FORMULATION AND EVALUATION OF MEDICATED NAIL LACQUER OF BUTENAFINE HCl FOR EFFECTIVE TREATMENT OF PARONYCHIA

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Abstract-

In the present research a medicated nail lacquer of Butenafine HCl had been developed for the treatment of paronychia. The main aim of the study was to provide a medicament over the nail for an extended period of time. The FTIR study was revealed that drug and all excipients are compatible. The antifungal activity of prepared nail lacquer was calculated against candida albicans & zone of inhibition was calculated by comparing with marketed cream. In this study demonstrating the effect of different penetration enhancer's like- thioglycolic acid, urea (H_2O_2) and 2-mercaptoethanol by ex-vivo permeation study. In the prepared nail lacquer penetration enhancers mainly act by breaking disulphide bond of the nail. The ex vivo permability study was carry out on goat hooves in the franz diffusion cell using phosphate buffer 7.4 as a medium. The formulation containing 1.5 gm of ethyl cellulose, along with 0.5 ml of thioglycolic acid showing the highest release (85.64%) and the formulation showing first order release kinetics and Super case II transport mechanism.

Keywords- Transungual, Nail lacquer, Butenafine HCl, Paronychia, Thioglycolic acid

1-Introduction:

The transungual drug delivery is related to delivery of drug into the nail plate (Keratinized) for attaining targeted delivery of drug, for the treatment of nail diseases. But this route is unfavourable for delivery of drugs because of its hardness & impermeability; however it is important to improve the topical delivery of these compounds for the effecious treatment of diseases of nail for e.g. Paronychia, onychomycosis and nail psoriasis, due to its localized effects, minimal adverse effects and improved adherence to the nail plate. [1] So for the improvement of nail drug delivery or effecious delivery of pharmaceutical ingredients over the nail, the anatomy and physiology of nail & its barriers are considerable. [2]

Previously for various nail diseases the oral drug treatment should be used but in conventional drug treatment there are various side effect (such as- systemic side effects are there, drug –drug interaction, these are not removable when not needed), also the topical formulations like- cream, gels having low permeability into the nail plate. [1]

For the accurate amount of a drug at the right place to the right time, some newer approaches there are like- chemical agents (such as- mercaptans, urea, sulfites & Keratolytic agents), physical methods (such as- Iontophoresis, laser, etching & UV-light etc) and mechanical methods (nail abrasion & nail avulsion), are used for maximum efficacy of drug at the site of application. [2]

Previously topical preparations of nail such as- nail enamel, nail lacquer and varish etc,are mostly used for enhancement of nails beauty, imparting color & luster of the nail ,but in recent times medicated lacquers are specially designed for the treatment of fungal diseases. [3]

Paronychia is an inflammation which involves the tissue of nail folds in the fingernail or toenail surroundings. It is the most usual infection of the hand which usually grow after an interruption between sealing of proximal nail fold & nail plate which will enables the entry for infecting organisms. The paronychia is developed mainly because of the some bacteria or yeast which called *Candida.* [4]

Butenafine HCl is a synthetic benzylamine antifungal agent. It works by inhibiting the synthesis of sterols by inhibiting squalene epoxidase , an enzyme responsible for the creation of sterols needed in fungal cell membrane. [5]

In the present study formulate a medicated nail lacquer of butenafine HCl for the treatment of paronychia. In this study use of various penetrations are there such as- thioglycolic acid,urea, 2-mercaptoethanol.

2. Material and method:

The drug Butenafine HCl was procured as a gift sample from glenmark Pharmaceuticals Ltd Solan. The other used excipients like- ethyl cellulose,Propylene glycol ,glycerine ,methanol, thioglycolic acid ,2-mercaptoethanol &Urea (H_2O_2)was purchased from Central drug house Pvt. Ltd. Delhi (IND).

In the current research work, the method used to formulate medicated nail lacquer was simple mixing method. In first step the ethyl cellulose was added slowly into the ethanol and making a homogeneous mixture by using magnetic stirrer at a constant speed. In second step the Butenafine HCl was then mixed with propylene glycol and glycerin and ethanol by continuous stirring. Then the homogenous mixture obtained from the step second are added slowly into step first mixture .To above homogenous clear solution thioglycolic acid ,2-mercaptoethanol and urea(H_2O_2) solution are then added and volume make up to 30 ml by adding ethanol. The 5 formulations are then prepared and it is showing in the table no.1. [6]

Preformulation Studies:

Preformulation testing is initial step in the development of a suitable dosage form by using different drugs and pharmaceutical agents. So it is defined as the process of examination of different physical and chemical properties of the drug alone or sometimes in combination with excipients.

