FORMULATION AND EVALUATION OF ALLYLAMINE AGENT FOR NAIL PREPARATION FOR MANAGEMENT OF FUNGAL INFECTION

Switi singh Parihar[1]*, Dr. Anupam kumar Sachan[2], Saurabh singh[3]

Article History : **Received - 30/04/2023** **Revised - 30/05/2023** **Accepted - 30/06/2023**

Abstract:
In this research, a medicated antifungal nail polish containing Terbinafine and Clobetasol propionate was developed. Long-term, sustained release of Terbinafine and Clobetasol propionate was investigated in the hopes of lowering the frequency of dosing. Toenail fungus, also known as onychomycosis, is quite common. Infection with dermatophytes, Candida, or non-dermatophytic molds can lead to onychomycosis. In terms of non-volatile content, drug release, drug content estimate, and inhibitory zone, the optimum formulation was a nail lacquer comprising 1-2 percent Terbinafine and Clobetasol propionate, as well as 3 percent ethyl cellulose. Up to 48 hours after administration, 98.12% of the drug was still active. FTIR tests confirmed that the drug and excipient were safe to use together. It was expected that this would improve clinical efficacy and patient compliance. The nail polish formulations were created by simply combining the necessary ingredients together, and then evaluated for non-volatile content, flowability, drug diffusion studies, and an estimate of the drug content. The selected optimized formulation, F4, showed no significant change in initial attributes throughout a month-long accelerated stability analysis performed at 40-20°C in accordance with ICH norms. The development and deployment of these systems pose no known dangers. Antifungal nail lacquer is a potential novel dosage form in the healthcare and pharmaceutical industries.

Keywords: Fungal infection, nail polish formulations, drug diffusion studies, DSC study allylamine agent.

[1*,2,3]Dayanand dinanath college institute of pharmacy Kanpur Email:-simmisinghindian1999@gmail.com

***Corresponding Author:** Switi singh Parihar
*Dayanand dinanath college institute of pharmacy Kanpur Email:-simmisinghindian1999@gmail.com

DOI:10.53555/ecb/2022.11.12.365

Introduction:

Some treatments for conditions like onychomycosis and psoriasis are applied to the nails directly, where they might offer benefits in terms of both protection and aesthetics. Nail infections are common among the elderly, affecting one in three people over 65 [3]. Even though only a small number of topical drugs penetrate the nail plate due to the structure and material of the nail, systemic adverse effects and medication interactions may occur with oral prescriptions. The keratinized layer of the nail plate must be penetrated for an active drug to reach the nail matrix and nail bed [2, 4]. The matrix, the nail bed, and the nail plate have all received insufficient attention. Therefore, the ungual system was neglected. Drugs are able to more easily enter the body through the horny nature of the nail plate. Due to the difficulty, only a small percentage of topical treatments are effective. As a result, there is no way to determine an effective therapeutic dose. Diminish the nail's natural shine, and you risk giving it an unnatural look [5]. Nail bed involvements and decreased blood flow, in addition to the fingernail plate's anatomical or chemical features, are to blame. This results in many different diseases. Nail drug delivery systems can be used to administer therapeutic dosages of medication [6]. Two of the most common nail illnesses are onychomycosis hematoma and onychomycosis hematoma, both of which can be caused by fungus, yeasts, and other bacterial and fungal infections. Lack of understanding of the barrier properties of nails and formulations that favor greater ungula diffusion [10, 11] reduces the efficacy of topical therapy for nail illnesses.

1. Methodology

Because of its film-forming and adhesive capabilities, ethyl cellulose was selected as a polymer. When compared to other polymers, this polymer exhibits a high compatibility with alcohols. Thioglycolic acid and dimethyl sulfoxide are used to increase medication penetration through the epidermis of the fingernails. As a plasticizer, dibutyl phthalate was used. These are drug-friendly, inexpensive, and readily accessible.

1.1Melting point

The melting points of Terbinafine and Clobetasol propionate were measured using a melting point instrument. One capillary tube with a lid was used to hold a little quantity of medication. The drug's melting temperature was measured when the capillary was submerged in a bath of silicone oil heated using an electrical heating coil. The results of three measurements were averaged and compared to pre-determined criteria.[4]

1.2 UV –visible spectrophotometric characterization of Terbenafine and Clobetasol propionate (λ_{max} determination)

It was then diluted with methanol to a stock solution of 1000g/ml by dissolving 100 mg Terbenafine and 100 mg Clobetasol propionate in 100ml volumetric flasks and diluting to the mark. Using methanol, 1 mL of this solution was reduced to 10 mL, and the result was tested. It was then determined that this solution (100g/ml) absorbed at a wavelength between 200 and 400 nm using a UV-visible spectrophotometer (Shimadzu 1700) [3].

1.3 Standard curve of Terbenafine and Clobetasol propionate.

100mg of Terbinafine was placed in a 100ml volumetric flask and weighed. After 30 minutes of sonication in 50ml methanol, this was diluted to 100ml with 1000g/ml methanol. When the stock solution was made by diluting one litre of the solution with another one, the concentration of the stock solution was set at 100 grammes per millilitre.

