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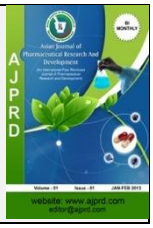

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Research Article

Formulation and Evaluation of Nail Drug Delivery System of Anti Fungal Drug

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A B S T R A C T

The purpose of this study was to prepare nail lacquer for nail drug delivery system of anti fungal drug in order to improve the physicochemical parameters that influence the drug permeation through a nail plate to reach the systemic circulation and the neighbouring target sites. The success of local topical therapy for onychomycosis depends on the achievement of effective chemical concentrations into/through the human nail plate; therefore, a suitable antifungal drug must be coupled with an appropriate delivery method. The method should maximize the effect of the active principle by aiding its diffusion into the nail bed to levels exceeding the minimum inhibitory concentration (MIC) against local infection by dermatophytes. Thus, a suitable carrier may be needed to enhance drug penetration through the nail barrier.

The nail lacquer formulations were prepared by simple mixing method and analyzed for non volatile content, gloss, smoothness to flow, drug diffusion studies, and % drug content. Among all formulations, nail lacquer prepared with 2% oxiconazole, 6% nitrocellulose, 1% ethyl cellulose, 15% salicylic acid, 10% propylene glycol and 10% 2-H β-CD exhibited good non volatile content, drug release, drug content estimation and zone inhibition i.e. F4 formulation. The drug release profiles were achieved 93.2% at 12 h. The *in vitro* ungual permeation studies revealed a good *in vitro in vivo* correlation. Nail lacquer were substantially stable after 1 month storage at 40±2°C.

Keywords: Onychomycosis, nail lacquer, nail growth, stability.

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INTRODUCTION

Topical treatment of skin and nail diseases is desirable in terms of patient acceptability and reduction of side effects associated with systemic drug delivery. This is particularly the case for nail diseases as they are frequently difficult to cure and also require long periods of treatment. (1)

The inadequate research and knowledge regarding the properties of keratinized nail plate, the nail bed and the nail matrix caused a lesser focus on ungual system. (2)

Horny structure of nail plate is responsible for penetration of drug across it. As it is hard enough, the penetration becomes difficult, only a fraction of topical drug penetrates across it. Hence the effective therapeutic concentration is not achieved. The nail plate may appear abnormal, as a result, variety of diseases occur. These diseases can be cured by achieving desired therapeutic concentration of drug by nail drug delivery system. (3)

The success of local topical therapy for onychomycosis depends on the achievement of effective chemical concentrations into/through the human nail plate; therefore, a suitable antifungal drug must be coupled with an appropriate delivery method. The method should maximize the effect of the active principle by aiding its diffusion into the nail bed to levels exceeding the minimum inhibitory concentration (MIC) against local infection by dermatophytes. Thus, a suitable carrier may be needed to enhance drug penetration through the nail barrier. (4)

The human nail plate consists of three layers; the dorsal & intermediate layer derived from the matrix, & the ventral layer from nail bed. The intermediate layer is three - quarter of the whole nail thickness & consists of the soft keratin. The upper layer, dorsal, are only a few cell layers thick but consisting of hard keratin, with a relatively high sulphur content, mainly in the form of amino acids cysteine, which constitutes 94 % by weight of nail. [5]

