8	40.67	42.88	44.46	46.67	47.66	48.28	48.68	49.18	50.45	53.38
12	49.42	52.22	58.46	60.34	61.89	63.23	64.78	65.90	66.89	67.53
24	50.43	55.44	59.26	67.14	70.13	76.88	78.18	84.81	89.81	92.43

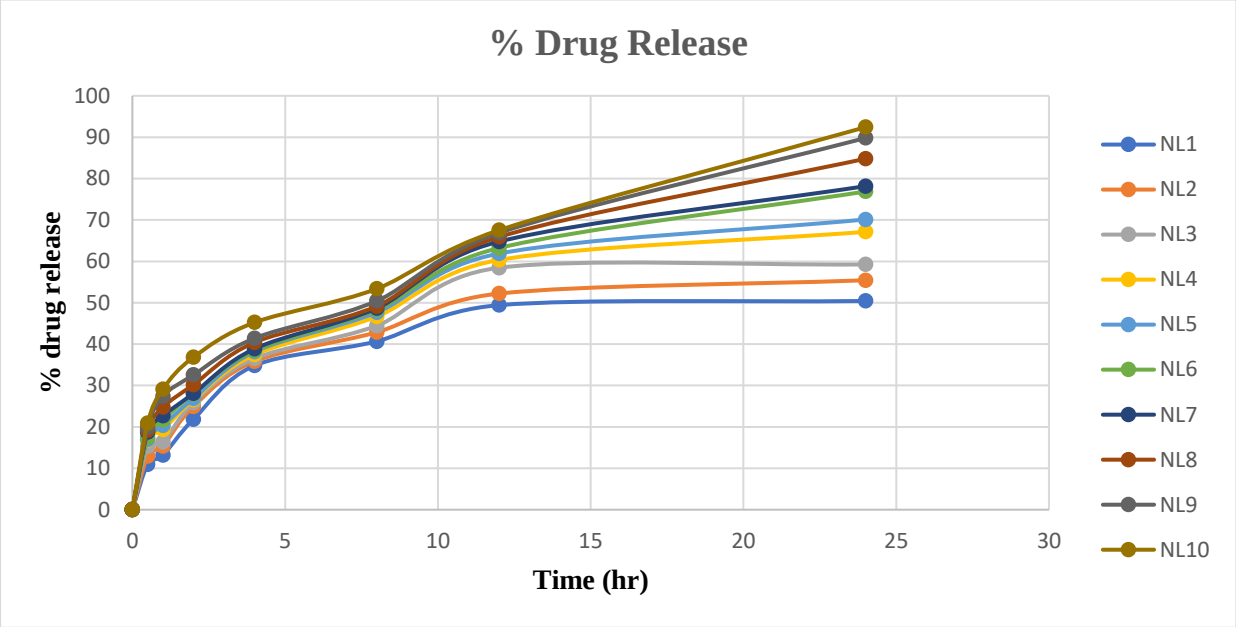

Figure 5: % drug release of various formulations

In vitro antifungal activity

A nutritional agar media was used to assess the antifungal effectiveness of an enhanced nail lacquer formulation against Candida albicans at various concentrations. Also contrasted were the positive and negative controls. When the zone of inhibition was studied, it was found that F10 had larger values of inhibition zone at varied concentrations, indicating stronger antifungal activity. (Figure 6,7). It was discovered that the zone of inhibition demonstrated by the improved formulation was bigger, measuring 7.01±0.56 mm and 7.98±0.16 mm, respectively.

Table 5: Zone of Inhibition of various formulation at different concentration

Formulation code	Zone of Inhibition	
	10mg/ml	20mg/ml
NL1	4.70±0.10	4.87±0.67
NL2	4.85±0.57	5.45±0.78
NL3	4.98±0.18	5.88±1.29
NL4	5.14±1.16	6.10±0.56
NL5	5.46±0.36	6.43±0.76
NL6	5.72±0.73	6.92±0.71
NL7	5.91±0.12	7.01±1.19
NL8	6.36±0.78	7.37±0.38
NL9	6.72±1.19	7.62±1.28