1.4 Difference scanning calorimeter (DSC)

Terbinafine and Clobetasol propionate were studied using DSC for their thermotropic characteristics and thermal behaviour. About 5mg of the sample were put in aluminium pans and heated at a rate of ten minutes at 40 to 300 degrees Fahrenheit in a nitrogen environment with a flow rate of 100ml/min [4].

1.5Infrared spectral (FTIR) analysis

The purity of Terbinafine and Clobetasol propionate was determined using FTIR spectroscopy. An FTIR spectrophotometer was used to record the infrared spectra of Terbinafine and Clobetasol propionate. There were 10 milligrammes of stuff that needed to be collected. The sample was tested in the range of 600 cm-1 to 4000 cm-1. It was then examined and compared to an established standard using the FFTIR spectrum [15-17].

1.6Optimization of formulation.

To find the optimal concentration for the making of films, scientists measured the film's thickness, strength at tensile stress, folding perseverance and water resistance.

Table 1 Composition of nail lacquer containing Terbinafine and Clobetasol propionate

Ingredients	Formulation					
	F1	F2	F3	F4	F5	F6
Terbinafine	250mg	250mg	250mg	250mg	250mg	250mg
Clobetasol propionate	250mg	250mg	250mg	250mg	250mg	250mg
Ethyl cellulose	2gm	2gm	2gm	2gm	2gm	2gm
Isopropyl alcohol	10ml	10ml	10ml	10ml	10ml	10ml
Ethyl acetate	5ml	5ml	5ml	5ml	5ml	5ml
Toluene	2ml	2ml	2ml	2ml	2ml	2ml
Thioglycolic acid	0.3ml	0.3ml	0.5ml	0.5ml	0.7ml	0.7ml
DMSO	0.4ml	0.5ml	0.6ml	0.4ml	0.5ml	0.6ml
Dibutyl pthalate	2ml	2ml	2ml	2ml	2ml	2ml

2. Evaluation of nail lacquer

2.1 Film thickness

A screw gauge accurate to within 0.01 mm was used to measure a variety of locations on the film. Five different spots were measured for film thickness, and an average of them was determined.

2.2 Folding endurance

The film's ability to withstand being repeatedly folded was evaluated employing a 2x2 cm sample folded till it snapped. The number of instances a piece of film is able to be folded without cracking is a fair measure of its folding resilience.

2.3Non-volatile content

The contents of a petri dish were weighed after 10 ml were placed onto them. The petri dish was baked for an hour at 105 degrees Celsius, then cooled, and finally weighted. The weight shift was clearly seen by onlookers. The average of three separate readings was calculated.

2.4 Drying time

A brush was used to apply a film sample to a petri plate. The production time for a film that is dry to the touch was timed using a stopwatch.

2.5Smoothness to flow

Visual inspection for smoothness was carried out on a glass plate that had been poured from a height of 1.5 inches before the sample was spread out horizontally on the plate.

2.6Viscosity

Spindle No. 3 was spun at 20 rpm in a room temperature viscosity test using a Brookfield Viscometer, model LVF.

2.7Water resistance

The ability of a film to withstand the passage of water through it will be evaluated using this method. This was accomplished by first soaking a surface that had a film coating on it, and then peeling off the film. The resistance to water decreased with each additional pound of weight.

2.8Drug content estimation

The drug concentration in 1 ml of nail polish was determined by dissolving the polish in methanol. After the appropriate dilution, absorbance at 260nm was measured using UV-1700, Shimadzu, Japan.

2.9Diffusion studies across artificial membrane

In this experiment, a Franz diffusion cell was used. Artificial membranes (cellophane) were used in the diffusion experiments. The membrane was immersed in a 7.4-pH phosphate buffer solution for an hour before the solvent was added to the receptor compartment. The membrane's surface was uniformly coated with a 10mg test vehicle. The membrane of the cell was positioned cautiously onto the membrane. The temperature was held at 37 degrees Celsius for the entire 10 hours, and the stirring speed was maintained at 600 revolutions per minute. After an hour, five milliliters of the drug sample were withdrawn and replaced with fresh solvent. Each test was taken a total of three times. A dual-beam UV spectrophotometer was used for drug analysis.

3.0 **Stability study** A sample was tested for two months while it was kept in a stability chamber at 40 degrees Celsius and 75% relative humidity. Water resistance, diffusion, nonvolatile content, and drying time were all tested using a synthetic membrane [58, 60].

4.0 RESULT

4.1 Melting point

Terbinafine and clobetasol propionate, in terms of melting points, were found to have values between 195 and 198 degrees Celsius, respectively. Lab experiments revealed that the melting point of terbinafine was 197.2 degrees Celsius, while that

of clobetasol propionate was 199.7 degrees Celsius.