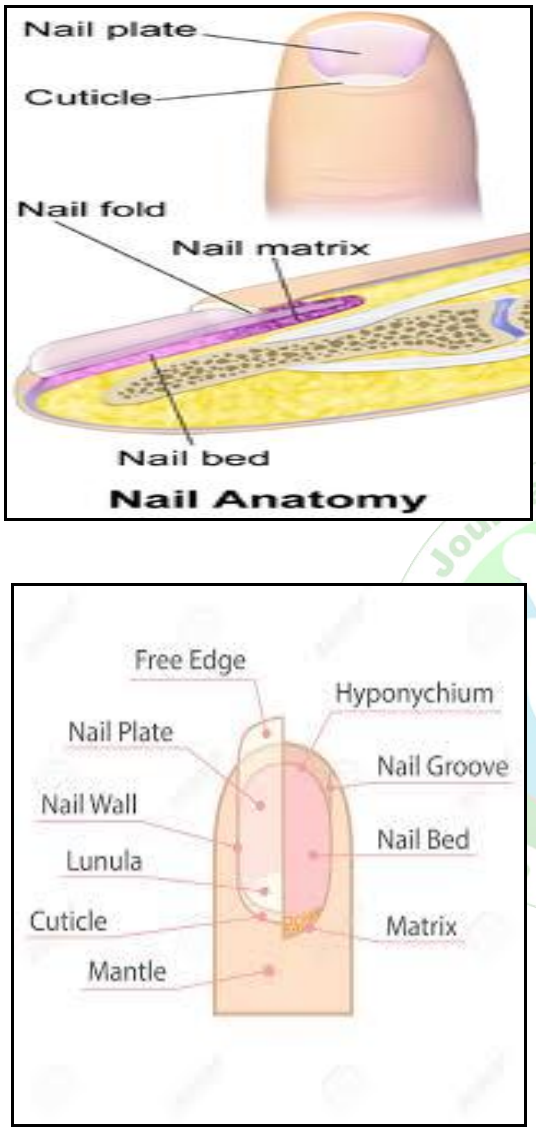

Figure 1: Structure of nail and nail anatomy

Structure and anatomy of human nail:

Located on the distal part of each digit, Nails (with hair, sebaceous and sweat glands) are known to be appendages of the skin. Nails are the invagination of the outer layer of the skin, the Epidermis and composed of very small cells, called onychocytes, which are mainly made up of keratin, a fibrous protein. Human nail is composed of many parts like nail plate, nail bed, matrix, nail cuticle, eponychium, hyponichium, specialized ligaments and nail folds.

Nail Plate: Nail plate is the hard translucent, most visible and functional part sits on and covers the nail bed and composed of keratin. Proximally and laterally the nail plate is surrounded by the nail folds, which covers its proximal and lateral margins. The nail plate is more porous than skin, hence water can pass through it more easily than through the skin. The nail plate looks like a single solid piece but it is made up of 100 layers of dead, flattened cells which are arise from the germinal matrix epithelium of the nail bed. The pinkish color of the plate is due to blood capillaries below the nail plate, which receives blood supply from ulnar and radial digital arteries. The Free edge or distal edge is the anterior cutting margin of the nail plate that extends over the tip of the finger and toe.

Bed: It is the living skin below nail plate or we can say that the area upon which the nail rests. It grows from the distal margin of lunula towards the epidermis of hyponichium (free edge) and looks pinkish due to blood capillaries visible through translucent nail plate. Bed epithelium (a thin layer of tissue) is act as junction between nail bed and nail epithelium. Nerves are also present in the nail bed.

Nail Matrix: The nail matrix is specialized epithelial structure that lies below the proximal nail fold. The nail matrix epithelium composed of basal cells which in turn differentiate into spinous cells and then into orthokeratotic cells that forms the nail plate. The nail matrix is also known as root of the fingernail. This portion composed most of the portion of the nail and the nail bed.

Lunula: It is the whitish visible semicircle (Half-moon) part at the base of the nail plate. At this half-moon part, the nail bed is so tightly packed with keratin that the capillaries are masked by the amount of keratin. The lunula is largest in the thumb and often absent in the little finger.

Cuticle and Eponychium: Generally, cuticle and eponychium create confusion with each other. They are not same. The cuticle is the dead skin (almost invisible) at the base of the finger nail or toenail and is often removed during manicure. But eponychium is the living skin that is present at the base of the nail plate and covers the matrix area. Cuticle seals the space between nail plate and the skin. This sealing prevents the entry of foreign particle and micro-organisms and helps in avoiding injury and infection.

Hyponichium: It is the most distal, soft, slightly thickened layer of skin that is located between the fingertip and the free edge of nail plate and forms a water proof protective barrier that prevents microorganisms from invading and infecting nail bed.

Nail Folds: These are the folds of normal skin that surrounds the nail plate and forms the nail grooves which furrows on the side wall.

The side wall is also known as lateral nail fold which is the skin overlapping the side of the nail.

