Formulation and Development of Antifungal Nail Lacquer Containing Miconazole Nitrate Use in Treatment of Onychomycosis

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

In this formulation used different type of the use in this preparation which is 2 hydroxy propyl beta cyclodextrin, ethyl cellulose, nitrocellulose, propylene glycol as well as drug formulate and obtain optimal release conclusion is success in this formulation.

Index Terms- Fungal infections, Nail Lacquer, Onychomycosis

I. INTRODUCTION

All over the last time period the treatment of illness has been carried out by administrating drugs to human body by many routes namely oral, parental, topical inhalation etc. The suitably treatment is accurate and demands by medical condition. As a matter of fact, the thought of solution of the patients disease with least harm done to the patient's health is said to be the main achieve of any therapy. However, a good treatment technique is needful by the knowledge of pharmacokinetics and pharmacodynamics of the stable drug.

Nails of human being do not have role of decorative as well as protective, but can also be considered as a substitute pathway for drug delivery in a special manner in nail disease such as onychomycosis or psoriasis. These nail diseases are to great degree of spread in the population,

In the pharmaceutical industry developing effective method for nail drug delivery system is important. .Conformity and decrease danger side effects of a drug cause from temporary overdose. Other advantageous is convenience, particularly noteworthy in patches that necessitate only once weekly use. Such a simple dosing regimen can helpful in patient attachment to drug therapy. Scheming an0d development of TDDS is multidisciplinary activity that comprehend cardinal feasibleness studies starting from the choice molecule of the drug to the presentation of sufficient drug flux in an in vivo and in vitro model followed by friction of a drug delivery system that fitting all the rigorous demand that are specific to the molecule of the drug

FUNGAL INFECTION- The fungus is crude organism and the fungi can live all over in the air, in the soil, on the plant and in the Fungal infection the classed by capable of causing harm fungi are very common determine, and it not so serious if they are diagnosed fast and right treated. All the same while fungal infections are solicitude, one of treated again injection can easy fall out, as fungi can be create problem to skill. The fungal are frequently present in the totality of surrounding conditions.

NAIL DISEASE-

The nail plate may seem not in normal as a conclusion of congenital defect, disease of dermis with attachment of the nail bed, systematic disease, minimize of blood supply, local trauma, infection of the nail folds, Infectious nail plate.

- GREEN NAIL SYNDROME-Pseudomonas is category of fungus which is cause the infection

B-PARONYCHIA-

1-ACUTE PARONYCHIA- Bacterial infections **e.g.** group. A streptococci .that is cause the swelling violent pain.

-CHRONIC PARONYCHIA- Mainly fall out in patients whose hands are an invariably in water with recurrent lower trauma prejudicial the cuticle so that throne can farther harm the nail fold. Generally get infected particularly with pseudomonas develops a green or black discoloration.

C-NAIL PSORASIS- Scurfy dermis the nail plate gets cavities dry and frequent tumble and also appears red, orange and brown with red dots.

D-YELLOW NAIL SYNDROME- A not widely known position qualify via yellow nail with lack of cuticle, develop slowly and it minimize or separated.

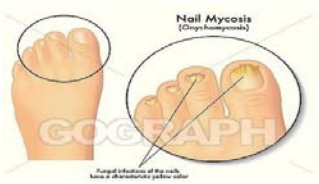
E-ONYCHOMYCOSIS- It is chronicle for third of integumentary fungal infection and one half of all nail disease.

PARAKERATOSIS- Presenting hyperkeratosis.

ONYCHOMYCOSIS-

People with infection are frequent feel shame about nail not in figure, because it can one time limits the quality of moving freely, it may indirectly minimize peripheral circulation because of that decline position that are several stasis and foot ulcers Fungal infections of the nails can also dispersed to another site of the body to another human.

ONYCHOMYCOSIS



CLASSIFICATION OF ONYCHOMYCOSIS-

A- **DISTAL SBUNGAL ONYCHOMYCOSIS-** The more general form may growth in the toenails, fingernails or both, infection is normally caused by trichophyton rubrum which attach in nail bed and the bottom of the nail plate, starting at migrating proximally done inherent nail matrix.

B- **WHITE SUPERFACIAL ONYCHOMYCOSIS-** Once 10% of cases which is caused by several fungus that direct attach the superficial layers of the nail plate and develop well represented opaque white island on the plate the nail is rough, soft and friable. This several of disorder can be treated with topical antifungal drug alone.

C- **PROXIMAL SUB UNGAL ONYCHOMYCOSIS-** It is fall out while infecting organism commonly attach the nail through proximal nail fold, penetrate the newer develop nail plate and then migrate distally.

D- **CANDIDA ONYCHOMYCOSIS-**It can category into three part-

1-Infection starting as infection structure encompassing the nail known felon.

2-Chronicle for lower than 1% of disorder this position is seen in immune via media patients and attach direct of the nail plates.

3-While nail plate has removed from nail bed.

TREATMENT OF ONYCHOMYCOSIS-

Several modalities can be used for the treatment of disease topical therapy, systemic therapy, combination therapy, nail removal and nail lacquer.

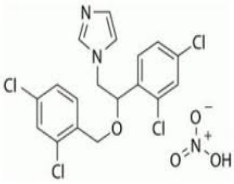
NAIL LACQUER-

Nail polish or nail varnish is used for people fingernail or toenail to decorate and/or protection the nail plate. Conventional nail lacquer have been applied as cosmetics since a large duration for beautification and protection of nails. Topical nail preparation like lacquer, enamel and varnish are integral part of today's beautification curative. It is help for defence to the nail plate, but most significantly it maximize their glowing, imparting colour. Formulation of active objects, large tissue concentration for capacity for the treatment of nail fungal disease.

The medicated drug are colourless and non-glossy to be applied for male patients, and more significant the drug are produce from the film so it can penetrate in to the nail the drug consisting polymer film may be considered as a matrix type controlled release the drug are closely spread with polymer and predicted the spread drug in polymer film before it is produce.

DRUG PROFILE

Miconazole Nitrate



Structure of Miconazole nitrate

Table No.2 Properties of Miconazole nitrate

Proprietary name	Desenex, Monistat, Zeasorb-AF
IUPAC Name	(RS)-1-2(2,4-Dichlorobenzyloxy)-2-(2,4 dichlorophenyl)ethyl-1H-imidazole
Molecular formula	$C_{18}H_{14}Cl_4N_2O$
Molecular weight	416.127g/mol
CAS No	22961 – 47 – 8
Melting Point	159-163 0C

Description: white crystalline and slightly smell

Solubility of Miconazole: Soluble in Ethanol, Acetone

Mechanism of action Miconazole interaction with 14-a dimethyl as, a cytochrome P—450 enzyme necessitate to alteration, lanostero to ergo sterol. As ergo sterol is a significance substance of the fugal cell membrane, conquer of its synthesis conclusion in largely cellular permeability for accountable leakage of cellular substance. Miconazole may also conquer endogenous respiration, interaction with membrane phospholopods, conquer the transformation of yeasts to mycelial forms, curb purine taking, and impair triglyceride and/or phospholide biosynthesis.

Pharmacokinetic The consumption of the oral drug delivery of the Miconazole (Nitrate) is come into possession to be 20% Volume of distribution is obtained to be 201/kg and plasma protein binding is 92%and plasma half – life is 24.1 hr

Dose The adult dose is 2% topically dose is 250mg and pediatric dose 0.330-0.500 mg/g

Category- **:** Anti – fungal

EXCIPIENT USED IN ANTI FUNGAL NAIL LACQUER-

- Nitrocellulose
- Propylene Glycol
- Ethyl Cellulose
- 2- Hydroxy propyl-B- Cyclodextrin

PREFORMULATIONS STUDIES

1 Recognition of Drug

A) Study of solubility

Saturated solubility of Miconazole nitrate was made by applying 10 ml of distilled water/ethanol/acetone in 25 ml volumetric flasks in thrice. Precaution was taken so that the drug dosage form stay in medium in spare. Then by using mechanical shaker, the flasks were shaken for 48 hours. The test sampling was done on 24^{th}& 48^{th} hour. The test sample is withdraw (1 ml after filtration) was soluble with suited medium and analyzed by using UV spectrophotometer at 223 nm.