4.2 Purity of drug

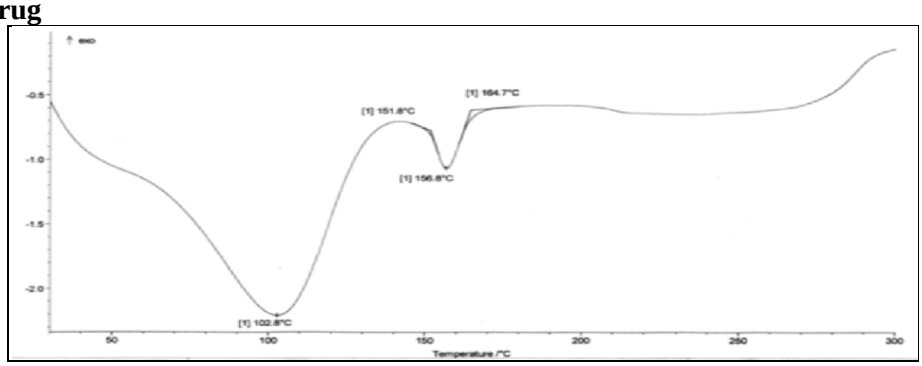

Fig. 1: DSC of Terbenafine

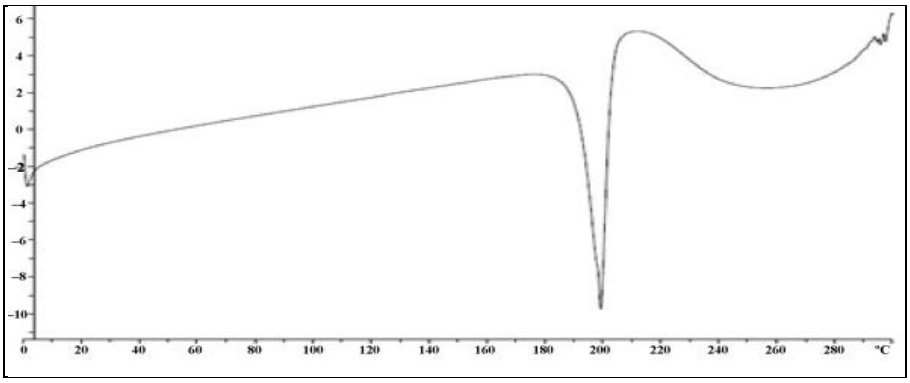

Fig. 2: DSC of Clobetasol propionate

Using a thermogram, the melting points of Terbenafine and Clobetasol propionate were determined to be 156.8 degrees Celsius and 199.6 degrees Celsius, respectively. The purity of the medicine can be seen in the DSC plot.

4.3 UV spectroscopy Terbenafine's maximum absorbance in phosphate buffer was recorded at 283 nm. The phosphate buffer Terbenafine standard calibration curve was generated using the following absorbance values at various concentrations.

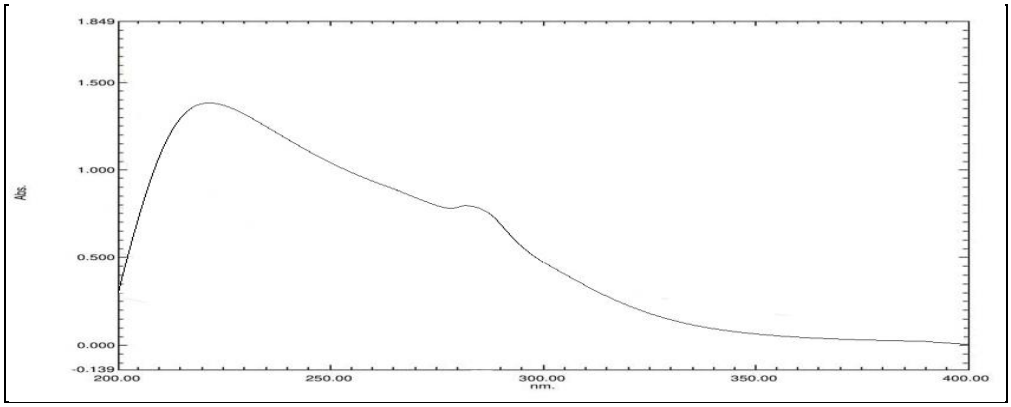

Fig. 3 Calibration curve of Terbenafine

4.4 Drug Excipient compatibility study The IR reference peaks for terbinafine and clobetasol propionate were also present in the spectra of the drug-polymer and drug-permeation enhancer-excipient combination, as indicated in Table No. spectra.

1. In other words, FTIR analysis showed no evidence of drug-permeation enhancer interactions. As a result, the drug and the permeability enhancer work well together. The Figures contained visual representations of the IR