Specialized Ligaments: It is a tough band of fibrous tissue that attaches the nail bed and matrix bed to the underlying bone. These ligaments are situated at the base of the matrix and around the wedges of nail bed.

Functions of nail:

- A healthy nail protects the distal phalanx, the finger tip, and the surrounding tissues from the injuries.

- It helps to enhance delicate movements of the distal digits through counter pressure exerted on the pulp of the finger.
- The nail acts as a counterforce when the end of the finger touches an object and hence enhancing the sensitivity of the fingertip.
- Without nails on the fingertips, it is not possible to grab and hold the things accurately or precisely. [6-7]

MATERIALS AND METHODS

MATERIALS

Oxiconazole and HP -β-CD were obtained as gift sample from Yarrow fine chemicals, Mumbai. Nitrocellulose and ethyl cellulose was obtained from Kemphasol, popatwadi, Mumbai. Salicylic acid and ethyl alcohol was obtained from nice chemicals, Pvt. Ltd, Cochin. Other chemicals were used for analytical grade.

Development of nail lacquer of oxiconazole

Development of nitrocellulose:

About 5 gm of cellulose base (cotton) was taken in a beaker and 50 ml of concentrated sulphuric acid and 25 ml of 70 % nitric acid was added. The above mixture was cooled to 5-10 min to obtain cellulose nitrate. Then cotton was removed and washed in cold water with sodium bicarbonate ($NaHCO_3$) solution to remove all acid residues. Then it was dried at room temperature.

Nitrocellulose film former

Table 1: Nitrocellulose film former

Formulation code	Nitrocellulose (% w/v)	Plasticizers (% w/v) PG	Glycerin	Ethanol (ml)
NF1	2	10	-	10
NF2	4	10	-	10
NF3	6	10	-	10
NF4	8	10	-	10
NF5	2	-	10	10
NF6	4	-	10	10
NF7	6	-	10	10
NF8	8	-	10	10

Four different concentrations of nitrocellulose, 2%, 4%, 6%, 8%, were prepared using two different plasticizers, propylene glycol and glycerin at 10% concentration as per table no 4. The optimum concentration for film formation was determined by evaluating the thickness, tensile strength, folding endurance and water resistance. [8]

Evaluation of nitrocellulose film

a. Film thickness

The thickness of the film was measured by using screw gauge with a least count of 0.01 mm at different spots of the films. The thickness was measured at five different spots of film and average was taken.

b. Folding endurance

Folding endurance of the films was determined by repeatedly folding a small strip of the film (approximate 2×2 cm) at the same place till it broke. The number of times film could be folded at the same place, without breaking gives the value of folding endurance. [9]

c. Tensile strength

The instrument used to measure the tensile strength was designed in pharmaceutics laboratory especially for this project work. The instrument is a modification of chemical balance used in normal laboratory. One pan of the balance was replaced with one metallic plate having a hook for attaching the film. The equibrium of the balance was adjusted by adding weight to the right pan of balance. The instrument was modified in such a way that the patch can be fixed up between two hooks of horizontal beams to hold the test film. A film of 2.5 cm length was attached to one side hook of the balance and other side hook was attached to plate fixed up to the pan.

Tensile strength (T) $T=Mg/Bt$ Dynes/cm^2

T= force at break
M= mass in grams
g= acceleration due to gravity 9.8 m/sec^2
B= breadth of the specimen in cm
t=thickness of sample in cm.

d. Water resistance

This is the measure of the resistance towards water permeability of the film. This was done by applying a continuous film on a surface and immersing it in water. The weight before and after immersion was noted and increase in weight was calculated. Higher the increase in weight lowers the water resistance. [10]

Formulation of nail lacquer

The mixture of oxiconazole and nitrocellulose film was dissolved in ethyl alcohol in the required quantity using a magnetic stirrer at a constant speed. To above clear solution required quantity of 2-HP-β-CD, salicylic acid and propylene glycol were mixed thoroughly and made up to the volume to 100 ml. The prepared nail laquer was transferred to a narrow mouthed, plastic screw capped glass bottle. [11].