B) Determination of the melting point

Melting point of drug determined by excellent measurement by fetching a few amount of drug in a capillary tube certain at once last and was attached in Thiel's melting point setup and temperature range at that the drug melted was presented. Mean of one of thrice readings was written.

C) λ max determination

100 mg of pure Miconazole nitrate was interpreted in a volumetric flask and soluble in a small few amount of phosphate buffer pH of 7.4 and volume made up to 100ml. 1ml of the trying firstly of dilution was taken and some diluted to 100ml. The trying test firstly solution scanned for excellent absorbance in double beam UV-Visible spectrophotometer in between the range of 400-200 nm against phosphate buffer pH 7.4 as the clean. Thrice reading were taken and mean was determined.

ANALYTICAL METHODS

A) Phosphate buffer solution preparation

0.2M Sodium hydroxide solution preparation

8gm of the sodium hydroxide was soluble in needful quantity of distilled H2O in a 1000ml volumetric medium and volume made up to 1000ml with distilled H2O.

0.2M potassium dihydrogen phosphate solution preparation –

27.218gm of potassium dihydrogen orthophosphate was soluble in needful quantity of distilled H2O in a 1000ml volumetric medium and volume was made up to 1000ml with distilled H2O.

The pH of phosphate buffer solution preparation

50ml of potassium dihydrogen phosphate solution was taken in a 200ml volumetric flask and 39.1ml of 0.2M sodium hydroxide solution was mixed and made up to 200ml with distilled H20.

B) Standard stock solution & Calibration curve of Miconazole nitrate preparation

Miconazole nitrate 100mg pure drug was right weighed and transfer into a 100ml volumetric flask of medium. And the volume was made up to 100ml with PBS of pH 7.4, to come into ownership standard stock solution of 100mcg/ml concentration. According above solution of 2ml, 4ml, 6ml, 8ml, 10ml, was pipetted out into other 100ml volumetric flask and made up to 100ml with PSB of pH 7.4 come into ownership a concentration range of 20µg/ml, 40µg/ml, 80µg/ml, and 100µg/ml solution. The analyzed of solution at 223nm by using UV-Visible spectrophotometer. The concentration versus absorbance was plotted on the graph. Drug constitute assessment and diffusion presented were aim on this calibration curve.

Drug-polymer compatibility determine

Pure drug FT-IR spectral analysis and polymer were portaged out singly and as composition. The compatibility between Miconazole nitrate, nitrocellulose, 2-HP-β-CD, propylene glycol and made development were carried out in the ratio 1:1. The test were located FT-IR window after mixing and triturating with potassium bromide.

Table-Drug-Polymer compatibility study

Composition	Ratio	250 C ±2 /60⁰ CRH	40⁰ C ±2 /75⁰C RH
Miconazole nitrate	100mg	6 Months	1 Month
Nitrocellulose	100mg	6 Months	1 Month
HP-β-CD	100mg	6 Months	1 Month
Propylene glycol	100mg	6 Months	1 Month
Miconazole + nitrocellulose	1:1	6 Months	1 Month
Miconazole + HP- β-CD	1:1	6 Months	1 Month
Final Formulation	NA	6 Months	1 Month

FORMULATIONS STUDIES

Preparation of nail lacquer of Miconazole nitrate

A) Making of Nitrocellulose

Approximate 5gms of cellulose base (cotton) is mixed to 50ml concentrated sulfuric acid and 25ml 70% nitric acid mixture and chilled to 5-10 ^{0}C to give cellulose nitrate. Then cotton was separated and washed in chilled water and with $NaHCO_3$ Solution separated all acid remain. It was then low at dried at room temperature.

B) Optimization of Nitrocellulose film former

Table-Optimization of nitrocellulose film former

Formulation Code	Nitrocellulose (% w/v)	Plasticizers (% w/v)		Ethanol (ml)
		PG	Glycerin	
NF1	3	10	....	10
NF2	5	10	....	10
NF3	7	10	....	10
NF4	9	10	....	10
NF5	3	....	10	10
NF6	5	....	10	10
NF7	7	....	10	10
NF8	9	....	10	10

4 different concentrations of nitrocellulose, 2%, 4%, 6%m 8%, were made applying 2 different plasticizers, Propylene glycol and glycerin at 10% concentration as per **Table No. 2 .**The optimal concentration for film formation was characterized by great determination by rating the thickness, tensile power, folding stress and H2O opposition.

Evaluation

a) Film thickness

The thickness of the flick was determined by applying screw gauge with a minimum count of 0.01 mm at many points of the films. The thickness was

b) Folding Endurance

Folding endurance of the films was measured by repeat foldaway a little strip of the film (approximately 2x2 cm) at the same site till it brittle. The numerous of times film could be crimped at the same site, without brittle gives the factor of folding endurance.

FORMULATIONS STUDIES

Preparation of nail lacquer of Miconazole nitrate

A) Preparation of Nitrocellulose

Around 5gms of cellulose base (cotton) is mixed to 50ml concentrated sulfuric acid and 25ml 70% nitric acid mixture and chilled to 5-10 ^{0}C to give cellulose nitrate. Then cotton was separated and washed in chilled H2O and with $NaHCO_3$ Solution to separate all acid remain. It was then easily slow dried at room temperature.

t=thickness of sample in cm.

b)-Water resistance

This is determine of the resistance to the aqueous permeability of the layer. This was by applying a continuous layer on a plane and plunging it in water. This weight before and after submergence was written and maximize in weight was calculated. Larger the maximize in weight lesser the water resistance.

Development of nail lacquer-

The Formulation was done according to formula shown .The Miconazole nitrate and Nitrocellulose was solublize in Ethyl alcohol in the important substance used a magnetic stirrer at an various speed. To clear the solution important substance of 2-HP-β-CD, Salicylic acid, and propylene glycol were mixed and volume to 100ml. The prepared nail lacquer was trans change to a narrow plastic screw capped glass bottle.

FORMULATION TABLE

Ingredients (%)	F0	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11
Miconazole nitrate	3	2	3	3	3	3	3	3	3	3	3	3
Nitrocellulose	7	7	7	7	7	7	7	7	7	7	7	7
Salicylic		6	11	16	21	16	16	16	16	16	16	16
2-H-β-CD	…	…	…	…	…	5	7.9	11	11	11	11	11
Ethyl cellulose	…	…	…	…	…	…	…	…	0.26	0.51	0.79	1.09
Propylene Glycol	11	11	11	11	11	11	11	11	11	11	11	11

Ethanol q.s	100	100	100	100	100	100	100	100	100	100	100	100

EVALUATION OF NAIL LACQUER

A) Nonvolatile content

10ml of preparation was take in a petri dish and firstly weighed were taken. This dish was put in the oven at 105^0C for 1hr, the petri dish was removed, cooled and weighed. This separated in weights was taken. Mean of one of three cycle readings was reported.

B) Drying time-A layer of formulation was used on a petri dish with the using by the brush.. The time for make a dry-to-hard layer was noted use by stop watch.

C) Smoothness to flow

The preparation was dip from a heighted of 1.5 inches into a glass plate and dispersed on a glass plate and made to wave vertically and see obtaining for smoothness of layer.