Melting Point: [7]
The sample was placed in to sealed melting point capillary. It was then put into a melting point apparatus. Sample was then heated and as the temperature increase the sample was observed to detect the phase change from solid to liquid phase .The temperature at which the phase changes occur shows the melting point.

Solubility study: [8]

The solubility of drug was determined in a set of solvents (ethanol, methanol, phosphate buffer 7.4).For this a saturated solution of Butenafine HCl was prepared in a 1ml of different solvents and undisturbed for 24 hours. Then the solution was sonicated for 5minutes and after that 0.1ml of pipette out from the test tube and make up the volume by different solvents. The amount of Butenafine HCl present in the solvent was then estimated using UV visible spectrophotometer after appropriate dilutions with respective solvents.

Preparation of standard calibration curve of Butenafine HCl: [9]

Preparation of standard calibration curve of Butenafine HCl in methanol-

Accurately weight 25 mg of drug was dissolved in 25 ml of methanol and thus 1000 µg/ml solution was prepared .Now from this solution 100 µg/ml solution was prepared and by using the present stock solution, appropriate dilutions was prepared by utilizing same solvent in the range of 10, 20, 30, 40, 50, 60 µg/ml . At λ max 280 nm, value of absorbance in different concentration was determined against methanol as blank and Standard curve was plotted between concentration and absorbance.

Preparation of standard calibration curve of Butenafine HCl in ethanol-

Accurately weight 25 mg of drug was dissolved in 25 ml of ethanol and thus 1000 µg/ml solution was prepared .Now from this solution 100 µg/ml solution was prepared and by using the present stock solution, appropriate dilutions was prepared by utilizing same solvent in the range of 10, 20, 30, 40, 50, 60 µg/ml . At λ max 280 nm, value of absorbance in different concentration was determined against ethanol as blank and Standard curve was plotted between concentration and absorbance.

Preparation of standard calibration curve of Butenafine HCl in pH 7.4 Phosphate   buffer-

Preparation of Phosphate buffer 7.4-Firstly take 50 ml of 0.2 M potassium dihydrogen phosphate in 200 ml of volumetric flask, &then add specific volume of 0.2 M of sodium hydroxide & add water to make up the volume.

Preparation of stock solution-Weigh 25 mg of drug & dissolved in 25 ml of 7.4 phosphate buffer and thus 1000 µg/ml solution was prepared. Now from this solution 100 µg/ml solution was prepared and by using the present stock solution, appropriate dilutions was prepared by utilizing same solvent in the range of 10, 20, 30, 40, 50, 60 µg/ml . At λ max 280 nm, value of absorbance in different concentration was determined against phosphate buffer 7.4 as blank and Standard curve was plotted between concentration and absorbance.

Fourier transform infra red spectroscopy: [10]
Infrared spectrum of Butenafine HCl was determined by using Fourier Transform Infrared Spectrophotometer using KBr disk method. The sample (0.5 to 1 mg) is finely grounded and intimately mixed with approximately 100 mg of dry potassium bromide powder. The Grinding and mixing can be done with mortar and pestle. The mixture is then pressed into a transparent disk in an evacuable die at sufficient high pressure. Suitable KBr disks or pellets can often be made by using a simpler device such as- a hydraulic press. The base line correction was done using dried potassium bromide. Then, the spectrum of dried mixture of drug and potassium bromide was scanned from 2000cm-1 to 400 cm -1.
Characterization of prepared medicated nail lacquer-

Gloss- [11]

To evaluate the gloss formulated nail lacquer was applied on the nail, then visually seen it was then compared with the marketed nail lacquer formulation.

Smoothness of flow- [12]

To calculate the smoothness of flow firstly take 2 Petri dishes,from 1 Petri dish sample was poured into another Petri dish, approximately from 1.5 inch height and then visually seen .

Repeat the same for all the formulations & compare the formulations for smoothness of flow.

Drying Time- [13]

To determine drying time of the formulations, firstly the petri dishes are taken and then a thin film of a formulated samples and marketed formulation was applied evenly with the help of brush. The time taken to form a dry to touch film , was noted by using watch or stopwatch.

pH- [14]

pH of the medicated nail lacquer were measured by using digital pH meter.

Water Resistance- [15]

To determine the resistance of the formulation into water the water resistance test is performed. The test was performed by applying a thin film onto the surface of glass slide &then immerses it into water. The before &after weight was then noted down after different time interval

Drug content Estimation- [16]

The drug content of formulated nail lacquers and marketed nail lacquer was estimated by accurately 5 ml of nail lacquer formulation dissolved in methanol and then different dilutions were prepared. After preparing different dilutions the absorbance was recorded, by the use of UV- visible spectrophotometer (UV- Japan) at lambda max 280 nm. Then by using standard curve slope,the drug content was determined & mean value was noted.