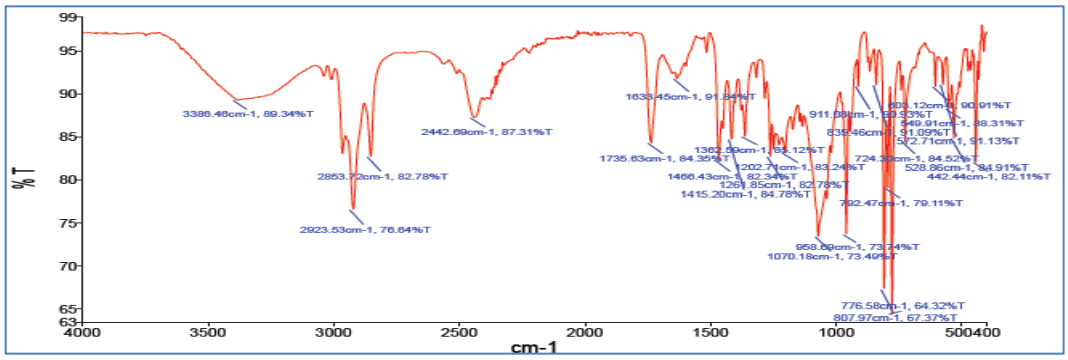

Fig. 4: FTIR spectra of Terbenafine

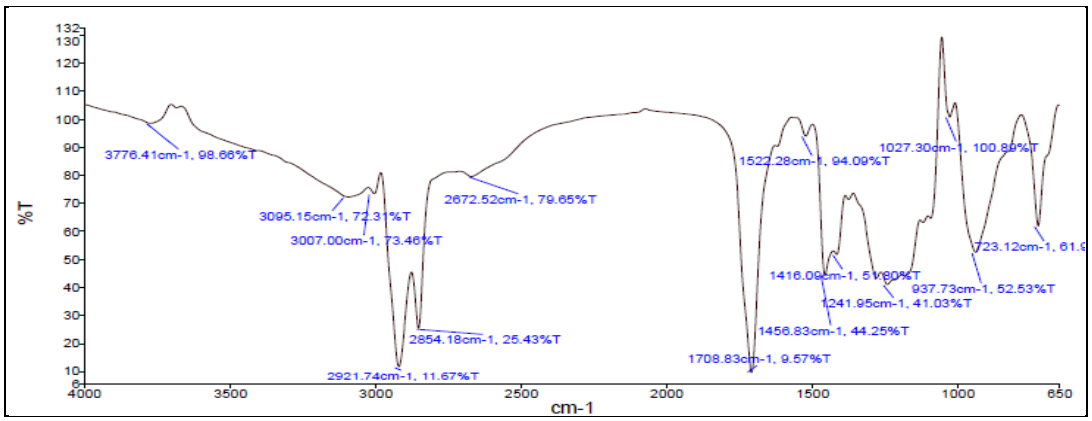

Fig. 5: FTIR spectra of Clobetasol propionate

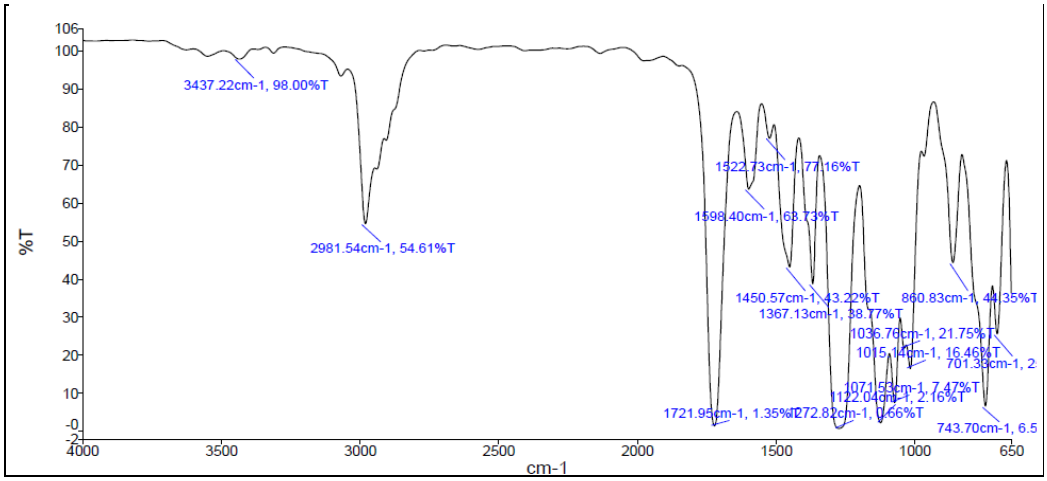

Fig.5: FTIR spectra of Drug + Ethyl acetate

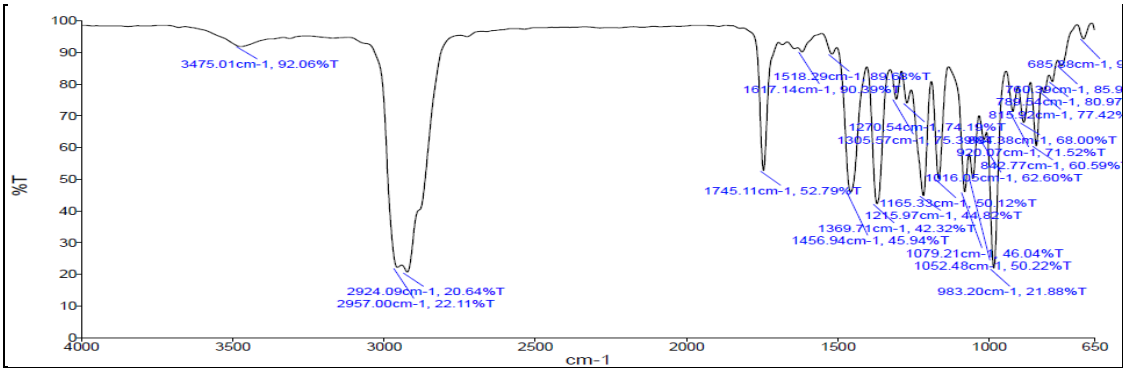

Fig. 6: FTIR spectra of drug + isopropyl alcohol

5.0 **Evaluation of Nail lacquer**

5.1 Thickness (µm)

The consistency of the formulations' thickness demonstrates the method's efficacy. All film thicknesses were measured with a micrometer screw gauge. The data showed that the formulation thicknesses ranged from 55 m to 59 m. A Table contains the data that was entered. The requested thickness range was found by combing through film literature, which provided data on film thickness.