Table 2: Formulation chart of nail lacquer

Ingredients (%)	F1	F2	F3	F4	F5	F6	F7
Oxiconazole	2	2	2	2	2	2	2
Nitrocellulose	6	6	6	6	6	6	6
Salicylic acid	5	10	20	15	15	15	15
2-HP-β-CD	-	-	-	10	10	10	10
Ethyl cellulose	-	-	-	1.00	0.75	0.50	0.25
Propylene glycol	10	10	10	10	10	10	10
Ethanol (q.s)	100	100	100	100	100	100	100

Preformulation studies of drug

Preformulation studies were performed on the drug (API), which included melting point determination, solubility and compatibility studies.

The following preformulation studies were performed for oxiconazole.

Identification of drug

Solubility Studies:

Saturated solubility of oxiconazole was prepared by using 10 ml of distilled water/ethanol/acetone in 25 ml volumetric flasks in triplicate. A precaution was taken so that drug remains in medium in excess. Then by using mechanical shaker, the flask was shaken for 48 h. The sampling was done on 24 and 48 h. The sample withdrawn (1 ml after filtration) was diluted with appropriate medium.

Determination of melting point:

Melting point of drug was determined by taking a small quantity of drug in a capillary tube sealed at one end and was placed in thiel's melting point apparatus and temperature range which the drug melted was noted. Average of triplicates readings was noted.

Scanning for drug absorption (λmax) using double beam spectrophotometer:

100 mg of pure drug was taken in a volumetric flask and dissolved in a little of phosphate buffer pH of 7.4 and volume made up to 100 ml. 1 ml of the above solution was taken and further diluted to 100 ml. The above solution scanned for maximum absorbance in double beam UV-visible spectrometer in between the range of 400-200 nm against phosphate buffer pH 7.4 as the blank. Triplicate readings were taken and average was calculated. [12]

Development of UV spectrophotometric method for analysis of oxiconazole:

Preparation of standard calibration curve:

The stock solution (1 mg/ml) was prepared by weighed accurately 50 mg of oxiconazole nitrate and transferred to a 50 ml volumetric flask then makeup the final volume with methanol. Different concentrations (2, 4, 6, 8, and10µg/ml) of solutions were prepared from the stock and measure the absorbance at 210 nm by using UV-Visible spectrophotometer and reagent blank. The data are compiled in table 8. [13]

FTIR study:

IR study was carried out to check purity of drug. It was determined by fourier transform region of 4000 to 400 cm^{-1} at resolution of 4 cm^{-1} by dispersing sample in KBr and compressing into disc by applying pressure of 5 tons for 5 min in hydraulic press. The pellet was placed in light path and the spectrum was obtained. Infrared spectrophotometer (FTIR-Shimadzu). [14-15]

Evaluation of nail lacquer

Nonvolatile content:

8 ml of sample was taken in a glass petri dish of about 8cm in diameter. Samples were spread equally. The dish was placed in the oven at 105ºC for 1 hr. The petri dish was removed, cooled, and weighed. The difference in weight of sample after drying was determined that gives the volatile content present. The difference in weights was recorded.

Drying time:

A film of sample was applied on a glass petri dish with the help of brush. The time to form a dry to touch film was noted using a stopwatch.

Water resistance:

This is the measure of the resistance towards water permeability of the film. This was done by applying a continuous film on a surface and drying, then immersing it in water. The weight before and after immersion was noted

and increase in weight was calculated. Higher the increase in weight, lower the water resistance.

Smoothness to flow:

The sample was poured on a glass slide on an area of 1.5 square inches and spread on a glass plate by making glass slide to rise vertically. And smoothness of flow was determined by comparing with standard marketed nail lacquer.

Gloss:

Sample of nail lacquer was applied over the nail and gloss was visually seen, compared with marketed cosmetic nail lacquer. [16-17]

Viscosity:

The viscosity of nail lacquer was determined using a Brookfield viscometer with spindle no 64. The sample was taken in a closed jar to minimize the solvent evaporation. Sample should be aged at least 8 h at 250 ºC before performing the test. At 250ºC, shake vigorously, start timer, insert spindle into the sample to the scored line, with the motor running at 60 rpm. Spindle should be in correct position in less than 1 min. Read the instrument at the end of 10 min then switch the speed control to 6 rpm and read the instrument again at the end of another 10 min. [18]