Nonvolatile content - [17]

To calculate nonvolatile content firstly 5 Petri dishes are taken and then mark as F_1, F_2, F_3, F_4, F_5. Then the initial weights of these petri dishes are taken and note it down .After that 5 ml of each sample was taken into Petri dishes and spread evenly. Then weight of each Petri dish with sample was recorded. The Petri dishes are then put it into a hot air oven at 105^0c, for 1 hour &after 1 hour the Petri dishes are again weighed and difference was recorded and then percent non volatile content was calculated.

Viscosity-[18]

The viscosity of the formulated Butenafine HCl nail lacquer was calculated by using Brookfield Viscometer (model LVF), in room temperature by using the spindle no.63 at different RPM.

Antifungal activity– [19, 20, 21]

Preparation of SDB (Sabourd Dextrose Broth)-

For preparing sabourd dextrose broth media, firstly all apparatus were sterilized by using hot air oven at 50 ^{0}c for 1 hour. Then take 1 gm of mycological peptone with 2gm of dextrose and suspended it in a 100 ml of distilled water, & the pH was adjusted to 5.6±0.2 at temperature 25^0c.Heat the above solution if necessary for complete dissolution of medium ,it was then sterilized by using autoclave at 15 lb ps pressure (121 ^{0}c) for 1 hour.

Preparation of Candida albicans suspension-

For preparing Candida albicans suspension, firstly all apparatus were sterilized by using hot air oven at 50 ^{0}c for 1 hour. After that Candida albicans sample was inoculated into a sabourd dextrose broth by using inoculation loop .Then after inoculation the Candida suspension was kept in a BOD (biological oxygen demand) for 17-24 hours. The incubated suspension was then used for further experiment of antifungal activity.

Determination of antifungal activity (Disc diffusion method)

After preparation of PDA media and SDB containing Candida albicans incubated suspension, the plates are placed in a laminar air flow. The previously sterilized discs are then dipped into different concentration of sample (Butenafine HCl dissolved in DMSO) for about 30 minutes. Then in the prepared PDA plates the Candida albicans suspension was applied with the help of sterilized cotton plug. The disc with sample of different concentration ratio (1:1,1 :2 ,1:3,1:4,1:5) and marketed formulation are then placed into a petri dishes containing c. albicans. These plates are then placed in a BOD incubator for about 17- 24 hours and then measure the zone of inhibition with the help of scale.

Transungual permeation studies: [22]

The ex-vivo transungual permeation study of formulated nail lacquer was performed in hooves from freshly slaughtered cattle, free from adhering tissue which was then soaked in a phosphate buffer pH 7.4 for 24 hours. Then the permeability of the formulation was performed by using franz diffusion cell, in which the nail was placed carefully into the cell. After that the formulated nail lacquer equivalent to 200 mg was then evenly applied onto the surface of the hooves.

The receptor compartment of the diffusion cell was then filled with a solution of phosphate buffer pH 7.4 &maintained the whole assembly at 37^{0}c by constant stirring for about 24 hours .The 5ml of nail lacquer sample was take after a time interval of 1hour and then replace it with fresh solvent of buffer. Then the analysis of drug was done by using a single beam UV spectrophotometer (shimandzu corporation).

Ex-vivo release kinetics: [23]

Determination of the release pattern of the prepared nail lacquer formulation, the data of ex-vivo release was considered & it is treated by several mathematical models which are zero order, first order, higuchi & korsmeyer- peppas model. In which the R (correlation coefficient), n (diffusion exponent) and K (release constant) values getting from curve fitting of release data were determined a model which is suitable for the nail formulation.

3. **Result and discussion:**

The five different formulations of Butenafine HCl nail lacquer was formulated by using different concentration of polymer and by using different amount of penetration enhancers.

The prepared formulations are then evaluated for various parameters like-gloss, drying time, smoothness of flow, water resistance, non volatile content, viscosity, antifungal activity and ex vivo permeation study and ex vivo release study.

Melting Point- The melting point of the Butenafine HCl was determined by capillary method and it was observed in between 206-208 ^{0}c.

Solubility Study- By measuring solubility of the drug in methanol, ethanol and phosphate 7.4 buffer it was observed that the drug is soluble in ethanol, phosphate buffer and in methanol.

