AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

Development and Optimization of Nail Lacquer Containing Fluconazole for Transungual Drug Delivery System

Amrita Sawant Desai[1]*, Shripathy D[1], A.R.Shabaraya[1]

1.Department of Pharmaceutics, Srinivas College of Pharmacy, Valachil, Mangalore-574143, Karnataka, India

ABSTRACT

The present investigation focuses on the Optimization and formulation of medicated nail lacquer containing Fluconazole for transungual drug delivery system using ethyl cellulose as polymer and two different penetration enhancers. Fluconazole is a tri azole antifungal drug having broad spectrum activity. It acts by inhibiting 14 – α demethylase, a cytochrome P450 enzyme which converts lanosterol to ergosterol. Ergosterol inhibition causes increase in permeability of cellular membrane of fungi and hence leakage of cellular components. In present study Formulations were designed according by the design expert software 8.0.7.1 and the central composite design was selected for designing of experiments. The prepared formulations were evaluated for the different parameters such as drying time, smoothness of flow, gloss, water resistance, non – volatile content, drug content, *in – vitro* diffusion studies, *in – vitro* permeation studies, drug release kinetic studies. By applying the available information from the evaluation of nail lacquer 35 optimized formulations were obtained and out of which three were selected for further studies. Three optimized products were subjected to different evaluation parameters, drug release kinetics, anti – fungal testing and stability studies.

Key words: transungual drug delivery, Fluconazole, optimization, penetration enhancers, *in – vitro* permeation studies, ethyl cellulose.

*Corresponding Author Email: amritasawantdessai@gmail.com

Received 25 March 2014, Accepted 02 April 2014

Please cite this article in press as: Desai AS *et al.*, Development and Optimization of Nail Lacquer Containing Fluconazole for Transungual Drug Delivery System. American Journal of PharmTech Research 2014.

INTRODUCTION

The most common route of administration is oral drug delivery system, but it have significant disadvantage in case of the drug which shows a high hepatotoxicity. Especially in case of the anti-fungal drug they show high hepatotoxicity when taken orally. In order to overcome this limitation of oral drug delivery, most of the anti-fungal drugs can be formulated in form of topical formulations[1, 2].

Topical formulations are highly desirable in treating the nail disorders due to its localized effects, which in turns causes reduction of the systemic side effects related to oral therapy in case of antifungal drug. However the effectiveness of the topical therapy for nail (transungual drug delivery- drug delivery through the nail) is limited minimal drug permeability through the nail plate. The nail permeability is quite low and limits topical therapy to early/mild disease state such as Onychomycosis, Leuconychia, and Onychogryops etc. Hence the absorption of the drug into the nail unit, the nail plate is highly desirable to treat this disease state. The nail plate behaves like a concentrated hydro gel to permeating molecules and the diffusion of the molecules through the nail plate has been compared to the diffusion of non – ionic electrolytes through the polymer gel[3, 4].

Medicated nail lacquers are viscous liquid formulations, containing a film forming agent, plasticisers, viscosity imparters, penetration enhancers, solvent etc[5]. After the application of nail lacquer on the infected nail, due to rapid evaporation of the solvent it leads to formation of an occlusive film which acts a “depot” leading to optimized and sustained release of the drug to the affected area. Hence a high tissue concentration of the drug is achieved which is needed for the treatment of the fungal infections[6, 7]. Medicated nail lacquer offers many advantages as compared to other topical formulations such as gels and creams. It causes better adherence of the drug to affected site, it is not easily removed by rubbing, washing and whipping, it is easy to apply and can be used in case of the elderly patient receiving multiple therapy[8].

Fluconazole is a tria azole derivative having broad spectrum activity. It has chemical formula of 2-(2,4-difluorophenyl)-1,3-*bis*(1*H*-1,2,4-triazol-1-yl)propan-2-ol. However it is associated with the side effect of causing high hepatotoxicity, which can be overcome by formulating in form of medicated nail lacquer for the treatment of fungal infections[9]. In present study optimization approach was applied for formulation of medicated nail lacquer in order to obtain a best possible formulation using ethyl cellulose as polymer and Thioglycolic acid and dimethyl sulfoxide as penetration enhancers.

MATERIALS AND METHOD

Fluconazole, ethyl cellulose, glycerine was purchased from Yarrow chemical, Mumbai, India. Propylene glycol was obtained from Lobo chemicals, Mumbai, India. Thioglycolic acid, Dimethyl sulfoxide and ethanol was purchased from Hi- media, Mumbai, India. Fluconazole nail lacquers were prepared accordingly the data obtained by Optimization software. All together data for 15 formulations were generated by the software. The nail lacquer was prepared by simple mixing method using ethyl cellulose in concentration range of 10%w/v to 12%w/v and Thioglycolic acid, dimethyl sulfoxide in range of 1%v/v to 2.5%v/v.

Spectrum Measurement:

The standard solution of Fluconazole was prepared by dissolving 100mg in 100ml of phosphate buffer pH 7.4, further diluted to get 100µg and was scanned between 400-200nm in UV-Visible spectrophotometer (Jasco V-630 UV/Visible spectrophotometer), to obtain λ max[10].