Drug content estimation:

Nail lacquer equivalent to 200 mg was dissolved in 50 ml phosphate buffer solution of pH 7.4. Then the solution was ultra sonicated for 15 min. The resulting solution was filtered, made up the volume up to 100 ml with phosphate buffer solution of pH 7.4. From the above solution take 10 ml and made up to100 ml with PBS of pH 7.4. Then the diluted solution was estimated spectrophotometrically at wavelength of 210 nm and determined the drug content. [19-20]

Diffusion studies across artificial membrane:

Diffusion studies were performed using artificial membrane (cellophane).The membrane was soaked for 1h in solvent system (phosphate buffer, pH 7.4), and the receptor compartment was filled with solvent. Test vehicle equivalent to 4 mg was applied evenly on the surface of the membrane. The prepared membrane was mounted on the cell carefully to avoid entrapment of air bubbles under the membrane. The whole assembly was maintained at 37°C, and the speed of stirring was kept constant (600 rpm) for 24 h. The 2 ml aliquot of drug sample was taken after a time interval of 2 h and was replaced by the fresh solvent. Each experiment was replicated at least thrice. The drug analysis was done using UV spectrophotometer at 210 nm. [21]

In- vitro transungual permeation studies:

In vitro transungual studies were carried out using Franz diffusion cells of volume 25 ml, were performed by using Franz diffusion cell at 37±5°C and phosphate buffer (pH 7.4) fitted with a custom made Teflon nail holder. Drug solution equivalent to 100 µg prepared in buffer was placed in the donor compartment. The receiver compartment was filled with phosphate buffer (pH 7.4) volume was 25 ml. The active diffusion area was 0.25 cm. The receiver compartment was stirred at 600 rpm with a 3 mm magnetic stir bar. Intermittent samples of 2 ml were drawn from the receiver compartment at 2 h intervals for 36 h and the amount of oxiconazole transported was measured. Equal volume of fresh buffer was replaced in the receiver compartment followed by each sampling. The drug analysis was by using double-beam UV spectrophotometer, at 210 nm. [22]

Determination of zone of inhibition:

Agar cup-plate method was used to determine *in vitro* antifungal activity against Candida albicans. Nutrient agar plates were prepared and sterilized by autoclaving at 120ºC, 15 pounds pressure for 15 min. 70 ml nutrient agar media was then inoculated with fungal strain i.e. C. albicans (2 ml of inoculums to 100 ml of nutrient agar media). The mixture was then poured in two sterilized petri plates and five wells of 5 mm diameters were prepared via sterile cork borer in each petri plate. 0.2 ml each of optimized formulation, control formulation were transferred to the cups aseptically and labeled accordingly as optimized and control formulation. Negative and positive controls were also prepared which consist of un-inoculated media and media seeded with test organism but deprived of antifungal agent, respectively. The prepared petri plates were maintained at room temperature for 2 h to allow the diffusion of the solutions in to the medium and then incubated at 28°C for 48 h. The diameter of zone of inhibition surrounding each of the well was recorded. [23]

Stability study:

Stability studies of nail lacquer were carried out as per ICH guidelines. The samples were stored at the temperature 40±2°C/75±5% RH for 1 month. Then the formulation was evaluated for drying time, non-volatile content, *in vitro* adhesion, water resistance and drug content. [24]

RESULTS AND DISCUSSION

Pre formulation studies

Solubility:

Oxiconazole was found to be freely soluble (1-10 parts of solvent required for 1 part of solute) in phosphate buffer of pH 7.4 and methanol, slightly soluble (100-1000 parts of solvent required for 1 part of solute) in ethanol.

Melting point:

The melting point of oxiconazole, was determined by capillary method using Digital Melting Point apparatus was found to be 137°C. The value was comparable with the literature value of 137 to 138°C. The melting point as obtained as corresponding the literature value confirms the purity of the sample.