D) Gloss

Development of nail lacquer was used on the nail and gloss needful and done with marketed cosmetic nail lacquer.

FORMULATIONS STUDIES

1 Development of nail lacquer of Miconazole nitrate

E) Viscosity using the brook field viscometer.

F) Adhesion

There are neither to amount of evaluation tools resultant to use the medicinal nail lacquer at this time of duration. The instruments is used of chemical balance applied in the general laboratory as showed. One pan of the balance was transfer with two stainless steel plates. In between the plates a film of 4 cm^2 was made and adhered. The poise of the balance was adjusted by mixing a weight to the right pan of balance. The force needful to pull away the plates determined and compared with a commercial cosmetic nail lacquer test sample.

Force of Adhesion = Mass x Acceleration due to gravity

= Kilogram. meter/second^2

= Neutons. meter/second^2

Adhesive Strength = Force of Adhesion (N) / Surface area (m^2)

G) Drug content appraisal-

Nail lacquer equivalent to 200mg was soluble in 50 ml phosphate buffer solution of pH 7.4. Then the solution was supersonic for 15 mints. Resultant solution was filtered, made up to 100 ml with phaphate buffer solution of pH 7.4. From the above solution carried at 10ml and made up to 100ml with PBS of pH 7.4. Then the diluted solution was assesssment spectrophotometrically at wavelength of 223 nm and determined the drug constiuents.

H) Diffusion studies across artificial membrane

Diffusion studies were tested by Franz cell applying artificial membrane (cellophane) of 0.8µm. The membrane was loaded for 24hrs in solvent system and the solvent fill the receptor compartment.

Nail lacquer equivalent to 200mg was used evenly on the surface of the membrane.

The made membrane was assembled on the cell carefully to avoid entrapment of air bubbles in the membrane. The all weldment was maintained at 37^0C, and the speed of stirrings was kept constant for 20hrs. The 5ml aliquot of drug sample was taken at time intervals of **2hr, 4hr, 8hr, 10hr, 12hr, 16hr, and 20hrs** and was replaced by the fresh solvent. Samples were analyzed by double-beam UV spectrophotometer as per method mentioned in drug content appraisal. Each experiment was recurrent thrice.

I) In vitro permeation studies

Hooves from freshly slaughter cattle, free of adhering tending to attach and cartilaginous tissue, were loaded in distilled water for 24hrs. Membranes of approximate 1mm thickness were cut form the distal part of hooves. In vitro permeation studies were tested by using from Franz diffusion cell, the hoof membrane was situated by paying attention on the surface of the nail membrane. The targeted receptor compartment was filled with solvent phosphate buffer solution of pH 7.4, and the all weldment was maintained at 37^0C with constant mixing for 48hrs. The 5ml factor of number of drug sample was taken after a time intervals of **2, 4, 6, 8, 10, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48hrs.** transfered by the fresh solvent. The drug analysis was done by using double-beam UV spectrophotometer at 223nm.

J) Determination of antimicrobial activity

Candida albicans were wages for testing antifungal act by the cup-plate method. The culture was take up on sobouraud's agar slants. 20ml of melted sabouraud's agar medium was confirm 72hrs. Old 0.2 ml suspension of *Candida albicans* in the Petri dish and allowed to standard by conformity undisturbed for 15 mints. The cups (10mm diameter) were slugged in the Petri dish and filled with 0.05 ml of a solution of the sample. The plates were taken for diffusion at 40^0C for 1hr, and followed by incubation at 30^0C for 48 hrs. After done the incubation time the zone of suppression in millimeter were determined. On with test solution in every petri dish one cup was filled up with solvent, which play as control. The zone of suppression was noted and compared with control.

K) Stability study

Stability studies of nail lacquers were according ICH guidelines. Test samples were at temperature of $25\pm2\ ^0$C/60 $\pm$5% RH for 6 months and 40 $\pm$ 2^0C/75 $\pm$ 5% RH for 1 month. Then the samples were analyzed for non-volatile content, drying time, gloss, smooth of flow, drug content and diffusion across artificial membrane.

II. RESULT AND DISCUSSIONS

Results for Analytical Study

1 Scanning of drug

Pure Miconazole nitrate sample was scanned using phosphate buffer solution (PBS) of pH 7.4 between 200nm to 400nm using UV visible spectrophotometer. The tallest peak of Miconazole nitrate was obtained at 223nm **(Figure 12)** and thus the λ_{max} of Miconazole nitrate was at 223nm and was used some spectrophotometric evaluations during the investigation.

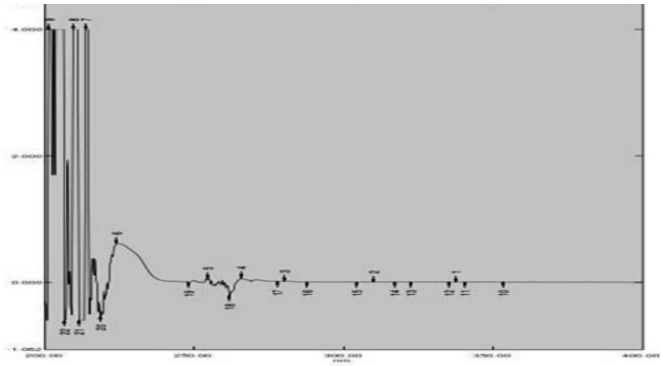
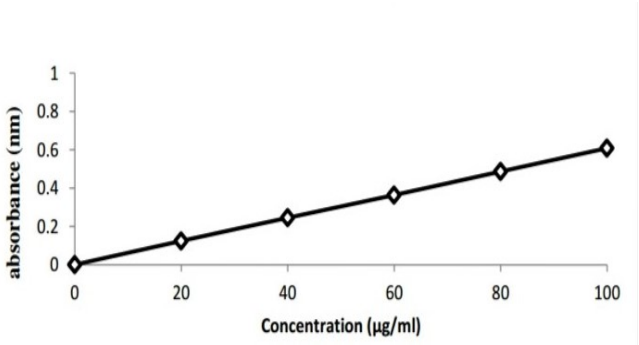


Figure 12: UV spectrum of Mixonazole nitrate in phosphate buffer solution of pH 7.4

Standard curve for Miconazole nitrate in phsphate buffer of pH 7.4

Standard solutions of Miconazole nitrate in various concentrations **(Table No. 13)** were made applying PBS pH 7.4 and their absorption was determined at 223nm. Drug concentration Vs. absorbance was plotted in **Figgure 13.**

Concentration(ug/ml)	Absorbance at 223nm
00	00
20	0.125
40	0.246
60	0.366
80	0.488
100	0.608



Calibration curve of Miconazole nitrate in phosphate buffer solution pH 7.4

2 PREFORMULATIONS STUDIES

1 Solubility studies of Miconazole nitrate

The result of solubility studies of pure Miconazole nitrate are given below:

Table No. 14: Solubility studies of Miconazole nitrate

Solvents	Solubility (mg/ml)
Ethanol	0.78
Water	0.03
Acetone	0.36

From the data, solubility profile of Miconazole nitrate was insoluble in water, soluble in ethanol and acetone.

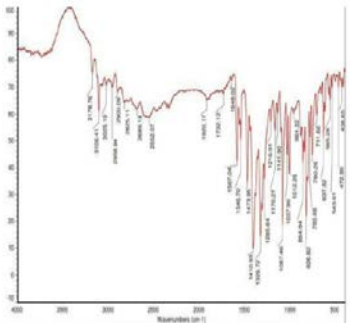
3. Melting point determination

The melting point was found to be $161^0C \pm 0.577$ and as per the IP 2007 melting point of Miconazole nitrate was within the range of 159-160 ^0C.