Construction of calibration curve:

A stock solution of Fluconazole was prepared by dissolving 100mg in 100ml of phosphate buffer pH 7.4. From this stock solution, suitable dilutions were prepared using the same solvent in the range of 10, 20, 30, 40, 50, 60, 70 & 80µg/ml. At λ max, the absorbance of all the concentration solutions was measured against phosphate buffer pH 7.4 as blank. Standard curve between concentration and absorbance was plotted and intercept (B) and slope (K) values were noted[10].

Drug excipients compatibility studies[10]:

FTIR can be used to investigate and predict any physiochemical interaction between different excipients. It was scanned from 4000 to 400 cm^{-1} in a FTIR spectrophotometer (F.T.I.R, Shimadzu). The IR spectrum of the physical mixture was compared with those of pure drug and polymer and peak matching was done to detect any appearance or disappearance of peaks.

Preparation of Nail lacquer[11]:

The mixture of Fluconazole and the polymer was dissolved in ethanol in required quantity using magnetic stirrer at constant speed. To this solution glycerin and propylene glycol were added and mixed thoroughly at constant speed. To above clear nail lacquer solution penetration enhancers i.e. dimethyl sulfoxide & Thioglycolic acids were added and mixed thoroughly. Prepared medicated nail lacquer was transferred to a narrowed mouthed, plastic screw capped glass bottles

Experimenting of design[12, 13]:

Central composite design is an experimental design technique, by which the factor involved and their relative importance can be assessed. In the present study the formulation, which is design,

based on central composite design containing 3 factor and the experimental trials were, performed at all possible combinations. To study all possible combination of all levels, a three factor, two- level full factorial design was constructed and conducted in full order.

The three independent formulation variable evaluated include:

Factor A: Amount of Ethyl cellulose (X_1), Factor B: volume of DMSO (X_2), Factor C: Volume of Thioglycolic acid (X_3)

Table 1. Actual level of different factors varied in optimization.

Coded values	Actual values		
	Ethyl Cellulose	DMSO	Thioglycolic Acid
-1	10mg	1.00ml	1.00ml
+1	12mg	2.50ml	2.50ml

The dependent variable measured were time for 80 % of drug release (hrs) and drying time (sec). High and low levels of each variable were coded as 1 and -1 respectively. The range of factor must be chosen in order to adequately measure is effects on response variables. The range of each factor was chosen from the preliminary studies. Stepwise regression analysis was used to find out the control factors that significantly affect response variables.

Table 2. Formulation details of Nail lacquer containing Fluconazole (F1 to F8).

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
Fluconazole(gms)	1	1	1	1	1	1	1	1
Ethyl cellulose(gms)	10	12	10	12	10	12	10	12
Propylene glycol(ml)	10	10	10	10	10	10	10	10
Glycerine(ml)	10	10	10	10	10	10	10	10
DMSO(ml)	1	1	2.5	2.5	1	1	2.5	2.5
Thioglycolic acid(ml)	1	1	1	1	2.5	2.5	2.5	2.5
Ethanol (ml)	100	100	100	100	100	100	100	100

Table 3. Formulation details of Nail lacquer containing Fluconazole (F9 to F10).

Ingredients	F9	F10	F11	F12	F13	F14	F15
Fluconazole(gms)	1	1	1	1	1	1	1
Ethyl cellulose(gms)	10	12	11	11	11	11	11
Propylene glycol(ml)	10	10	10	10	10	10	10
Glycerine(ml)	10	10	10	10	10	10	10
DMSO(ml)	1.75	1.75	1	2.5	1.75	1.75	1.75
Thioglycolic acid(ml)	1.75	1.75	1.75	1.75	1	2.5	1.75
Ethanol (ml)	100	100	100	100	100	100	100

The amount of one polymers Ethyl cellulose and the volume of two different penetration enhancers DMSO and Thioglycolic acid were selected as independent variable factor A, factor B, and factor C respectively. As variant concentration of the polymer and penetration enhancers combination will affect the drug release pattern. Amount of one polymer Ethyl cellulose and two different penetration enhancers were coded values in table 1.

Central composite design- design expert software (8.0.7.1 Stat Ease Inc.) was consider, according to the model total 15 experiment were conducted.

EVALUATION PARAMETERS:

Drug content

Drug content of nail lacquer was determined by dissolving accurately 1ml of nail lacquer in ethanol. After suitable dilution absorbance was recorded by using UV- visible spectrophotometer (UV – 1700, Shimadzu, Japan) at 260 nm.

Nonvolatile content[14, 15]

1gm of sample was taken in a glass Petri dish of about 8cm in diameter. Samples were spread evenly. The dish was placed in the oven at 105^0 C for 1hr 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 amount of volatile content was then subtracted from 1gm weight of nail lacquer

Drying time[14, 15]

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.

Smoothness of flow[14, 15]

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[14, 15]

Gloss of the film was visually seen, comparing it with a standard marketed nail lacquer

Water resistance[14, 15]

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 increases in weight lower the water resistance.

Diffusion studies across artificial membrane[14, 15]

Diffusion studies were performed using artificial membrane (cellophane). The membrane was Soaked for 1hr in solvent system (phosphate buffer, pH 7.4), and the receptor compartment was filled with solvent. Test vehicle equivalent to 10mg 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 10hrs. The 5ml aliquot of drug sample was taken after a time interval of 1h and was replaced by the fresh solvent. Each experiment was replicated at least thrice. The drug analysis was done using double-beam UV spectrophotometer (U.V.1700 Shimadzu Corporation).