NL10	7.01±0.56	7.98±0.16

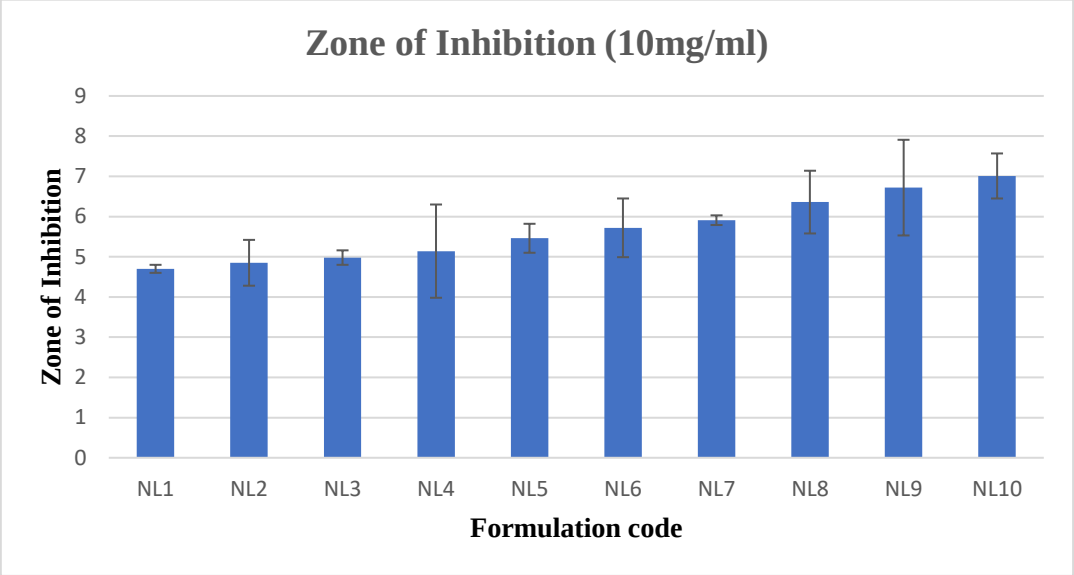

Figure 6: Zone of Inhibition (10mg/ml) of various formulations

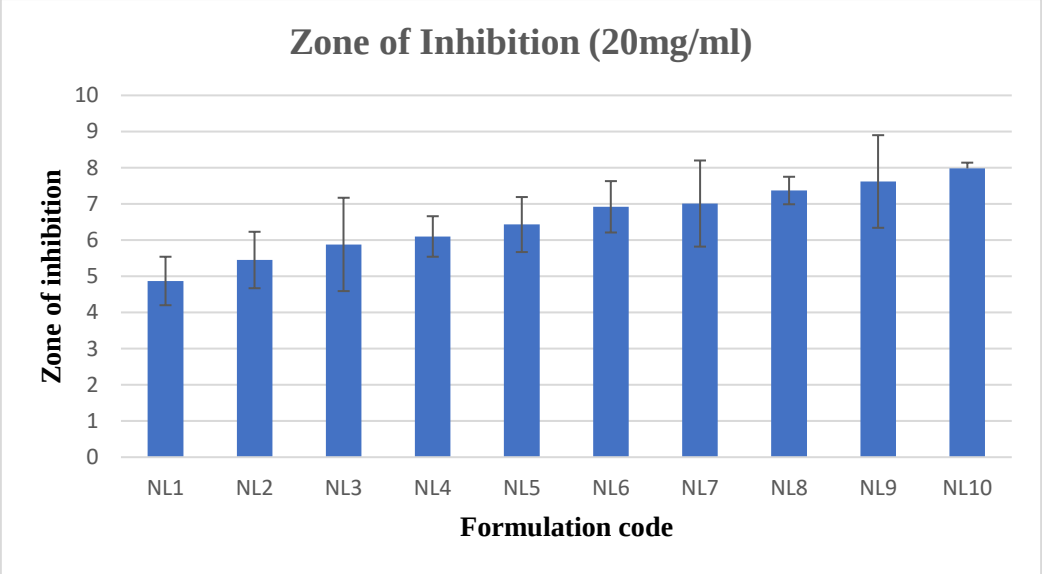

Figure 7: Zone of Inhibition (20mg/ml) of various formulations

Stability studies

Stability studies were used to determine how long a product could be stored before spoiling and how it should be stored. As part of our investigation, we rushed through a variety of stability tests on NL10 for a whole month. After making the necessary changes, expedited stability tests were conducted in accordance with ICH guidelines. Researchers looked at things

like drying time, % drug content, and non-volatile content to ensure that they had indeed changed. The outcomes are shown in Tables No 6.

Non-volatile content, drying time, and drug content were not significantly different from pre-stability charging data when formulations were re-evaluated after stability charging. Therefore, it was concluded that the formulations' stabilities were in accordance with ICH criteria.

Table 6: Stability study parameter of optimized batch (NL10)

Sl. No.	Parameter	Initial	After
1	Non-volatile content	36±0.38	35±0.84
2	Drying time (sec)	58	59
3	Drug content	98.55	98.03

CONCLUSION

In conclusion, this study aimed to utilize nail lacquer as a drug delivery system to improve the stability and antifungal efficacy of an antifungal drug. The researchers thoroughly characterized the nail lacquer formulation, evaluating various parameters such as drying time, smoothness, gloss, non-volatile oil content, viscosity, drug content, adhesion, diffusion studies, in vitro antifungal activity, and stability studies.

The results demonstrated that the nail lacquer formulation had a drying time of 40 to 77 seconds, providing uniform smoothness and gloss. It exhibited a non-volatile oil content range of 36±0.38 to 46±0.56, with viscosity measurements between 135 and 172 centipoises, and the percentage drug content ranged from 87.55% to 98.99%.

Furthermore, diffusion studies revealed that the nail lacquer formulation achieved drug release percentages ranging from 50.43% to 92.43% at 24 hours. In vitro antifungal activity testing demonstrated zone of inhibition values of 7.01 ± 0.56 mm and 7.98 ± 0.16 mm at different concentrations, indicating potent antifungal properties.

Stability studies conducted in accordance with ICH guidelines suggested that the nail lacquer formulation exhibited excellent stability, controlled release properties, and promising antifungal activity, making it a potentially effective option for onychomycosis treatment.

However, the conclusion also emphasizes the need for further research to validate the long-term effectiveness, safety, and therapeutic potential of the nail lacquer formulation. Additional studies are required to assess its durability, potential side effects, and clinical efficacy.

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Consent for Publication: Not applicable.

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