5.2 Folding endurance The length of time a sheet of polymer film can be folded indicates how flexible it is. The films' adaptability to folding was measured by conducting endurance tests. A film's ability to withstand folding is indicated by counting the number of folds it can make before snapping. The developed films had a value more than 135, and all figures between 127 and 184 were also present in the table. Films made with any amount of polymer demonstrated remarkable folding endurance, indicating they were flexible enough to endure mechanical stress. The film's ability to withstand repeated foldings is a key indicator of its pliability.

5.3 Tensile strength The phrase "tensile strength" refers to the amount of mechanical force that may be applied to film without it tearing or breaking. Tensile strength values vary depending on the polymer:plasticizer ratio and the polymer solution concentration. The strength of the tensile force was measured by means of analytical instruments. Table No.16 showed that the average tensile strength was lowest for the film with a contents of 8% ethyl cellulose and highest for the film with a concentration in order of 6%.

Table 4.5 thickness, folding endurance and tensile strength

Formulations	Thickness (µm)	Folding Endurance	Tensile Strength (kg/cm^2)
F1	58 ± 0.01	165	2.74 ± 0.12
F2	54 ± 0.01	137	2.68 ± 0.04
F3	59 ± 0.04	168	2.47 ± 0.09
F4	57 ± 0.02	158	2.52 ± 0.16
F5	58 ± 0.02	156	2.83 ± 0.24
F6	56 ± 0.01	163	2.53 ± 0.03

5.4 Water resistance This is the standard for assessing the impermeability to water. This appearance was achieved by coating the surfaces and then submerging them in water. Immersion weight loss or increase could be determined. The resistance to water is decreased when a person gains weight. When compared to a film made of 15% ethyl cellulose, one made of 6% ethyl cellulose is lighter and more resistant to water. A table was used to organize the information.

Table 6. Water resistance of nail lacquer

Formulation	**W1**	**W2**
F1	6.85	6.92
F2	6.83	6.95
F3	6.88	6.90
F4	6.92	7.14
F5	6.81	6.90
F6	6.84	6.91

The optimal amounts of ethyl cellulose (6 percent w/v) and Thioglycolic acid (10 percent w/v) were determined based on the results of the research mentioned above, and so the F3 formulation was chosen.

5.6 Drying time

Table 7. drying time of nail lacquers

Formulation	**Drying time (sec)**
F1	50
F2	52
F3	127

F4	52
F5	58
F6	59

5.7 Viscosity

The sample's viscosity varied between 100 to 220 centipoise, and it was clear and lustrous at a centipoise value of 140 to 160. Both adhesion and flow improved with increased thickness. Because to clouding and a dulling of luster, this viscosity range is unfit for cosmetic use.

Table 8.Viscosity of nail lacquer

Formulation	Viscosity (centipoise)
F1	100
F2	116
F3	120
F4	127
F5	135
F6	184

5.8 Percentage drug content determination As can be seen in the table below, the drug content of the lacquers was calculated to be anywhere from 86.25 percent to 99.01 percent. Maximum drug concentration was 99.01 percent (F4), with minimum concentration of 86.25 percent (F2). If a formulation has more than 90% active ingredients, then the formulation process and components used will not compromise the stability of the drug. There is an adequate amount of prescription medication in the sample, so perhaps the treatment will work.