In vitro transungual permeation studies[14, 15]

In Hooves from freshly slaughtered cattle, free of adhering connective and cartilaginous tissue, were soaked in distilled water for 24 h. Membranes of about 1-mm thickness were then cut from the distal part of hooves. In vitro permeation studies were carried out by using Franz diffusion cell (respective volume, 100 ml), the hoof membrane was placed carefully on the cell, and the surface area available for permeation was 1.4 cm^2. Then the test vehicle equivalent 10mg was applied evenly on the surface of the nail membrane. The receptor compartment was filled with solvent A (phosphate buffer, pH 7.4), and the whole assembly was maintained at 37°C with constant stirring for 30 h. The 5 ml aliquot of drug sample was taken after a time interval of 2 h and was replaced by the fresh solvent A. Each experiment was replicated at least thrice. The drug analysis was done by using double-beam UV spectrophotometer (Jasco Corporation, Japan).

Determination of zone of inhibition[16]

Antifungal activity was checked by cup plate method. In this method a previously liquefied molten sabouraud dextrose agar media was inoculated with 0.2 ml of fungal suspension of *Candida albican* having a uniform turbidity at temperature of 4 to 8°C. 20 ml of culture medium was poured into the sterile petri dish having an internal diameter of8.5 cm. Care was taken for the uniform thickness of the layer of medium in different plates. After complete solidification of liquefied inoculated medium, the wells were made aseptically with cork borer having 6mm diameter. In one plate formulation (nail lacquer) and in another plate pure drug solution was placed carefully. Plates were kept for pre diffusion for 30 mins. After it normalized to room temperature; the plates were incubated at 22-27°C for 72hrs. After incubation period was over, the zone of inhibition was measured with help of scale.

Stability studies

Stability studies were carried out at 40 ± 2^0C/75 ± 5% RH for two months, sample was stored in stability chamber. The sample was evaluated for nonvolatile content, drying time, gloss, and smoothness of flow, water resistance and diffusion across artificial membrane.

Kinetic release studies[17]

For determination of drug release kinetics from the buccal tablet, the *in- vitro* release data were

analyzed by zero order, first order, Higuchi and Korsmeyer and Peppas equations.

Zero order release Kinetic

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

$$dQ/dt = K_o$$

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

First order Release Kinetic

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

$$dQ/dt = K_1 Q$$

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

Higuchi Release Model

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

$$Q = K_H t^{1/2}$$

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

Korsmeyer and Peppas Kinetics

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

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

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

RESULTS AND DISCUSSION:

The λ maximum was found at 260 nm. The standard graph was ontained between range of 10 to 100µg/ml and was found to be linear with regression value of 0.998, shown in figure 1.

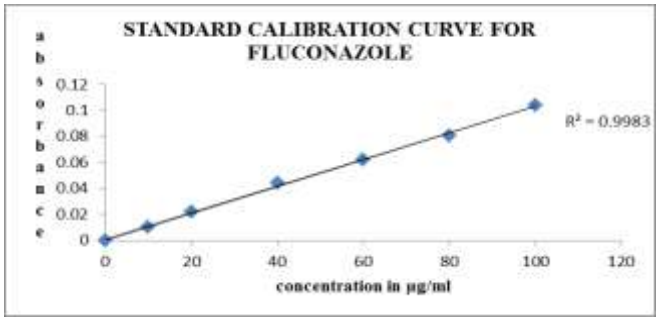

Figure1. Standard calibration curve for Fluconazole

The FTIR studies revealed that there was no chemical interaction between drug and the polymer used. All the formulation F1 to F15 were evaluated for smoothness of flow. Formulation F1, F3, F5, F6, F7 and F9 showed good smoothness of flow, were as formulation F2, F4, F6,F8,F10, F11, F12, F13, F14, F15 showed satisfactory smoothness of flow. It was noticed that as the polymer concentration increased the smoothness of flow decreased. The increase in the concentration causes increase in the viscosity of the solution,decreases in the smoothness of flow. Gloss of nail lacquer was evaluated by comparing with the marketed product. It was found to be satisfactory when compared to marketed product.

It was seen that as the polymer concentration increases from 10%w/v to 12%w/v the non – volatile content increases. The formulation which had higher concentration of polymer showed higher non – volatile content as the amount of polymer present in the sample for determination of non – volatile content was more as compared to the formulation which contained lower concentrations of polymer. Non – volatile content depends and vary upon the concentration of polymer used. The non – volatile content values for all the formulations are given in table 4.

Table 4. Non – volatile content of Nail Lacquer

Formulation code	Non – volatile content (%)*	Formulation code	Non – volatile content (%)*
F1	21.3±0.57	F9	20.3±0.20
F2	27.3±0.57	F10	27.7±0.75
F3	20.6±0.50	F11	25.0±0.50
F4	27.3±0.57	F12	24.4±0.55
F5	20.6±0.76	F13	24.1±0.32
F6	26.6±0.72	F14	23.8±0.26
F7	20.3±0.57	F15	24.8±0.76
F8	26.6±0.57		

*Average of three trials (n=3)

The drying time for all 15 formulations was found to be in the range of 64 to 86 seconds. In water resistances test it was found that as the polymer concentration increases the water resistance increases i.e. the amount of water absorbed by the nail lacquer film after keeping in water for 24 hours is less. The value of amount of difference in weight of nail lacquer film before and after keeping in water for 24 hours is given in table 5.