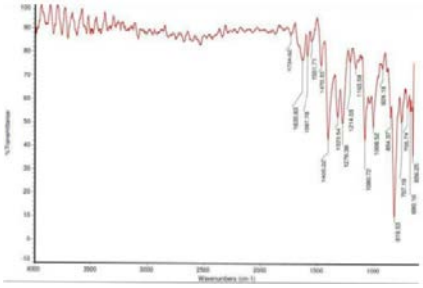
4 Drug excipient compatibility study

All the reference IR peaks of the pure drug Miconazole nitrate were also present in the spectra of mixture of drug-polymer and drug-permeation enhancer-excipients as mentioned in the above **Table No. 10.**

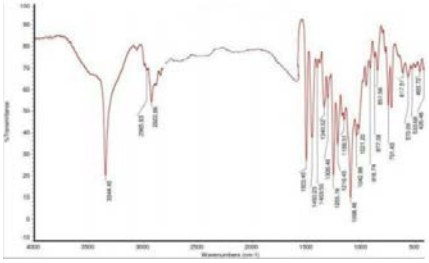
So FTIR study showed that there is no interaction between drug and permeation enhancer. So the drug and permeation enhancer are compatible. The IR spectrums were given in the **Figure 14 to 20.**



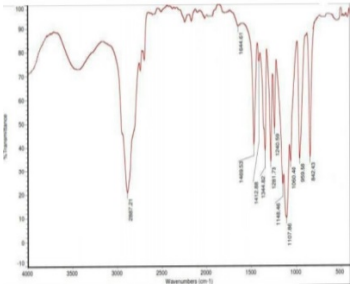
IR spectra of miconazole nitrate



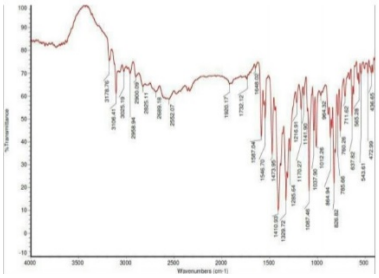
IR spectra of nitrocellulose



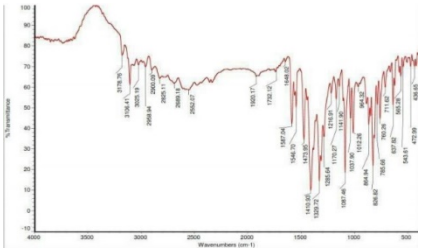
IR spectra of ethyl cellulose



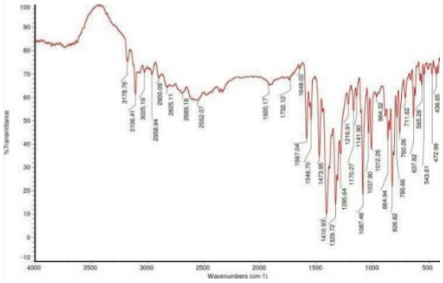
IR Spectra of the beta hydroxyl propyl cellulose



IR Spectra of Miconazole nitrate and nitrocellulose



IR Spectra of Miconazole nitrate and beta hydroxyl propyl cellulose



IR Spectra of Miconazole nitrate optimized Nail lacquer

TABLE NO. 15L FTIR COMPATIBILITY STUDY INTERPRETATION

FTIR spectra of pure Mixonazole nitrate		**Miconazole nitrate Optimized Nail Lacquer Formulation (F11)**	
Wave number (cm^{-1})	**Functional group**	**Functional group**	**Wave number (cm^{-1})**
3281.6	Imidazole C-N stretch	Imidazole C-N stretch	3178.79
3254.79	Aromatic CH stretch	Aromatic CH stretch	3106.43
2972.94	Aliphatic CH_2 stretch	Aliphatic CH_2 stretch	2958.96
2885.65	Aliphatic CH stretch	Aliphatic CH stretch	2900.10
1448.74	-CH_2- bending	-CH_2-bending	1773.97
1416.05	C-H bending (aliphatic)	C-H bending (aliphatic)	1410.95
1329.04	C-N stretch	C-N stretch	1329.74
1083.85	C-C stretch	C-C stretch	1087.48
		C=C aromatic	1587.06
		C=C aromatic	1546.75
		C-H bending (aromatic)	711.66

After spectral comparison it was confirmed that not compatibility reaction took place between drug and additives, as all main properties IR peaks of Miconazole nitrate are present in the physical mixture with individual additives and also in the final optimized formulation, F11. All the additives peaks were obtained to be entire indicating nice compatibility.

6.4 Formulation development of Nail Lacquer

The aim of the present study was to furnish a preparation for conquer fungal developed on toe nails or finger nails so that the looks of the nails are valuable. Preparation consists a film former nitrocellulose, permeation enhancer such as 2-H-β-CD, keratolytic agent like salicylic acid and an antifungal agent (Miconazole nitrate) and ethanol as solvent. Preparation is made by simple mixing method.

5 Optimization of nitrocellulose film former

Various concentration of film forming polymers were applied for film formation and then applied for optimization of film. Various concentrations were tried between 2-8%. From the conclusion, it was obtained that by maximizing the concentration polymer up to 6%, thickness and strength of film was coveted. While maximizing concentration more than 6%, sticky films were generated. Thus, 6% concentration of polymer was needful for some obtained of plasticizer. Plasticizer tried were Glycerin and Propylene glycol in 10% concentration each. Glycerin showed more sticky film which was unable to detach from surface. Thus, 6% nitrocellulose and 10% propylene glycol, due to its excellent film forming nature was choose for some optimization research.

A) Thickness (μm)

Unvarying thickness bespeak the unvarying of the preparation because of that suitableness of the executed procedure. Thickness of all the films determined by applying a micrometer screw gauge. Obtained result presented that thickness of all preparation varied from 55 to 59 μm.

The determined values were shown in the **Table No. 16.** Data for film thickness was duplicate within the coveted range of thickness identified through review of literatures for films.

B) Folding endurance

Folding endurance bespeak the flexibility of the polymer film. In order to evaluate the flexibility, the made films were subjected to folding endurance research. The numerous of bend a film can sustain without interruption will dictate its folding endurance. The computed measured determined were above 125 in all of the generated layers and are noted in **Table No. 16** and it was in the range of 126-178 for all the generated films. Regardless of polymer concentration applied, all the films presented nice folding endurance, bring out that the made films were having the capability to produce hold up the mechanical pressure along with nice flexibility. The folding endurance is a significant evaluation, which assure the flexibility of the generated films. Larger the folding endurance values better will be the flexibility of the films. 6% film (NF3) presented good folding endurance, because of that ensuring good flexibility.

Table No. 16: Optimization of nitrocellulose film former

Nitrocellulose Concentration (%w/v)	1	2	3	4
Thickness (μm)	59 ± 0.02	60± 0.02	56 ± 0.04	59 ± 0.03
Folding endurance	156	127	179	178
Tensile strength (Kg/cm^2)	2.57 ± 0.01	2.59 ± 0.01	2.61 ± 0.04	2.56 ± 0.02

B) Water Resistance

This is the determined of the opposition towards water permeability of the layer. This was done by applying uninterrupted layer on a surface and plunge it in water. The weight before and after immersion was noted and maximize in weight was determined. Large maximize in weight low the water opposition. Here Nitrocellulose Film of 6% (NF3) has relatively, low weight and has the better water resistance. The data were shown in **Table No. 17.**

Table No. 17: Water (W) resistance of nail lacquers

Formulation code	W_1 (g)	W_2 (g)
NF1	6.86	6.92

NF2	6.84	6.93
NF3	6.89	6.90
NF4	6.93	7.15
NF5	6.82	6.92
NF6	6.85	6.92
NF7	6.90	6.95
NF8	6.92	7.05

Having a base on above studies it was distinct that, NF3 formulation has the excellence properties needful for a nail lacquer and thence 6% w/v of nitrocellulose and 10% w/v of Propylene glycol was determined to be the optimum concentrations.