Table 9. Percentage drug content determination

Formulation	Drug content (%)
F1	90
F2	91.50
F3	93.75
F4	99.01
F5	86.25
F6	94.28

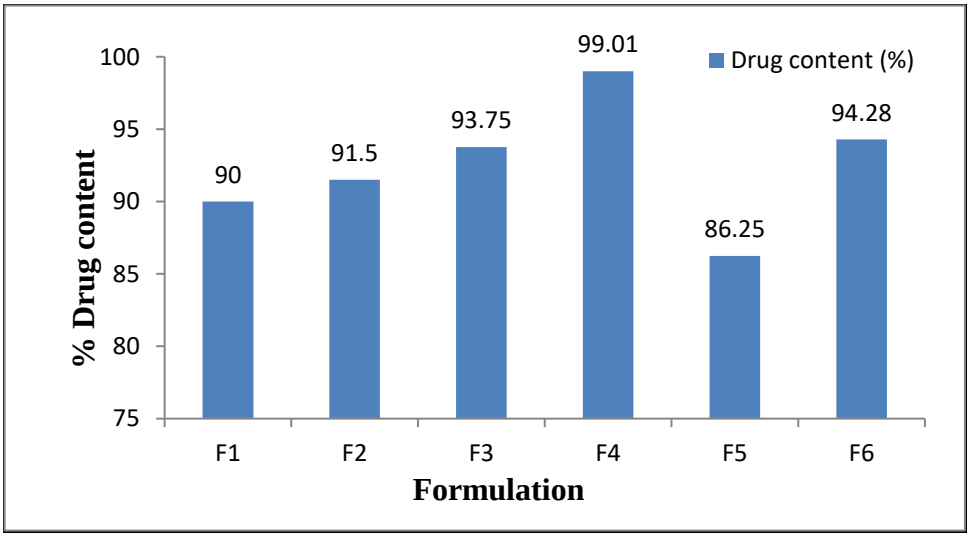

Fig. 7 Percent drug content

5.9 Diffusion studies across artificial membrane
Each mixture was subjected to a 48-hour test using a cellophane membrane (artificial membrane, 0.8m in thickness). All of the Table formulas were tested in diffusion studies.An in vitro diffusion analysis only detected 64.18 percent of the medication released after 48 hours in the initial batch F1 and F2, both of which contained 0.3ml permeation enhancers. Diffusion trials using 0.5ml (F3), 0.7ml (F4), and 0.8ml (F5) of a permeation enhancer showed that only 64.18 %, 65.10 %, 99.12 %, and 69.10 % were discharged in 48 hours. The keratolytic effect of the penetration enhancer greatly improved drug uptake. Medicine was only partially absorbed, and researchers discovered that increasing the dosage had no effect. Salicylic acid concentrations of 15% w/v were determined to be optimal.

Table 10: Diffusion studies across artificial membrane

Time (hrs)	Percentage drug release					
	F1	**F2**	**F3**	**F4**	**F5**	**F6**
0	0	0	0	0	0	0
2	9.82	11.22	13.35	12.82	15.25	26.25
4	1 0.20	12.05	14.98	27.12	16.88	32.23
6	13.28	14.35	16.35	28.31	17.22	38.51
8	16.42	17.88	18.85	32.72	20.13	46.52
10	26.58	28.95	32.05	46.25	30.35	48.22
12	32.45	36.33	40.20	50.21	36.15	56.28
16	43.10	42.30	48.38	58.65	42.95	65.15
20	48.22	49.98	51.80	60.21	50.10	76.45
24	49.65	50.80	52.61	68.11	54.32	79.92
28	52.55	54.89	56.80	70.22	58.38	82.40
32	56.25	58.75	59.33	78.85	60.21	80.25
36	58.95	59.98	61.28	84.15	63.45	79.45
40	60.18	62.15	63.92	88.85	66.21	77.31
44	62.52	63.25	65.99	90.25	68.84	76.65
48	64.18	65.10	68.34	98.12	69.10	74.71

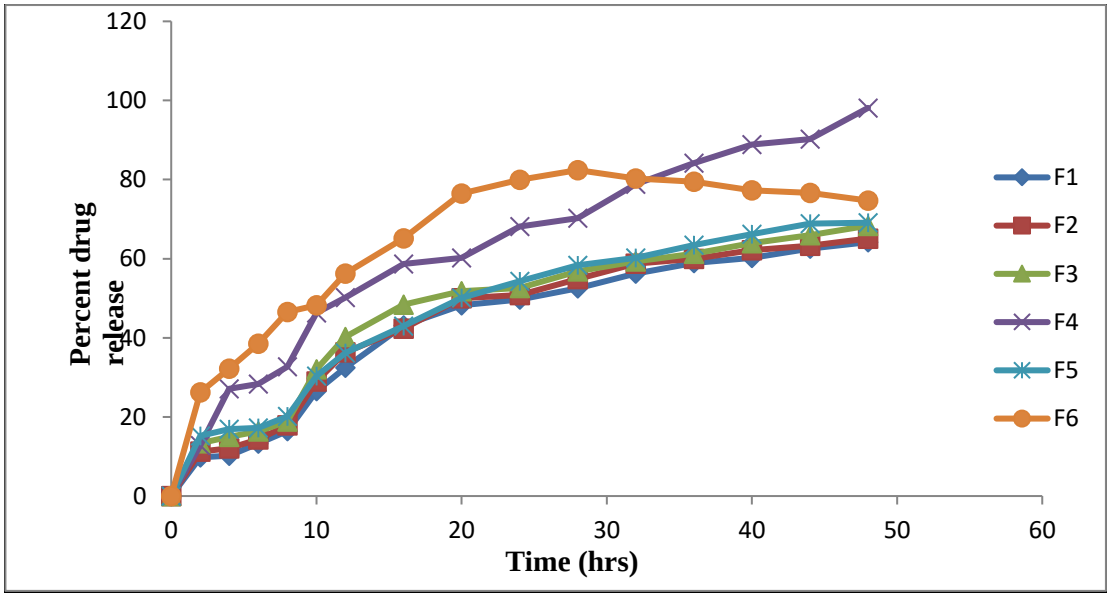

Fig. 8 Percent Drug release between artificial membranesAnti-microbial study

6.0 Antimicrobial study
The typical zone of inhibition is 21 mm, but other formulations showed zones of inhibition between 18 and 23 mm. All of the compositions were susceptible to infection by the yeast Candida albicans. A table and a diagram depict the findings.