Compatibility studies:

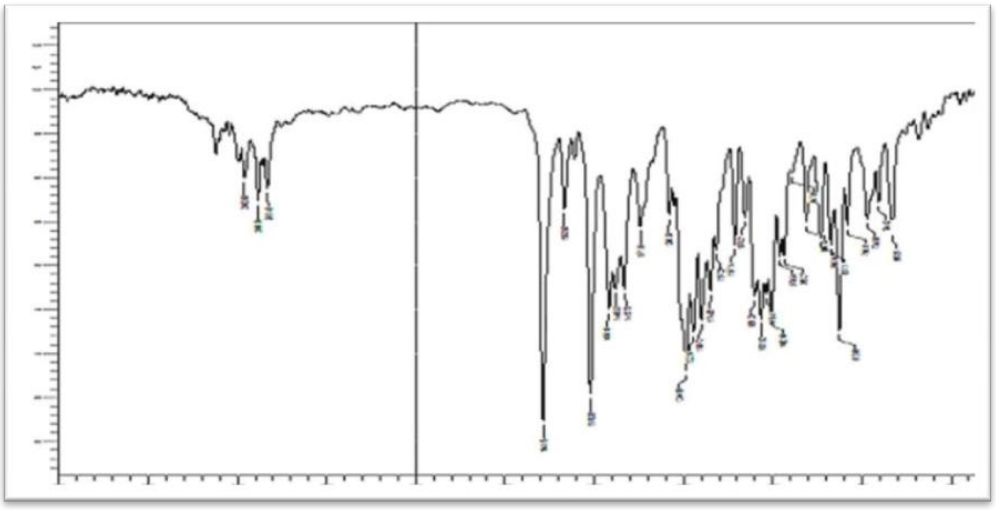

Figure 2: FTIR spectra of oxiconazole

All the characteristic IR peaks related to pure drug, oxiconazole were also appear in the IR spectrum of mixture of drug-polymer, so there was no any chemical incompatibility between drug and polymer.

Table 3: FTIR spectral of pure oxiconazole

Functional group	Wave number (cm^{-1})
C=C stretching	1510.501
C-Cl stretching	735.109
C-H stretching	2945.077
C=N stretching	1441.093
N-O stretching	1370.643

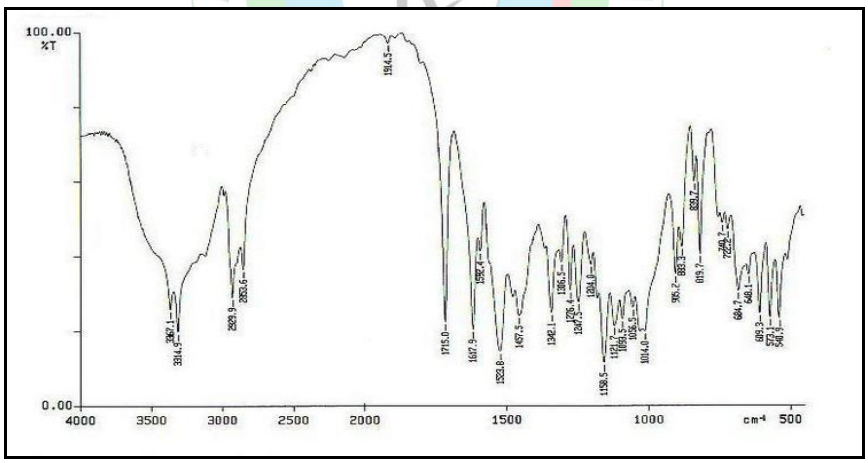

Figure 3: FTIR spectra of physical mixture of drug

Table 4: FTIR spectral comparison of pure drug and physical mixture

Function group	Wave number (cm^{-1})	
	Pure drug	Physical mixture
C=C stretching	1510.501	1568.411
C-CI stretching	735.109	684.210
C-H stretching	2945.077	2934.116
C=N stretching	1441.093	2462.014
N-O stretching	1370.643	1560.542

Evaluation parameters

Evaluation of nitrocellulose film

Table 5: Nitrocellulose film former

Nitrocellulose concentration (%w/v)	1	2	3	4
Thickness (µm)	57±0.03	58±0.02	56±0.04	59±0.02
Folding endurance	154	127	177	176
Tensile strength (kg/cm^2)	2.55±0.02	2.59±0.01	2.60±0.03	2.56±0.02