Table 5. Water resistance test for Nail lacquer.

Formulation	W_1 (g)	W_2(g)	W1 – W2(g)	Formulation	W_1 (g)	W_2 (g)	W1-W2(g)
F1	7.00	7.24	0.24	F9	7.00	7.22	0.22
F2	7.00	7.10	0.10	F10	7.00	7.12	0.12
F3	7.00	7.22	0.22	F11	7.00	7.16	0.16
F4	7.00	7.12	0.12	F12	7.00	7.16	0.16

F5	7.00	7.22	0.22	F13	7.00	7.15	0.15
F6	7.00	7.13	0.13	F14	7.00	7.15	0.15
F7	7.00	7.22	0.22	F15	7.00	7.14	0.14
F8	7.00	7.11	0.11				

W_1 & W_2 - are weight of glass slide along with nail lacquer before and after dipping in water respectively

The drug content was found to be in range of 98.10% to 99.98% and hence there was a good uniformity of drug content in the all the formulations.

***IN – VITRO* DIFFUSION STUDIES:**

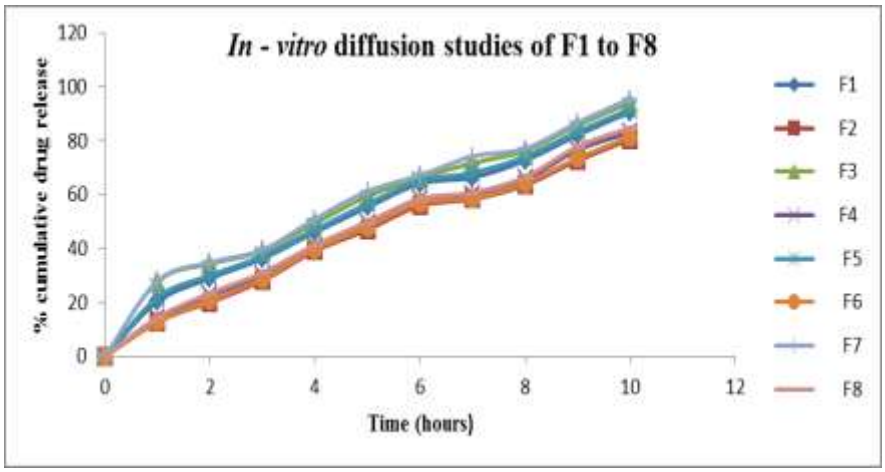

Figure 2. *In – vitro* diffusion study of F1 to F8

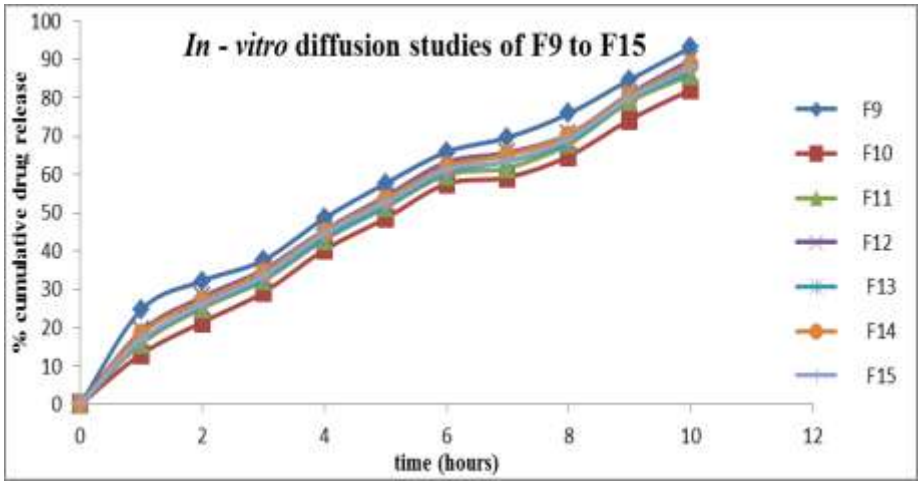

Figure 3. *In – vitro* diffusion study of F9 to F15

From *in – vitro* diffusion studies it was found that formulation F7 showed the highest release of 95.55% at the end of 10 hours containing 10%w/v of ethanol, 2.5%v/v of Thioglycolic acid and 2.5%v/v of dimethyl sulfoxide. Whereas formulation F2 (12%w/v of ethyl cellulose, 1.00%v/v of Thioglycolic acid and 1.00%v/v) showed the most sustained release of 80.54% at the end of 10 hours.