U.V. spectroscopy - The standard curve of butenafine HCl was plotted in between concentration and absorbance and measured in ethanol,methanol and phosphate buffer 7.4 and the value of R^2 in methanol ,ethanol and phosphate buffer was 0.989, 0.9924 and 0.9884 at lambda max 280 nm and it indicates linearity in equation.(table no. 2) (fig 1,2 &3).

FTIR- Identification of drug was done in pure drug and also with polymer (ethyl cellulose) and it was observed that the obtained peaks are matched with standard peaks of the drug so the drug is identified as butenafine HCl. (table no.3)(fig no.4)

Gloss- The gloss of formulated nail lacquer was evaluated by comparing it with the marketed product. It was found that gloss of formulated nail lacquer was satisfactory when compared with the marketed product. (table no.)

Smoothness of flow- The smoothness of the flow into the formulated nail lacquer F1, F2, F3, F4 & F5 was found good when compared with the marketed medicated nail formulation. (table no. 4)

Drying time-The drying time of the formulated nail lacquer F1 to F5 was found in between 65-72 seconds and it was observed that drying time increases with increasing the polymer concentration .The drying time of the marketed formulation was observed 55 seconds and the drying time of the formulated nail lacquer was nearer to marketed formulation. (table no. 4)

pH- All the observed pH of the formulations is nearer to pH of marketed formulation and it matches with the pH of the nail, which signify that formulation having no irritation on the nail. (table no. 4)

Water resistance test-The water resistance test was performed in prepared formulation from F1- F5. (table no.5)

Non-volatile content- The non-volatile content in different formulated nail lacquer from F1-F5 and in marketed formulation was measured and the observed nonvolatile content was mentioned in the (table no. 6)

Viscosity- The viscosity of the formulated nail lacquer from F1 to F5 formulation was determined by using Brookfield viscometer and the viscosity of the formulated nail lacquer was in between 179.2 to 180.8 cps. (table -7,8,9,10 and 11)(fig-5-10).

Antifungal activity- In the formulated medicated nail lacquer the range of zone of inhibition was observed in between 12-22 mm and the formulation F1 (with 22 mm zone of inhibition)was effective as marketed formulation(25 mm zone of inhibition) ,as the zone of inhibition of the best formulation is nearer to the marketed formulation zone of inhibition.(table no. 12) (fig no. 11).

Ex vivo transungual permeation study -The Ex-vivo transungual permeability study in formulated Butenafine HCl nail lacquer was performed in franz diffusion cell. By performing permeation study it was showing that the formulation F2 (85.64), F4 (84.95) and F5 (84.98) showing highest release as compared to F1 (81.78) and F3(81.56).(table no. 13)

Ex-vivo release kinetics- The ex- vivo release study was performed for determination of a release order of a formulated nail lacquer and it was observed data the highest value of R^2 showing the best fitting model in

formulated nail lacquer formulation, and it was observed that the prepared formulation showing first order kinetics which states that the release is dependent on concentration. (table no. 14-19) (fig no. 12-19)

Table no.1- Composition of Butenafine HCl nail lacquer

Ingridients	F1	F2	F3	F4	F5
Butenafine HCl(gm)	1	1	1	1	1
Ethyl cellulose(gm)	1	1	1.5	1.5	1.5
Propylene glycol(ml)	2.8	3	2.8	3	2.8
Glycerin(ml)	2	2	2	2	2
Thioglycolic acid(ml)	0.3	0.5	-	-	-
2-mercaptoethanol(ml)	-	-	0.3	0.5	-
Urea H$_2$O$_2$solution (1gm/100ml)	-	-	-	-	0.3
Methanol (ml)	30	30	30	30	30

Table no.2: Standard curve of Butenafine HCl at 280nm in Methanol, ethanol and phosphate buffer 7.4-

Concentration	Absorbance		
	Methanol	Ethanol	Phosphate buffer 7.4
10	0.2589	0.2536	0.2456
20	0.3365	0.3267	0.3265
30	0.5130	0.5381	0.5012
40	0.6476	0.6476	0.6476
50	0.7943	0.7904	0.7904
60	0.9262	0.8968	0.8893