6 Evaluation of nail lacquer

All preparations presented coveted layer make, smoothness of flow was nice. Coveted quantity of nonvolatile substance (31-41%) was observed with complete evaporation of volatile matter leaving a thin layer; Conclusion were plotted in **Table No. 18.** Drying time was obtained within 52-127 sec. Demur for F2, where it presented 127 sec, all formulation showed fast drying rate. That is less than 60 seconds. The numerous amount were shown in **Table No. 19.**

A) Nonvolatile content

The non-volatile content of all formulation has been shown in the **Table No. 18,** given below

Table No. 18: Nonvolatile content of nail lacquers.

Formulation code	Non-volatile content (%)	Formulation code	Non-volatile content (%)
F0	34 ± 0.38	F6	38 ± 0.81
F1	34 ± 0.38	F7	37 ± 0.70
F2	42 ± 0.81	F8	33 ± 0.40
F3	40 ± 0.40	F9	36 ± 0.41
F4	38 ± 0.81	F10	34± 1.22
F5	38 ± 0.71	F11	38 ± 0.81

B) Drying time

Table No. 19: Drying time of nail lacquers

Formulation code	Drying time (sec)	Formulation code	Drying time (sec)
F0	51	F6	57
F1	53	F7	60
F2	129	F8	57
F3	53	F9	60
F4	59	F10	59
F5	60	F11	58

C) Smoothness of flow and Gloss:

Both these parameters was obtained to be acceptable as can be received. The nail lacquer dipped onto the glass plate was obtained to dispersed and resultant in unvarying smooth layer. The gloss of the applied lacquer was worthy of comparison with marketed cosmetic test sample achieving the cosmetic credence.

D) Viscosity

The viscosity of the test sample ranged from 100 to 220 centipoise it was obtained that between140to160 centipoise the product was clean and glossy. Furthermore this viscosity range furnished nice attachment and flow property. Viscosity outside this range generate translucence and minimize gloss which will not be cosmetically satisfactory.

Table No. 20: Viscosity of nail lacquers

Formulation code	Viscosity	Formulation code	Viscosity
F1	100	F7	200
F2	111	F8	140
F3	122	F9	142
F4	133	F10	146
F5	184	F11	146
F6	198		

E) Adhesive strength

The adhesive strength of the implied batch was shown to be worthy of comparison with marketed sample and thence can be arrived to exhibit equal adhesive strength on applied nail surface.

Table No. 21: Adhesive strength of nail lacquers

Formulation Code	Force of Adhesion (N)	Adhesive strength (N/m^2)
F11	0.6	12.6
MARKET	0.7	16

SAMPLES		

F) Percentage drug content determination

Percentage drug ingredients for all the lacquers were obtained to be satisfy and in between 86.25-99.01% which is shown in **Table No. 22.** Largest % of drug constituents was obtained to be 99.01% (F11) and the smallest % of drug content was 86.25% (F3). Drug content more than 90% in the Preparation shows the large no. of quantity of drug present in the Preparation, Confirming that the methods of preparation and the constituents choose are not poignant the stability of drug. Large drug constituents also show to confirm that, a nice curative result can be arrived.

Table No. 22: Percentage drug content

Formulation Code	Drug content (%)	Formulation code	Drug content (%)
F0	90.01	F6	89.38
F1	91.52	F7	90.13
F2	93.76	F8	98.02
F3	86.27	F9	98.24
F4	94.30	F10	97.56
F5	95.82	F11	99.03

G) Diffusion studies across artificial membrane

Diffusion research of all the preparations were obtained by artificial membrane (cellophane membrane -0.8μm) for 48 hrs. The diffusion studies were made on all formulations as per shown in **Table No. 12.**

The top formulated batch F0 did not dwell of any permeation enhancers and in vitro diffusion revealed that only 27.10% drug released till 48 hrs. Thus trials were planned to incorporate a permeation enhancer. Salicylic acid at concentrations of 5% (F1), 10% (F2), 15% (F3) and 20% (F4) was tested out. The diffusion studies shown that only 64.18%, 65.10%, 68.34% and 69.10% respectively was obtained in 18 hours. It was clean that salicylic acid has valuable the drug permeation due to its keratoytic activity. But it was also determined that the drug permeation was not yet done and some maximize in salicylic acid concentration is not arrived to valuable permeation. Thence it was declared to choose 15% w/v of salicylic acid as the optimum concentration.

To further improve drug diffusion it was decided to include 2-H-β-CD in concentration of 5% (F5), 7.5% (F6) and 10% (F7) into formulations. The drug release and diffusion across membrane was found to improve in presence of 2-HP-β-CD. At concentration of 5%, 82.40% diffusion in 28% hour was observed. In case of F6, 89.0% diffusion as observed at 28th hours. It was also observed that as concentration of 2-HP-β-CD increased drug diffusion also improved drastically as clear from almost complete drug diffusion of 98.40% release in 20th hour with 7.5% concentration.

Though, inclusion of 2-H-β-CD has improved drug diffusion to 98.40%, it was observed that the release was found to be complete within 20 hours. Therefore to sustain the drug release over an extended period it was decided to include a rate controlling polymer ethyl cellulose at concentration of 0.25% (F8), 0.5% (F9) and 0.75% (F10) and 1.0% (F11) into formulation. The result showed an extended and completed release of 96.80% at 28th hr. in F8 and 93.0% till 36th hour in F9. In F10, a drug diffusion of 97.20% was observed at 40th hr. And finally when the concentration of ethyl cellulose was increased to 1% in F11, a drug diffusion of 98.12 percent which sustained over a period of 48 hours was achieved.

The formulation F11 was selected as the optimized nail lacquer formulation based on drug diffusion studies.

Table No. 23: Comparative study and optimization of salicylic acid concentration

Time (hr)	PERCENTAGE DRUG RELEASE (μg/ml)			
	F1	F2	F3	F4
0	0	0	0	0
2	9.83	11.23	13.37	15.27
4	10.21	12.07	14.99	16.89
6	13.29	14.37	16.37	17.26
8	16.43	17.89	18.87	20.15
10	26.59	28.97	32.06	30.38

12	32.46	36.35	40.23	36.17
16	43.12	42.32	48.39	42.97
20	48.24	49.99	51.83	50.12
24	49.66	50.83	52.62	54.35
28	52.56	54.90	56.84	58.40
32	56.27	58.77	59.35	60.23
36	58.97	59.99	61.29	63.47
40	60.19	62.19	63.95	66.25
44	62.53	63.27	65.97	68.86
48	64.19	65.15	68.36	69.12

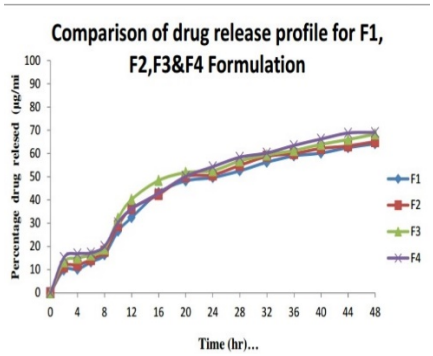


Figure 22: Comparative Dissolution profile of F1 v/s F2 v/s F3 v/s F4

Table No. 24: Comparative study and optimization of 2-HP-β-CD concentration

Time (hr)	PERCENTAGE DRUGT RELEASE		
	F5	F6	F7
0	0	0	0
2	26.26	32.13	39.32
4	32.24	43.56	49.86
6	38.52	52.83	59.66

8	46.53	61.66	67.73
10	48.23	69.36	76.46
12	56.29	76.26	85.06
16	65.16	80.03	92.16
20	76.46	83.36	98.42
24	79.96	88.97	96.26
28	82.42	89.08	94.25
32	80.26	86.35	93.17
36	79.46	84.17	91.84
40	77.33	82.18	90.09
44	76.66	80.88	89.18
48	74.74	78.26	88.98