Fig 9. Zone of inhibition of Formulated Nail Lacquers

Table. 11 Zone of inhibition of nail lacquers

Formulation	Zone of inhibition (in mm)	Standard zone of inhibition (in mm)	% Zone of inhibition
F1	23	27	85.18%
F2	19	27	70.37%
F3	22	27	18.48%
F4	23	27	85.18%
F5	18	27	66.66%
F6	17	27	62.96%

6.1 Stability studies

Stability studies determined shelf life and storage circumstances. F4 underwent rapid stability testing for a month. Stability studies were ICH-compliant after adjustments. Non-volatile content, drying time, and active component % all varied across the studied temperature range of 40 to 20 degrees Celsius. The duration of the tests was one month. Table 1 summarizes the findings.

Table. 12 stability studies data of F4

Parameters	Initial	After
Non-volatile content	37±0.92	36±8.47
Drying time (sec)	57	59
Drug content	99.12	98.75

Table 13 : In vitro Diffusion profile of F4 upon stability studies

Time (hrs)	Percentage drug release (µg/ml)	
	Before stability	After stability
0	0	0
2	12.82	10.6
4	27.12	24.9
6	28.31	26.45
8	32.72	30.25
10	46.25	39.95
12	50.21	45.75
16	58.65	52.55
20	60.2	58.81

24	68.11	62.5
28	70.22	72.05
32	78.85	76.8
36	84.15	81.25
40	88.85	90.53
44	90.25	92.2
48	98.12	97.75

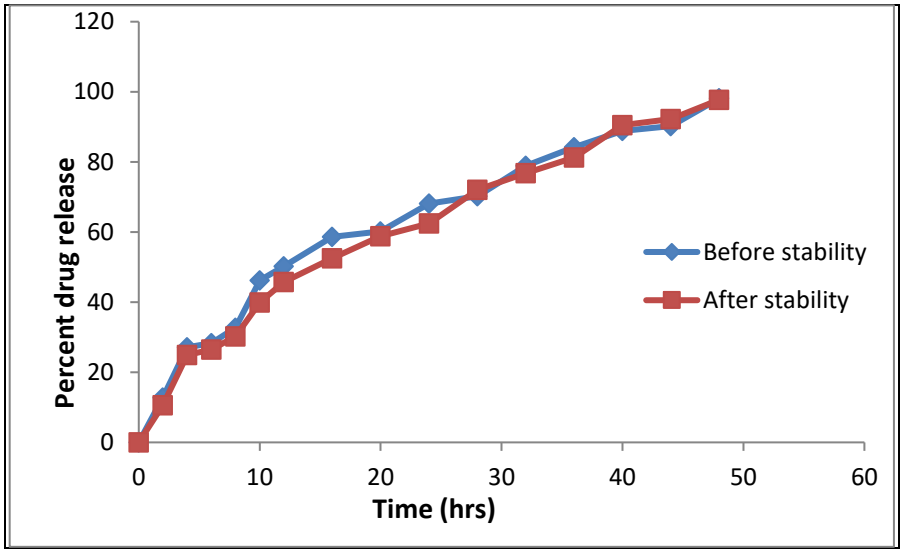

Fig. 10: In vitro Diffusion profile of F4 upon stability studies

Stability charge had no effect on non-volatile content, drying time, percent drug content, or drug diffusion when compared to data acquired before and after the charge. After conducting ICH stability testing, it was confirmed that all formulations were in compliance.

6.2 CONCLUSION

The primary objectives of this research were to compare the effectiveness of two nail lacquers often used for the treatment of onychomycosis, terbinafine and clobetasol-nitrate. The FTIR analysis showed that the formulations were safe to use, as the medication was compatible with the excipients. The film strength, drying time, flow, and volatile content were all satisfactory in all of the tested formulations. In a microbiological study, it was found that Candida albicans was vulnerable to the formulations. For one month, formulations were stable at 40 degrees Celsius. There is likely to be a solid correlation between in-vitro and in-vivo ungual permeation investigations.Formulation F4 kept a steady concentration of medicine for more than 48 hours in in vitro tests. The F4 formulation's keratolytic component worked as an intestinal permeability enhancer at an amount of 0.5 ml. The percentage of non-volatile material in the F4 formulation was 37.92.The amount of non-volatile material lost to vaporization was perfect for our purposes. The F4 formula dries rapidly. With a viscosity of 127, the F11 formulation shone and was transparent. When compared to a commercial sample, the F4 formulation's adhesive strength on the applied nail surface performed satisfactorily. The overall drug content in F4 was 99.01 percent. Therefore, the prognosis for a successful treatment is good. Diffusion tests performed over artificial membranes have showed that drug diffusion is increased by F4 by 98.40 percent. According to the results of these studies, medicated nail lacquers are an improved means of administering antifungal medication to the ungual area for the treatment of onychomycosis. Nail infections can be treated using medicated nail lacquers, but they can also be used for nail art. The patient is much more likely to follow instructions and accept treatment.

Acknowledgments: The authors delicately acknowledge the Department of Pharmacy, Dayanand dinanath college institute of pharmacy Kanpur U.P. for providing supported laboratory facilities for different invitro study.

Conflicts of interest: Authors declared that

there are no conflicts of interest.