Calibration curve of Butenafine HCl in methanol

$y = 0.014x + 0.050$
$R^2 = 0.989$
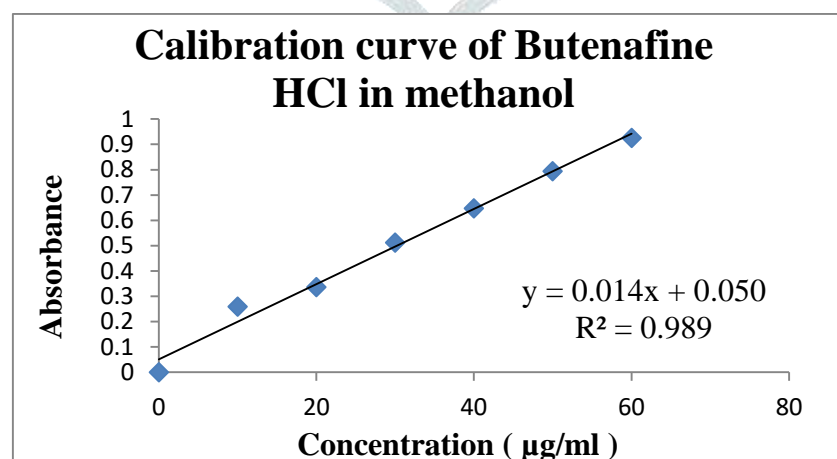
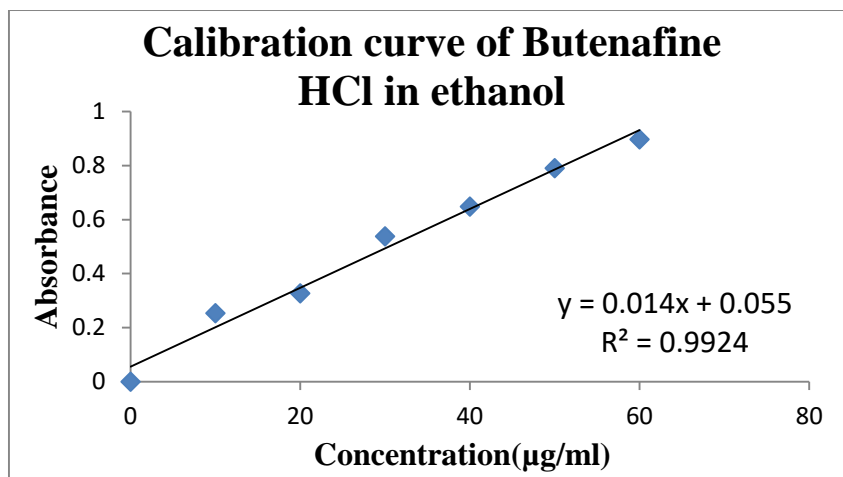**Figure no.1: Calibration curve of Butenafine HCl at 280nm in methanol**

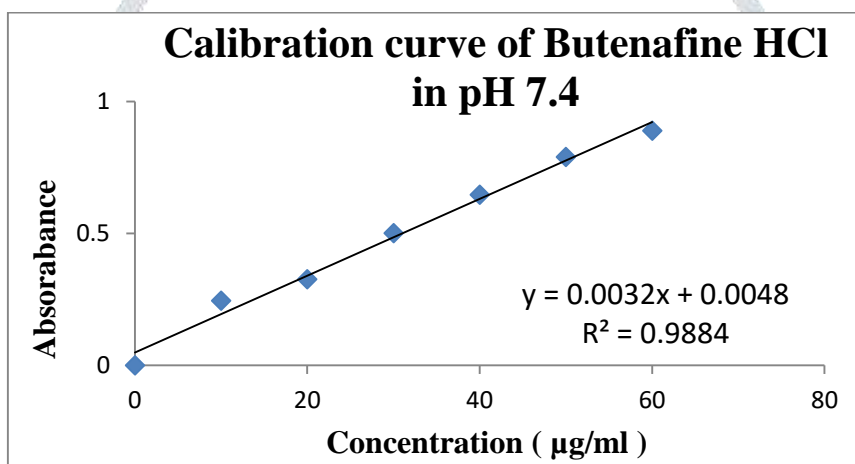**Figure no.2: Calibration curve of Butenafine HCl at 280nm in ethanol**