TRANSUNGUAL PERMEATION STUDIES:

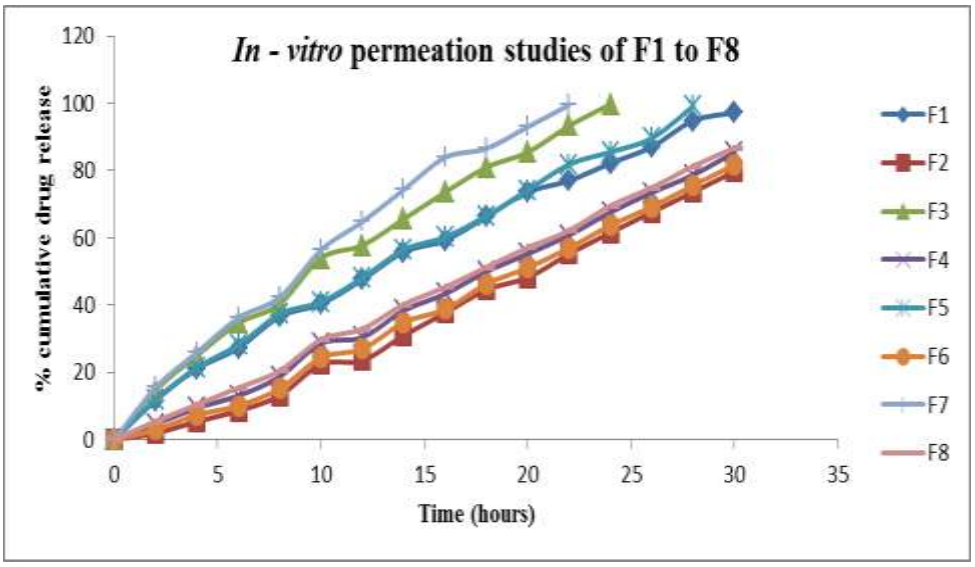

Figure 4. *In – vitro* permeation study of F1 to F8

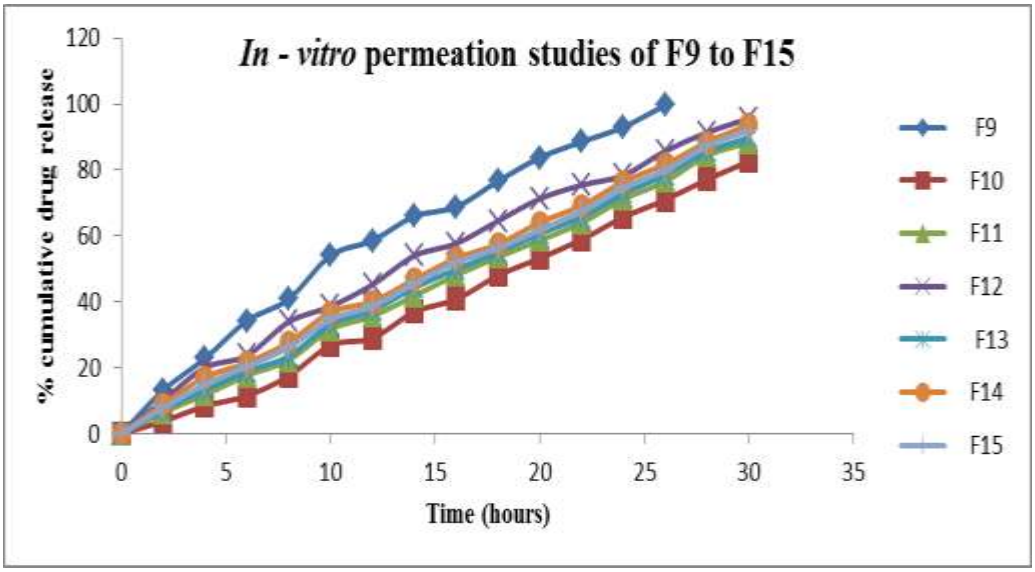

Figure 5. *In – vitro* permeation study of F9 to F15

From the *in – vitro* permeation studies it was found that formulation F7 showed a release of 99.52% at the end of 22 hours, whereas formulation F2 showed the most sustained release of 79.76% at the end f 30 hours. It was seen from both the in – vitro diffusion as well as in – vitro permeation studies that as the polymer concentration decreases and permeation concentration increases, the release of the drug increases from the formulation. Among both the permeation enhancers it was found that the Thioglycolic acid was a better penetration enhancer as compared to dimethyl sulfoxide. The effect of Thioglycolic acid was attributed to its small molecular weight and damage caused on the keratin network and decrease in lipid content in the dorsal nail layer; this act which loosened the nail structure, allowing Fluconazole to penetrate easier.

Optimization:

Design and summary of response:

Table 8: Summary of response

Std	Run	Factor 1(Ethyl cellulose)%w/v	Factor 2 (Thioglycolic Acid)%v/v	Factor 3 (DMSO) %v/v	Response 1 (drying time)	Response 2 (%CDR)
9	1	10.00	1.75	1.75	66	93.12
10	2	12.00	1.75	1.75	85	82.09
8	3	12.00	2.50	2.50	83	84.77
14	4	11.00	1.75	2.50	74	88.74
6	5	12.00	1.00	2.50	85	81.41
4	6	12.00	2.50	1.00	86	83.15
13	7	11.00	1.75	1.00	74	86.81
15	8	11.00	1.75	1.75	73	87.86
3	9	10.00	2.50	1.00	65	94.11
1	10	10.00	1.00	1.00	64	90.77
2	11	12.00	1.00	1.00	84	80.54
11	12	11.00	1.00	1.75	72	85.95
12	13	11.00	2.50	1.75	75	89.90
7	14	10.00	2.50	2.50	64	95.55
5	15	10.00	1.00	2.50	66	91.75