Table 6: Evaluation of nail lacquer

Formulation code	**Non volatile content (%)**	**Drying time (sec)**	**Viscosity**	**Drug content (%)**	**Zone inhibition (mm)**
F1	31 ± 1.42	51	100±0.45	89.56 ± 0.42	18
F2	33 ± 0.32	53	111±0.33	90.00 ± 0.32	20
F3	35 ±0.41	50	122±0.23	91.75 ±0.47	17
F4	42± 0.84	125	160±0.65	94.34± 0.98	23
F5	39 ± 0.40	59	146±0.72	93.23 ± 0.40	22
F6	37 ± 0.93	58	152±0.41	92.50 ± 0.93	19
F7	35± 0.71	56	140±0.69	91.87± 0.78	20

*Standard Deviation (n=3)

It was seen that as the polymer concentration increases from 1% w/v to 2% w/v the non-volatile content increases. Drying time for formulations F4 to F7 was found between 56 seconds to 125 seconds. It was found that as the polymer concentration increases, the drying time increases respectively. The viscosity of the sample ranged from 100 to 220 centipoises and it was observed that between 140 to 160 centipoises the product was clear and glossy. Drug content more than 90% in the formulation shows the high amount of drug present in the formulation, ensuring that the methods of formulation and the ingredients selected are not affecting the stability of drug. The zone of inhibition obtained were determined in candida albicans organism and compared with oxiconazole standard. From the analysis, formulation showed comparable zone of inhibition with that of oxiconazole standard solution.

Table 7: Water resistance of nail lacquer

Formulation code	**W1(g)**	**W2(g)**	**Difference in weight (g)**
F1	6.00	6.23	0.23
F2	6.00	6.21	0.21
F3	6.00	6.22	0.22
F4	6.00	6.51	0.51
F5	6.00	6.50	0.50
F6	6.00	6.45	0.45
F7	6.00	6.39	0.39

Smoothness to flow and gloss:

Figure 4: Smoothness to flow and gloss of nail lacquer

***In vitro* diffusion studies across artificial membrane:**

Table 8: *In vitro* diffusion studies across artificial membrane

Sl. No	Time (h)	Cumulative percentage drug release(±SD*)						
		F1	F2	F3	F4	F5	F6	F7
1	0	0	0	0	0	0	0	0
2	1	2.9±0.9	3.0±0.2	3.0±0.81	5.9±9.91	4.8±8.40	3.00±2.11	2.99±0.06
3	2	3.37±2.48	4.0±3.27	5.08±8.8	10.9±9.21	5.3±8.99	5.05±8.72	5.69±1.06
4	3	8.93±2.46	9.15±0.3	15.6±8.6	36.4±2.34	15.9±0.41	9.87±6.54	21.7±1.39
5	4	13.5±0.76	13.9±4.3	33.1±1.5	42.9±3.94	33.3±3.33	17.2±3.38	34.0±5.95
6	5	27.2±3.31	29.2±1.64	41.1±0.3	50.9±7.53	41.1±7.65	31.2±0.69	41.9±0.27
7	6	33.1±1.55	38.3±1.66	47.5±6.7	66.0±1.96	57.5±6.72	52.7±6.91	48.2±9.34
8	8	49.6±7.32	48.9±7.4	55.4±8.2	79.9±9.96	65.4±8.29	59.0±1.96	56.2±0.92
9	10	54.9±0.21	56.3±5.44	62.8±9.0	89.2±8.69	75.4±3.79	65.5±5.56	60.2±0.33
10	12	64.3±4.28	67.7±0.01	70.7±3.8	94.3±1.50	91.0±6.12	79.9±7.36	74.1±8.26

*Standard Deviation (n=3)

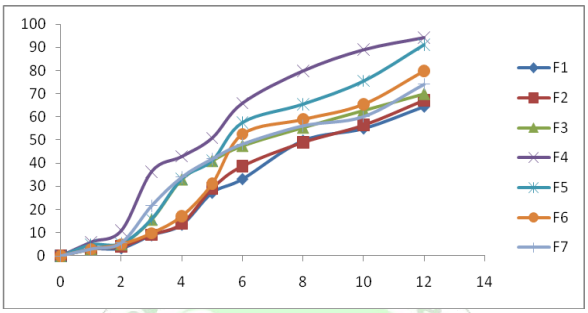

Figure 5: *In vitro* diffusion studies across artificial membrane

Formulation F4, F5 containing highest concentration of penetration enhancer (2-HP-β-CD ethyl cellulose, salicylic acid) showed the highest release of 94.3% and 91.0%. It was found that as the penetration enhancer concentration increases, the release of drug increases.