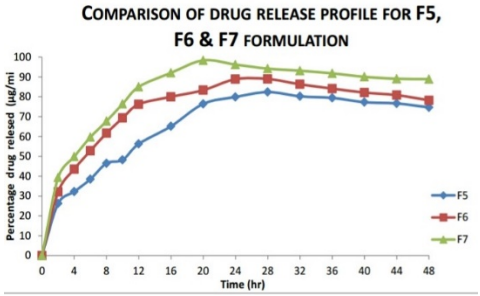


Figure 23: Comparative Dissolution profile of F5 v/s F6 v/s F7

Table No. 25: Comparative study and optimization of Ethyl cellulose concentration

Time (hr)	PERCENTAGE DRUG RELEASE (µg/ml)			
	F8	F9	F10	F11
0	0	0	0	0
2	29.66	26.53	19.46	12.83
4	34.13	31.96	30.46	27.13
6	45.57	40.44	36.92	28.32
8	51.17	44.92	48.85	32.73
10	62.36	53.23	50.75	46.26
12	69.76	60.14	56.80	50.22
16	75.94	68.67	60.25	58.67
20	88.46	72.33	65.72	60.22

24	93.24	83.46	72.68	68.13
28	96.82	89.77	80.52	70.23
32	95.06	95.85	85.73	78.86
36	94.58	93.79	90.63	84.16
40	93.15	90.73	97.57	88.86
44	90.77	89.88	94.23	90.26
48	89.03	88.74	91.32	98.13

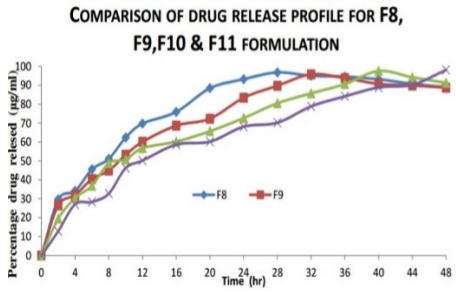


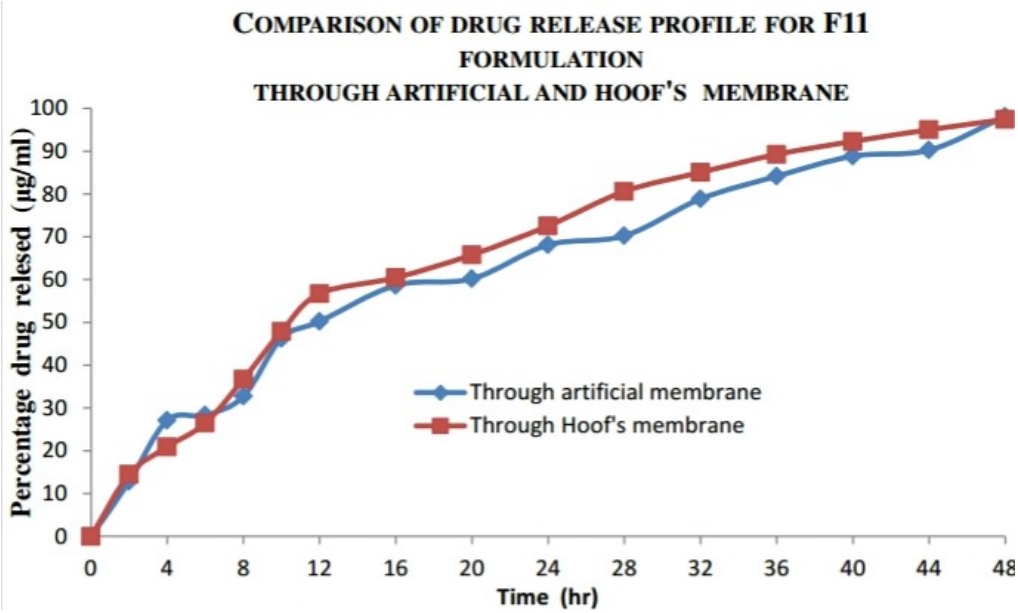
Figure 24: Comparative Dissolution Profile of F8 v/s F9 v/s F10 v/s F11

H) In vitro ungual permeation studies

To excite and constituting an imitation diffusion research with that of *in vivo* conditions, i.e. across nail plate, a diffusion study across hooves resultant form freshly slaughtered cattle was done. There was no importance difference and drug release data obtained across artificial hoof's membrane. This research achieve sureness which is nice *in vitro in vivo* correlation can be demur.

Table No. 26: Comparison of drug diffusion across artificial membrane and hoof's membrane

Time	PERCENTAGE DRUG RELEASE (µg/ml)	
	Drug diffused through artificial membrane	% drug diffused through hoof's membrane
0	0	0
2	12.83	14.51
4	27.13	20.91
6	28.32	26.46
8	32.73	36.76
10	46.26	47.91
12	50.22	56.73
16	58.66	60.44
20	60.21	65.83
24	68.12	72.56
28	70.23	80.61
32	78.86	85.06
36	84.16	89.26
40	88.86	92.32
44	90.26	95.05
48	98.13	97.46



Comparison of drug diffusion across artificial membrane and hoof's membrane

I) ANTI-MICROBIAL STUDY

The zone of inhibition for the many preparation was investigated, and it was obtained range from 17-22mm, which is allow to compare with that standard with 21mm. The show that all the formulations were sensitive to the microorganisms *Candida albicans.* Conclusion are shown in **Table No. 26.**

Table No. 27: Zone of inhibition of Miconazole nitrate Nail lacquers

Formulation Code	Zone of Inhibition (mm)	Formulation code	Zone of Inhibition (mm)
F1	23	F7	19
F2	19	F8	25
F3	22	F9	18
F4	23	F10	24
F5	18	F11	23
F6	17	Standard	22

J) Stability studies

Stability studies were applied to obtain the shelf life and storage condition of a product. In this determination F11 were subjected to speed up stability studies for as per day of 1 month. Stability studies were performed in according to ICH guidelines with importance adjustments.