A. Response 1: Drying time.

Table 9: Model summary statistics

Source	Std deviation	R – squared	Adjusted R –squared	Predicated R –squared	PRESS
Linear	**1.30**	**0.9809**	**0.9757**	**0.9636**	**35.62(suggested)**
2FI	1.19	0.9884	0.9798	0.9642	35.04
Quadratic	1.06	0.9943	0.9840	0.9528	46.24
cubic	1.00	0.9990	0.9857	-2.0878	3024.79

Table 10: ANOVA for Response Surface Linear Model

Source	Sum of squares	df	Mean square	F value	p – value prob > F
Model	960.90	3	320.30	188.41	<0.0001 (significant)
A: Ethyl cellulose	960.40	1	960.40	564.94	<0.0001
B: Thioglycolic acid	0.40	1	0.40	0.24	0.6371
C: DMSO	0.10	1	0.10	0.059	0.8128
Residual	18.70	11	1.70		
Core total	979.60	14			

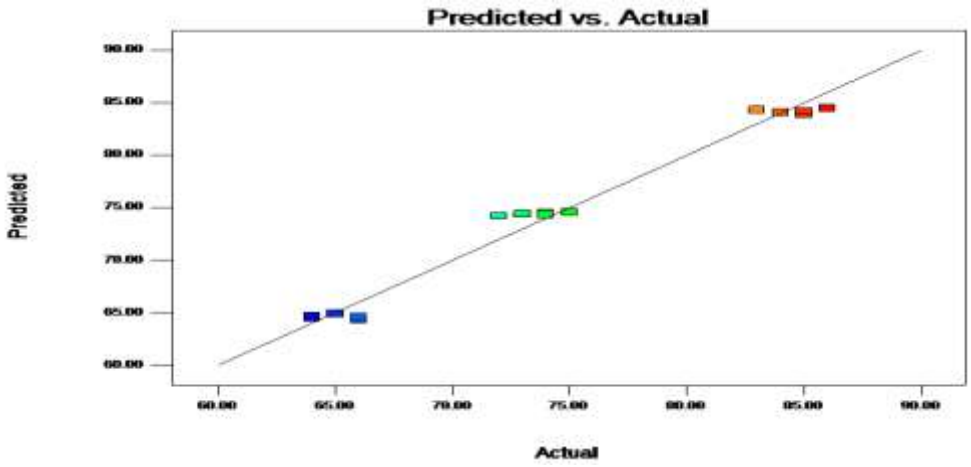

Figure 6: Predicted v/s actual graph for drying time

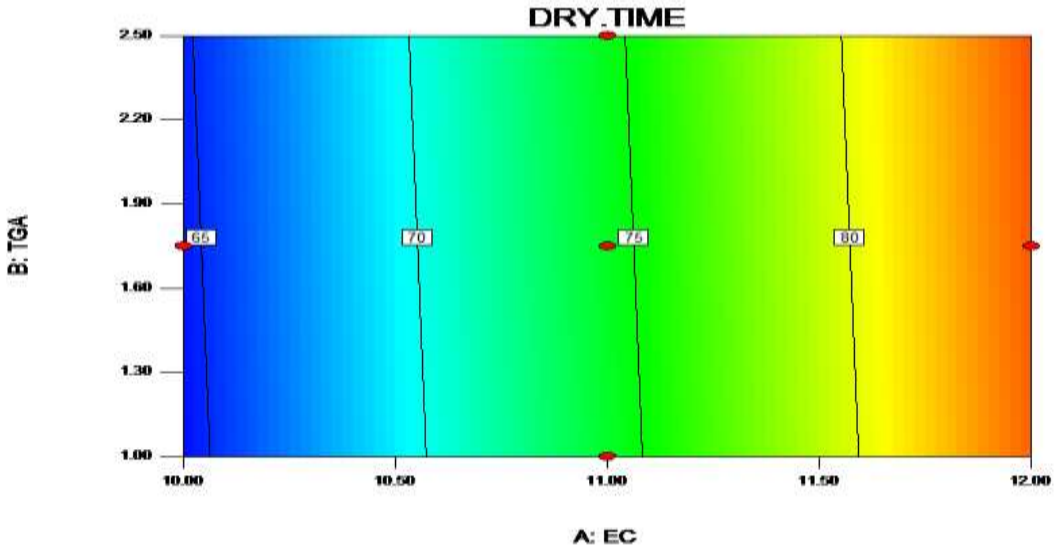

Figure 7: Contour plot for drying time against amount of Thioglycolic acid and Ethyl cellulose