In vitro transungual permeation studies:

Table 9: *In vitro* release study of formulations F1-F7 in phosphate buffer pH 7.4

Sl. No	Time (h)	Percentage drug release(±SD*)						
		F1	F2	F3	F4	F5	F6	F7
1	0	0	0	0	0	0	0	0
2	1	2.2±0.9	3.0±0.2	3.0±0.81	4.8±9.91	3.8±8.40	3.00±2.11	2.99±0.06
3	2	3.37±2.48	3.4±3.27	5.08±8.8	12.0±9.21	5.3±8.99	5.05±8.72	5.69±1.06
4	3	8.93±2.46	9.15±0.3	15.6±8.6	35.4±2.34	15.9±0.41	9.87±6.54	21.7±1.39
5	4	13.5±0.76	13.9±4.3	33.1±1.5	40.7±3.94	33.3±3.33	17.2±3.38	34.0±5.95
6	5	27.2±3.31	26.2±1.64	41.1±0.3	51.9±7.53	41.1±7.65	31.2±0.69	41.9±0.27
7	6	33.1±1.55	32.3±1.66	47.5±6.7	65.0±1.96	57.5±6.72	40.7±6.91	48.2±9.34
8	8	49.6±7.32	48.9±7.4	55.4±8.2	77.6±9.96	65.4±8.29	59.0±1.96	56.2±0.92
9	10	54.9±0.21	56.3±5.44	62.8±9.0	87.2±8.69	75.4±3.79	65.5±5.56	60.2±0.33
10	12	64.3±4.28	68.7±0.01	70.7±3.8	93.2±1.50	90.1±6.12	80.8±7.36	75.9±8.26

*Standard Deviation (n=3)

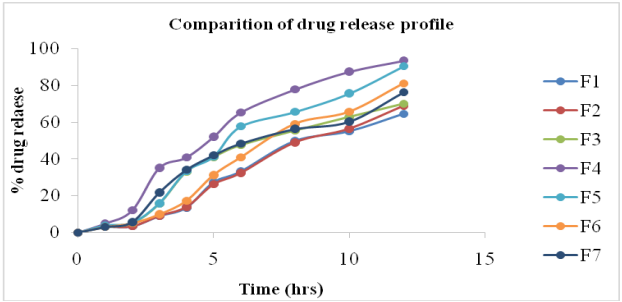

Figure 6: *In vitro* transungual permeation studies

In vitro permeation studies, it was found that formulation F4 showed release of 93.2% at the end of 12 h. Figure 6 illustrates the comparative *in vitro* drug release profile for nail lacquer for formulations F1 to F7.

Table 10: Accelerated stability studies for optimized formulation F4

Parameters	Before	After
Non volatile content	42± 0.84	41± 0.34
Drying time (sec)	125	122
Drug content (%)	94.34± 0.98	93.34± 0.56

The stability study data indicated that the medicated nail lacquer, showed good stability for 1 month when it was stored at temperature of 40±02ºC. There is no significant change is observed in colour, volatile content, drying time, % drug content and *in vitro* drug diffusion.

CONCLUSION

Oxiconazole was chosen as a model drug, the formulations were prepared with permeation enhancers (2-hydroxypropyl)- β-cyclodextrin and keratolytic agent and salicylic acid. Then, these lacquers were evaluated for drying time, non volatile content, drug content and drug diffusion. The results obtained from the *in vitro* studies indicate that formulation F4 showed a complete drug release which sustained over a period of 12 h. The F4 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 and ethyl cellulose as rate controlling polymer. This indicates that the combination of permeation enhancer and keratolytic agent resulted in an improved permeation and also a complete sustained drug release.

The medicated nail lacquers proved to be a better tool as a drug delivery system of an antifungal drug in the treatment of onychomycosis.

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