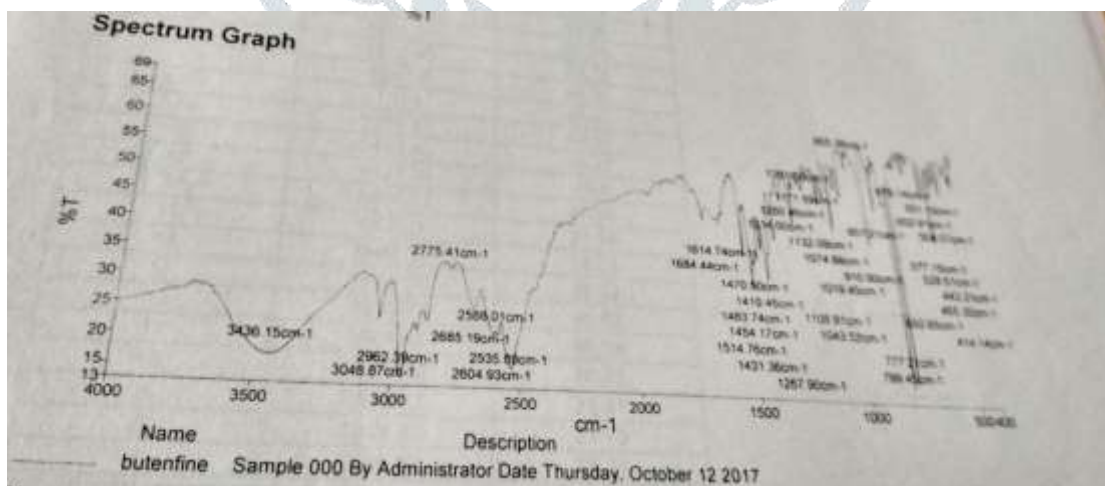**Figure no.3: Calibration curve of Butenafine HCl at 280nm in phosphate buffer 7.4**

Figure no.4: Observed Graph of Butenafine HCl

Table no. 3: Functional group detection of Butenafine HCl

S.no.	Observed peak(cm^{-1})	Standard frequency range (cm^{-1})	Interpretation
1	799.45cm^{-1}	690-900cm^{-1}	-C-H aromatic, out of plane
2	2962.39cm^{-1}	2850-3000cm^{-1}	-C-H Alkane
3	1074.88cm^{-1}	1000-1350cm^{-1}	C-N Amines
4	1483.74cm^{-1}	1475-1600cm^{-1}	C=C aromatic
5	1410.45cm^{-1}	1375-1450cm^{-1}	CH3 ,bending

**Table no. 4: Representation of gloss, smoothness of flow, drying time and pH of   Butenafine HCl nail lacquer**

Formulation code	Gloss	Smoothness of flow	Drying time (sec)	pH
F1	Good	Good	64 ± 0.81	5.1 ±0.005
F2	Good	Good	65±0.81	4.9 ±0.081
F3	Good	Good	69±1.24	5.2± 0.081
F4	Satisfactory	Good	71±0.47	5.3 ±0.081
F5	Satisfactory	Good	70±0.47	5.2 ±0.047
Std(Marketed formulation)	Very good	Very good	55±1.24	5.5±0.083

Table no. 5: The water resistance of the formulated medicated nail lacquer

Formulation code	%water uptake			
	Time(hrs)			
	1	2	3	4
F1	4.086	11.04	19.76	34.13
F2	3.88	10	20.86	33.09
F3	2.92	9.5	20.39	30.09
F4	2.42	9.2	19.98	29.83
F5	2.89	9.3	20.17	29.98

Table no.6: Representation of Percent nonvolatile content

Formulation code	Nonvolatile content (%)
F1	78.51 ±0.1084
F2	80.72 ±0.0374
F3	82.41 ±0.032
F4	81.56 ±0.0449
F5	83.62 ±0.8075
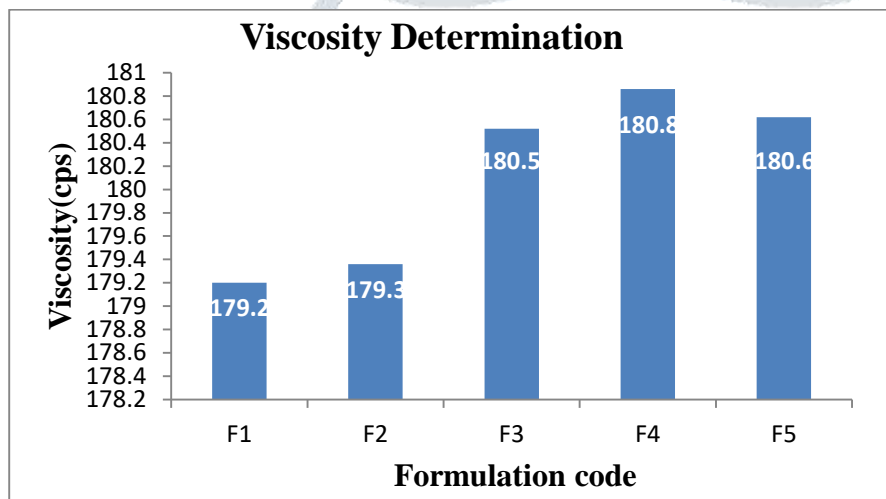
Figure no.5: Viscosity measurement in different formulation from F1 to F5