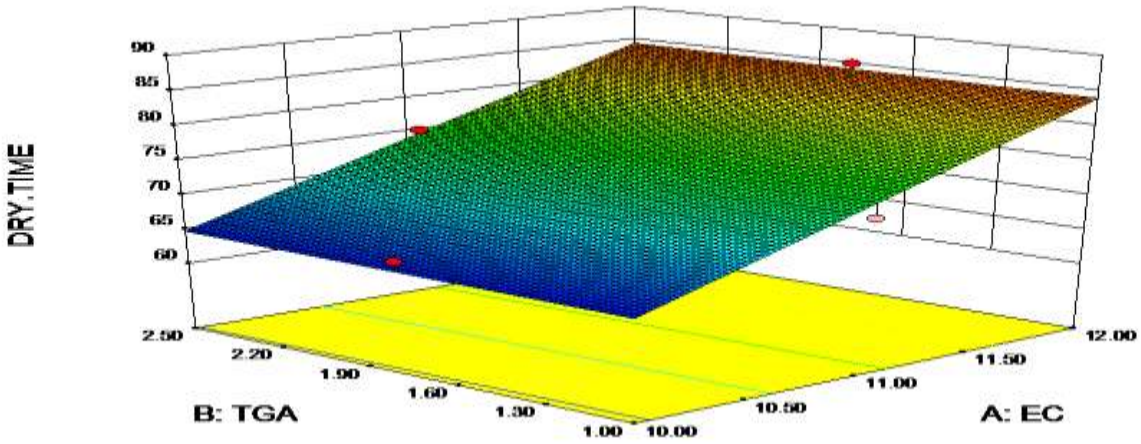

Figure 8: 3D plot for drying time against amount of Thioglycolic acid and Ethyl cellulose

A. Response 2: percentage cumulative drug release (%CDR)

Table 11. Model summary statistics

Source	Std deviation	R – squared	Adjusted R – squared	Predicated R – squared	PRESS
Linear	0.29	0.9971	0.9963	0.9943	1.83(suggested)
2FI	0.27	0.9982	0.9968	0.9929	2.26
Quadratic	0.31	0.9985	0.9958	0.9861	4.42
cubic	0.074	1.0000	0.9998	0.9478	16.66

Table 12. ANOVA for Response Surface Linear Model

Source	Sum of squares	df	Mean square	F value	p – value prob > F
Model	318.33	3	106.11	1241.88	<0.0001 (significant)
A: Ethyl cellulose	284.52	1	284.52	3329.85	<0.0001
B: Thioglycolic acid	29.14	1	29.14	341.02	<0.0001
C: DMSO	4.68	1	4.68	54.76	<0.0001
Residual	0.94	11	0.085		
Cor total	319.27	14			

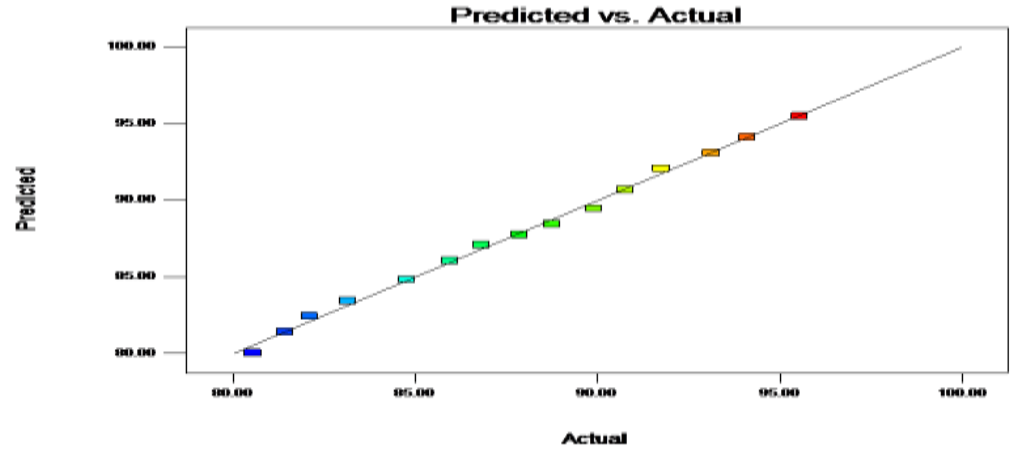

Figure 9: Predicted v/s actual graph for %CDR

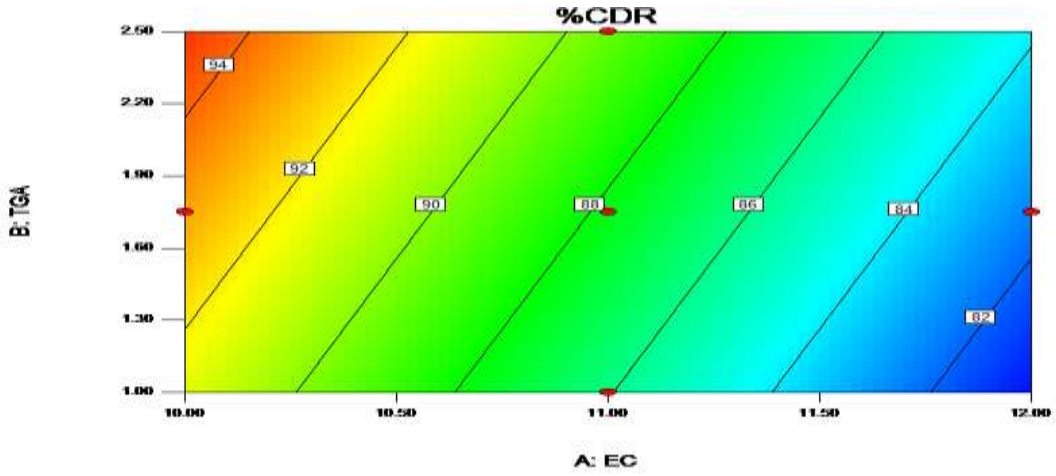

Figure 10: Contour plot for %CDR against amount of Thioglycolic acid and Ethyl cellulose