References

1) Aggarwal, Rohan, Monika Targhotra, P. K. Sahoo, and Meenakshi K. Chauhan. "Onychomycosis: Novel strategies for treatment." *Journal of Drug Delivery Science and Technology* 57 (2020): 101774.
2) Alam G, Singh MP, Singh A, Vishwakarma DK, Patel R, Srivastava SP. Transungual drug transport: advancement and challenges. J Pharm Res 2012;5(5):2574-79.
3) Baden, Howard P., Lowell A. Goldsmith, and Barbara Fleming. "A comparative study of the physicochemical properties of human keratinized tissues." *Biochimica et Biophysica Acta (BBA)-Protein Structure* 322, no. 2 (1973): 269-278.
4) Baker, Stephen J., Xiaoying Hui, and Howard I. Maibach. "Progress on new therapeutics for fungal nail infections." *Annual Reports in Medicinal Chemistry* 40 (2005): 323.
5) Bohn, Manfred, and Karl Th Kraemer. "Dermatopharmacology of ciclopirox nail lacquer topical solution 8% in the treatment of onychomycosis." *Journal of the American Academy of Dermatology* 43, no. 4 (2000): S57-S69.
6) Caputo, R., K. De Boulle, J. Del Rosso, and R. Nowicki. "Prevalence of superficial fungal infections among sports-active individuals: results from the Achilles survey, a review of the literature." *Journal of the European Academy of Dermatology and Venereology* 15, no. 4 (2001): 312-316.
7) Choi, Ki-Choon, Je-Yong Bang, Pyoung-Il Kim, Chan Kim, and Chae-Eun Song. "Amphotericin B-incorporated polymeric micelles composed of poly (d, l-lactide-co-glycolide)/dextran graft copolymer." *International journal of pharmaceutics* 355, no. 1-2 (2008): 224-230.
8) Cilurzo, Francesco, Francesca Selmin, Chiara GM Gennari, Luisa Montanari, and Paola Minghetti. "Application of methyl methacrylate copolymers to the development of transdermal or loco-regional drug delivery systems." *Expert opinion on drug delivery* 11, no. 7 (2014): 1033-1045.
9) De Berker, D. A. R., R. Baran, and R. P. R. Dawber. "Normal nail anatomy and physical signs in nail disease." *Handbook of Diseases of the Nails and their Management. Blackwell Science Ltd, Oxford, 1995a* 131 (1995).
10) Elewski, Boni E. "Onychomycosis: pathogenesis, diagnosis, and management." *Clinical microbiology reviews* 11, no. 3 (1998): 415-429.
11) Elewski, Boni E. "Onychomycosis: pathogenesis, diagnosis, and management." *Clinical microbiology reviews* 11, no. 3 (1998): 415-429.
12) ELEZOVIĆ, A., S. Hadžović, Š. HADŽIDEDIĆ, and S. Kostić. "Characterization of antifungal nail lacquer formulations containing fluconazole." *Scientia Pharmaceutica* 78, no. 3 (2010): 624.
13) Elkeeb, Rania, Ali AliKhan, Laila Elkeeb, Xiaoying Hui, and Howard I. Maibach. "Transungual drug delivery: current status." *International journal of pharmaceutics* 384, no. 1-2 (2010): 1-8.
14) Faergemann, J., and R. Baran. "Epidemiology, clinical presentation and diagnosis of onychomycosis." *British Journal of Dermatology* 149 (2003): 1-4.
15) Fortune, D. G., C. J. Main, T. M. O'sullivan, and C. E. M. Griffiths. "Quality of life in patients with psoriasis: the contribution of clinical variables and psoriasis-specific stress." *British Journal of Dermatology* 137, no. 5 (1997): 755-760.
16) Godge, Ganesh Raosaheb, S. C. Bharat, A. B. Shaikh, B. B. Randhawan, M. A. Raskar, and S. N. Hiremath. "Formulation Perspectives in Topical Antifungal Drug Therapy: A Review." *Journal of Drug Delivery and Therapeutics* 13, no. 5 (2023): 110-119.
17) Gupchup, Gouri V., and Joel L. Zatz. "Structural characteristics and permeability properties of the human nail: A review." *Journal of cosmetic science* 50, no. 6 (1999): 363-385.
18) Gupta, A. K., C. W. Lynde, H. C. Jain, R. G. Sibbald, B. E. Elewski, C. R. DANIEL III, G. N. Watteel, and R. C. Summerbell. "A higher prevalence of onychomycosis in psoriatics compared with non-psoriatics: a multicentre study." *British Journal of Dermatology* 136, no. 5 (1997): 786-789.
19) Heydendael, Vera MR, Corianne AJM De Borgie, Phyllis I. Spuls, Patrick MM Bossuyt, Jan D. Bos, and Menno A. De Rie. "The burden of psoriasis is not determined by disease severity only." In *Journal of Investigative Dermatology Symposium Proceedings*, vol. 9, no. 2, pp. 131-135. Elsevier, 2004.

20) Jodh, Rahul, Mukund Tawar, Aparna Kachewar, Vishal Mahanur, Yash Surekha, and Virendra Atole. "Preparation and Evaluation of Nail Lacquer containing Luliconazole as Ungual Drug Delivery System." *International Journal of Pharmaceutical Sciences and Nanotechnology (IJPSN)* 15, no. 3 (2022).