Table no. 7: Viscosity determination in formulated butenafine HCl nail lacquer F1

S.no.	Spindle no.	RPM	Viscosity	% torque	Viscosity average
1	63	20	186.7	4.9	
2	63	30	181.6	6.2	
3	63	50	179.3	7.9	179.14
4	63	60	176.8	8.2	
5	63	100	171.6	9.3	

Figure no.6: Viscosity determination in formulation F1

Table no. 8: Viscosity determination in formulated Butenafine HCl nail lacquer F2

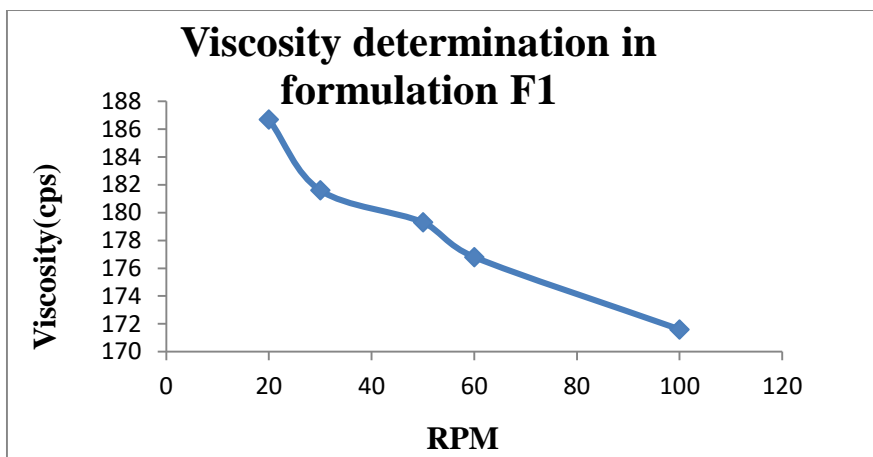| S.no.	Spindle no.	RPM	Viscosity	% torque	Viscosity average
1	63	20	186.9	4.9	
2	63	30	181.8	6.3	
3	63	50	179.5	7.9	179.36
4	63	60	176.8	8.2	
5	63	100	171.8	9.1	

Figure no. 7: Viscosity determination in formulation F2

Table no. 9: Viscosity determination in formulated Butenafine HCl nail lacquer F3

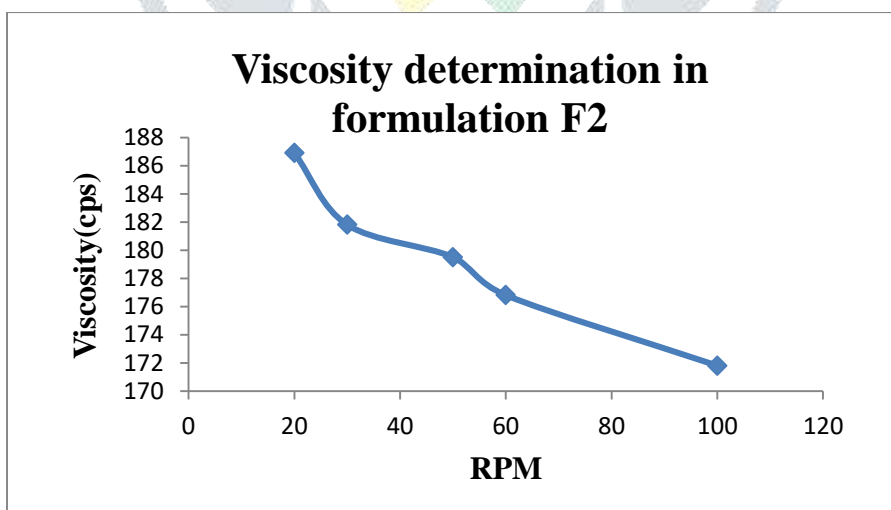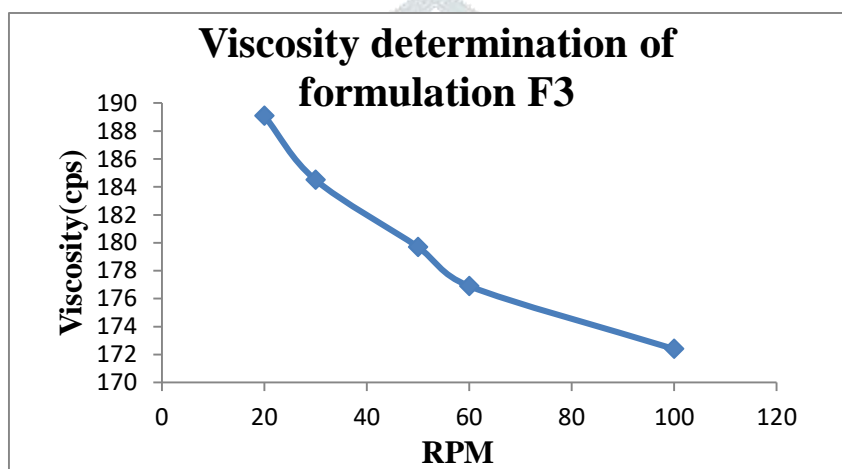| s.no.	Spindle no.	RPM	Viscosity	% torque	Viscosity average
1	63	20	189.1	5.3	
2	63	30	184.5	6.0	180.52
3	63	50	179.7	7.8	
4	63	60	176.9	8.1	
5	63	100	172.4	8.9	