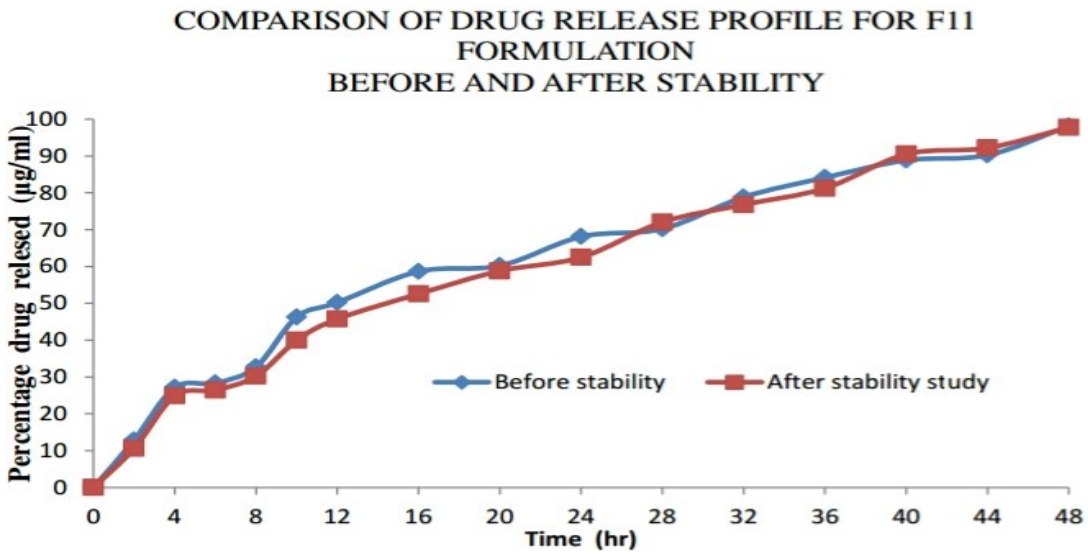
The studies were obtained to ascertain the changes in physical properties such as Non-volatile content, Drying time, % drug content, drug diffusion at three different conditions f higher temperature (40 ± 2^0C) for 1 month. The conclusion are shown in **Table No. 28, 29.**

Table No. 28: Stability studies data of F11

Parameter	Initial	After
Non content	36±0.82	35±0.36
Dryintin (sec)	57	59
Drug content	99.04	98.52

Table No. 29: Invitro Diffusion profile of F11 upon stability studies

Time	PERCENTAGE DRUG RELEASE (µg/ml)	
	Before stability	After stability
0	0	0
2	12.83	10.61
4	27.13	24.91
6	28.32	26.44
8	32.73	30.26
10	46.26	39.96
12	50.22	45.76
16	58.66	52.56
20	60.21	58.82
24	68.12	62.51
28	70.23	72.06
32	78.86	76.82
36	84.16	81.27
40	88.86	90.54
44	90.26	92.21
48	98.12	97.75



In vitro diffusion profile of F11 upon stability studies

The evaluation of formulation after stability study presented there was no important change with respect Non-volatile content, Drying time % drug content and drug diffusion with respect to result obtained before stability charging. Thence it was received that the formulation were obtained to acceptable stability compliance needful as per ICH guidelines.

III. CONCLUSION

- The main of the today studies was to formulate and evaluate the Miconazole nitrate nail lacquer as an ungual drug delivery system for the treatment of onychomycosis.
- Miconazole nitrate selected as a drug, the preparation were prepared with Salicylic acid. And by the FTIR research, resultant that the drug and the additives applied in the Preparation. Proved the formulations are sensitive to the required volatile contents by the microbial study.
- The Preparation are sensitive to the microorganism *Candida albicans.* Confirmed by the microbial study.
- The preparation were survived at 40^0c for 1 month .confirmed by stability study.
- By In vitro permeation study is proved in vitro in vivo correlation can be acceptable.
- Conclusion is achieved by the *in vitro* studies shown that formulation F11 given a complete drug release which sustained over 48 hours. The F11 formulation had salicylic acid at concentration of 15% w/v as keratolytic agent and 10% w/v of **(2-Hydroxypropyl)-β-cyclodextrin**as permeation enhancer. Shown result that the combination of permeation enhancer and keratolytic

agent resulted in an improved permeation rate and also a complete and sustained drug release.

- ❖ The formulation of F11 was choose as the nail lacquer formulation based on optimization as well as drug diffusion studies.
- ❖ There was no more interchangeable in the values after stability test confirmed by the stability study. It was obtained that the preparations were achieved to confirmed stability compliance necessary as per ICH guidelines.

By the above research, it can obtained that medicated lacquers shown to be a nice base as a drug delivery system for the ungual drug delivery of an antifungal in the treatment of onychomycosis, which is applying in the treating of the nail infections, the medicated nail lacquers can be also applied for glowing and glamorous of nails with easily and time consuming useful for applying which is improves patient compliance.

REFERENCES

[1] Gupchup GV, Zatz JL. Structural characteristics and permeability properties of the human nail: A review. j Cosmet Sci 1999;50:363-385.

[2] Rajendra VB, Baro A, Kumari A, Dhamecha DL, Lahoti SR, Shelke SD. Transungual Drug Delivery: An Overview. J Appl Pharm Sci 2012;2(1):203-09

[3] Patel RP, Naik SA, Patel NA, Suthar AM. Drug delivery across human nail. Int J Curr Pharm Res Vol1Issue1 2009;01:01-7

[4] Suryavanshi KA, Basru PR, Katedeshmukh RG. Review on Nail Transungual Drug Delivery System. Am. J. PharmTech Res. 2012;2(5):222-04.

[5] Sabreen J, Divyakumar B, Kiran B. Preungual drug delivery systems of terbinafine hydrochloride nail lacquer. Asian J Pharm 2008;02:53-06.

[6] Shirwaikar AA, Thomas TA, Lobo R, Prabhu KS. Treatment of Onychomycosis: An Update. Ind J Pharm Sci 2008 Nov-Dec;70(6):710-14.

[7] Rajendra VB, Baro A, Kumari A, Dhamecha DL, Lahoti SR, Shelke SD. Transungual Drug Delivery: An Overview. J Appl Pharm Sci 2012;2(1):203-09

[8] Patel RP, Naik SA, Patel NA, Suthar AM. Drug delivery across human nail. Int J Curr Pharm Res Vol1Issue1 2009;01:01-7

[9] Suryavanshi KA, Basru PR, Katedeshmukh RG. Review on Nail Transungual Drug Delivery System. Am. J. PharmTech Res. 2012;2(5):222-04.

[10] Sabreen J, Divyakumar B, Kiran B. Preungual drug delivery systems of terbinafine hydrochloride nail lacquer. Asian J Pharm 2008;02:53-06.

[11] Shirwaikar AA, Thomas TA, Lobo R, Prabhu KS. Treatment of Onychomycosis: An Update. Ind J Pharm Sci 2008 Nov-Dec;70(6):710-14.

[12] Lalit SK, Panwar SA, Darwhaker G, Jain DK. Formulation and Evaluation of Fluconazole Amphiphilogel. Der Pharmacia Lettre, 2011; 3 (5):125-31

[13] Lalit SK, Panwar SA, Darwhaker G, Jain DK. Formulation and Evaluation of Fluconazole Amphiphilogel. Der Pharmacia Lettre, 2011; 3 (5):125-31

[14] Kobayashi Y,Komastu T,Sumi M,Numajiri S,Miyamoto M,Kobayashi D, Sugibayashi K,Morimoto Y.In vitro permeation of several drugs through the human nail plate:Relationship between physicochemical properties and nail permeability of drugs.Eur.J.Pharm.Sci.2004;21:471-477.

[15] 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.

[16] Walters,K.A, Flynn,G.L, Marvel,J.R.Peneration of the human nail plate:the effects of vehicle pH on the permeation of miconazole. J.Pharm.Pharmaco.1985;37:498- 499.

[17] Pravin DC, Shilpa PC, Pramod KK, Bothiraja C. Drug delivery through nail 2006 cited 2010 Nov 29. Available from: URL : http://www.pharmainfo.net/reviews/drugdelivery-through-nail-review

[18] Boni E. Elewski, Onychomycosis: Pathogenesis, Diagnosis, and Management, Clin. Microbiol. Rev. July 1998 vol. 11 no. 3 415-429

[19] Jason A. Winston , Jami L. Miller, Treatment of Onychomycosis in Diabetic Patients, Clinical.diabetesjournals.org 2008 Nov-Dec; 70(6): 710–714

[20] Westerberg DP, Voyack MJ. Onychomycosis: current trends in diagnosis and treatment. American family physician. Dec 2013. 88 (11): 762–70.