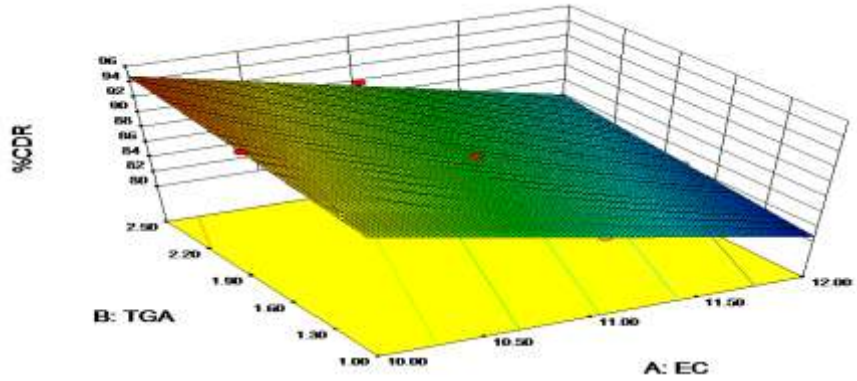

Figure 11: 3D plot for %CDR against amount of Thioglycolic acid and Ethyl cellulose

Table 13. Optimized formulae obtained and their desirability

Number	Ethyl cellulose (gm)	Thioglycolic acid (ml)	DMSO (ml)	Drying time (sec)	%CDR (%)	Desirability
OF1	10.01	2.42	2.48	64.93	95.10	1.000
OF2	10.00	2.35	2.41	64.82	94.14	1.000
OF3	10.03	2.30	1.43	64.91	94.82	1.000

All the three optimized formulations were evaluated for drug content, drying time and *in – vitro* diffusion studies. The data obtained after evaluation was found to be with the limit of predicted value given by software. And comparison of predicted and actual value is given in table no.

Table 14. Comparison of predicted and actual experimental values

Optimized formulations		OF1	OF2	OF3
Drying time (sec)	Predicted	64.93	64.82	64.91
	Actual	64.50	64.00	64.00
	%Error	-0.006	-0.012	-0.014
%CDR (%)	Predicted	95.10	94.14	94.82
	Actual	95.30	94.10	94.64
	%Error	0.002	- 0.0004	- 0.001

It can be seen that there no much deviation between the predicted and actual values (% error) for all the three formulation OF1, OF2, OF3, all were within the limit suggested by the model.

ANTI FUNGAL TESTING:

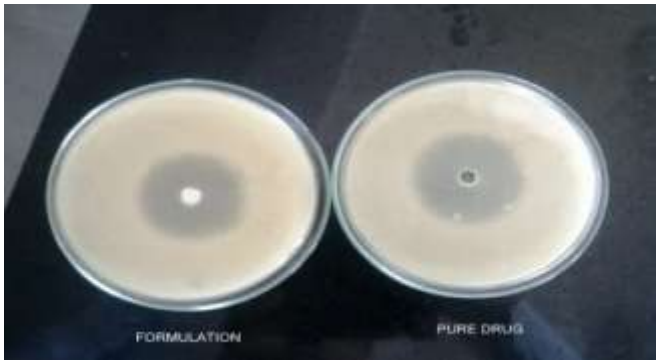

Figure 12: Zone of inhibition for anti fungal activity

Table 15. Zone of inhibition for pure drug and optimized formulation.

Micro-organisms	Diameter of Zone of Inhibition (mm) After 72hrs	
	Pure Drug	Optimized formulation (OF1)
Candida albicans	26mm	25.4mm

The anti fugal activity test showed that optimized formulation OF1 is as effective as pure drug.

KINETICS DRUG RELEASE STUDIES:

Table 16. Regression analysis (r^2) of release data based on best curve-fitting method for optimized formulations

Formulation code	Zero order r^2	First order r^2	Higuchi model r^2	Best fit release mechanism
OF1	0.9558	0.8912	0.9869	Higuchis
OF2	0.9643	0.899	0.9794	Higuchis
OF3	0.9565	0.8957	0.9852	Higuchis

The different kinetics models were applied to optimized formulations. The release kinetics data for Optimized formulations OF1, OF2, OF3 is given in table no.38 from the data obtained it was found that formulations followed zero order release, as the regression value (r^2) is higher as compared to the first order release. Formulations followed Higuchis model for the release mechanism as the regression value is higher as compared to that of kosmeyers - peppas model.

It was seen from stability studies that there was not much change in the parameters of nail lacquer and hence the nail lacquers were found to be stable over the period of two months of stability testing.

CONCLUSION:

Fluconazole is an antifungal drug and it show high hepatotoxicity in body when administered orally for treatment of fungal infections of nail. In order to overcome this side Fluconazole had been formulated in form of medicated nail lacquer. Here optimization approach was applied to obtain best possible formulation. Ethyl cellulose was used as film forming agent and Thioglycolic acid, dimethyl sulfoxide was used as penetration enhancers. Three optimized formulation were obtained based on the primary evaluations data. The optimized formulation were evaluated for different parameters such as anti fungal testing, drying time, cumulative drug release, kinetic studies and stability studies and showed satisfactory results for all the parameters. It can be concluded that medicated nail lacquer owes many advantages as compared to the oral formulations in treatment of fungal infections.

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