[21] Weinberg JM, Koestenblatt EK, Tutrone WD, Tishler HR, Najarian L. Comparison of diagnostic methods in the evaluation of onychomycosis. J. Am. Acad. Dermatol. 2003. 49 (2): 193–7

[22] Elewski, BE; Hay, RJ. Update on the management of onychomycosis: highlights of the Third Annual International Summit on Cutaneous Antifungal Therapy. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America. August 1996. 23 (2): 305–13

[23] Phillip R, And Bassler M, Treating Onychomycosis, University of Michigan Medical School, Ann Arbor, Michigan, Am Fam Physician. 2001 Feb 15;63(4):663-673.

[24] Cohen PR, Scher RK. Topical and surgical treatment of onychomycosis. J. Am. Acad. Dermatol. 1994; 31:S74–S77.

[25] Gupta AK, Lynde CW, Jain HC, Sibbald RG, Elewski BE, Daniel CR, Watteel GN, Summerbell RC. A higher prevalence of onychomycosis in psoriatics compared with non-psoriatics: A multicentre study. The British journal of dermatology. 1997. 136 (5): 786–789.

[26] Shireesh KR, Chandra SB, Vishnu P, Prasad MVV. Ungual Drug Delivery System Of Ketoconazole Nail Lacquer. Int J Appl Pharm 2010;2(4):17-19.

[27] Shivkumar HN, Vaka SR, Madhav NV,Chandra H, Murthy SN. Bilayered nail lacquer of terbinafine hydrochloride for treatment of onychomycosis, J Pharm Sci, 2010, 99(10): 4267-76.

[28] Pati Nikunja Basini , Dey Biplab Kr., Das Sudip , Sahoo Subhas. Nail Drug Delivery System: A Review. J. Adv. Pharm. Edu. R.2012;2(3):101-109.

[29] Xiaoying H, Thomas CKC, Sherry B, Christine L, Howard I, Ronald CW. Enhanced econazole penetration into human nail by 2-n-nonyl-1,3-dioxolane. J Pharm Sci 2002;92:142-8.

[30] Pati N B, Biplab D K, Sudip D, Subhas S. Nail Drug Delivery System: A Review, Journal of Advanced Pharmacy Education & Research.2012. 2 (3) : 101-109.

[31] Tandel A, Agrawal S, Wankhede S, Transungual permeation of the voriconazole nail lacquer against trichophyton rubrum, Journal of Drug Delivery & Therapeutics; 2012. 2(1) :162-8.

[32] Merekar A N , Pattan S R, Parjane S K, Dighe N S, Nirmal S A, Gore S T, Phad M B, Preungual Drug Delivery System Of Enalapril Maleate Nail Lacquer. Inventi Impact: Ndds . 2012 , Article Id- " Inventi:Pndds/366/12:102-5

[33] Hadzidedic S. Elezovic A, Hadzovic S, , Kostic S. Characterization of antifungal nail lacquer formulations containing fluconazole. Sci Pharm 2010;78:624.

[34] Ghannoum MA, Long L, Pfister WR. Determination of the efficacy of terbinafine hydrochloride nail solution in the topical treatment of dermatophytosis in a guinea pig model. Mycoses 2009;52:35-43.

[35] Sigurgeirsson B, Olafsson J, Steinsson J, Kerrouche N, Sidou F. Efficacy of amorolfine nail lacquer for the prophylaxis of onychomycosis over 3 years. J Eur Acad Dermatol Venereol 2010; 24(8):910-5

[36] Monti D, Saccomani L, Chetoni P, Burgalassi S, Senesi S, Ghelardi E, et al. Hydrosoluble medicated nail lacquer: in vitro permeation and corresponding antimycotic activity. Br J Dermatol 2010;162(2):311-7.

[37] Sudaxshina M. Design of antifungal nail lacquer formulations containing antifungal. Sci Pharm 2012;622:29.

[38] Togni G, Mailland F. Antifungal activity, experimental infections and nail permeation of an innovative ciclopirox nail lacquer based on a water-soluble biopolymer. J Drugs Dermetol 2010 May; 9(5):525-30.

[39] Bohn M, Kraemer KT. Dermatopharmacology of ciclopirox nail lacquer topical solution 8% in the treatment of onychomycosis. J Am Acad Dermatol 2000 Oct; 3(4):S57-69.

[40] Nadkar S, Lokhande C. Current Trends in Novel Drug Delivery-An OTC Perspective. Pharma times 2010 Apr; 42(4):17-23.

[41] Roberts DT, Taylor WD, Boyle J. Guidelines for treatment of onychomycosis. B J Dermatol 2003; 148: 402–410.

[42] Andrea M K , Elizandra S , Mauro L B, Tânia U N ,Celso V N , Antifungal Activity and Nail Permeation of Nail Lacquer containing Piper regnellii

(Miq.) C. CD. var. pallescens (C. DC.)Yunck (Piperaceae) Leave Extracts and Derivatives, 2010, ISSN 1420-3049

[43] Alessandro S, Monti D, Togni G, Mailland F. Ciclopirox: Recent Nonclinical and Clinical Data Relevant to its Use as a Topical Antimycotic Agent. Drugs 2010 Nov; 70(16):2133-2152.

[44] Mitkari B V , Korde S A ,Mahadik K R and Kokare C R, Formulation and Evaluation of Topical Liposomal Gel for Fluconazole, Indian J.Pharm. Ed. Res. 44(4), Oct - Dec, 2010

[45] Tulli A, Ruffilli MP, De Simone C,The Treatment Of Onychomycosis With A New Form Of Tioconazole, Chemioterapia. 1988 Jun;7(3):160-3

[46] Scher RK, Breneman D, Rich P, Savin RC, Feingold DS, Konnikov N, Shupack JL, Once-Weekly Fluconazole (150, 300, Or 450 Mg) In The Treatment Of Distal Subungual Onychomycosis Of The Toenail, J Am Acad Dermatol. 1998 Jun;38(6 Pt 2):S77-86.

[47] Bentley B Phillips. The Treatment Of Onychomycosis with Miconazole Tincture, Atr Med Journal. 1982; 62: 57-58.

[48] Indian Pharmacopoeia, Government of India, Ministry of Health and Family Welfare. Vol. II Delhi: Controller of Publications.2007:771

[49] Tripathi KD. Essentials of medical pharmacology. New Delhi:Jaypee;2008. 428-30

[50] P. P. Sharma. Cosmetics- Formulation, Manufacturing & Quality control. 3rd ed. Vandana publications; Delhi; 2005; 467-479.

[51] Academie BDEL, Sciences PDES. Structure of Cellulose — Nitric Acid Knecht Compounds . I . Spectroscopic Examination. 1965;XIII(6):377–83.

[52] Handbook of pharmaceutical excipients. USA: American pharmaceutical association; 1986 ; 210,262,592.

[53] Murd S. Drug delivery to the nail following topical application. Int. J. Pharm. 2002; 236. 1–26.

[54] Kiran, S., and Shekar C. Ungual drug delivery system of ketoconazole nail lacquer. Asian J Pharm. 2010; 1-3.

[55] Mertin D, Lippold B C, In-vitro permeability of the human nail and of a keratin membrane from bovine hooves: penetration of chloramphenicol from lipophilic vehicles and a nail lacquer. Department of Pharmaceutical Technology, Heinrich-Heine-University, Düsseldorf, Germany. 2011

[56] Venjnovic I, Huonder C, Betz G. Permeation studies of novel terbinafine formulations containing hydrophobins through human nails in vitro. Int J Pharm 2010;397(1-2):67-76.

[57] Rudresh S P. Transdermal drug delivery system for Diclofenac sodium. Dissertationsubmitted to Rajiv Gandhi University of Health sciences. Jan

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