Figure no.8: Viscosity determination in formulation F3

Table no. 10: Viscosity determination in formulated Butenafine HCl nail lacquer F4

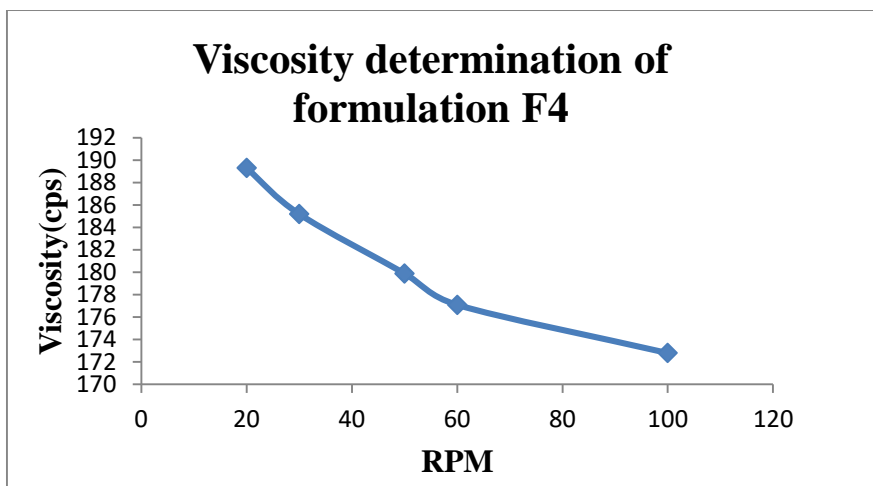| s.no.	Spindle no.	RPM	Viscosity	% torque	Viscosity average
1	63	20	189.3	5.2	
2	63	30	184.5	5.8	
3	63	50	179.9	7.6	180.86
4	63	60	177.1	8.0	
5	63	100	172.8	8.6	

Figure no.9: Viscosity determination in formulation F4

Table no.11: Viscosity determination in formulated Butenafine HCl nail lacquer F5

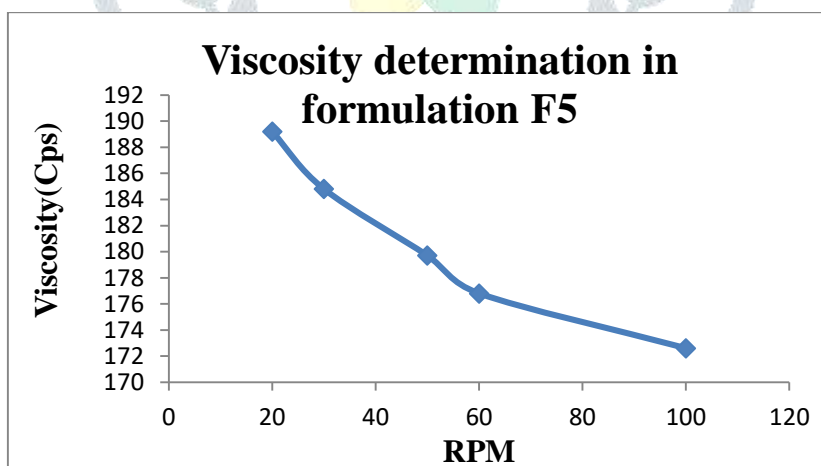| s.no.	Spindle no.	RPM	Viscosity	% torque	Viscosity average
1	63	20	189.2	5.2	
2	63	30	184.8	6.2	
3	63	50	179.7	7.8	180.62
4	63	60	176.8	8.3	
5	63	100	172.6	8.8	

Figure no.10: Viscosity determination in formulation F5

Table no.12: The zone of inhibition of prepared nail lacquer and marketed cream

Formulation code	Zone of inhibition(mm)
F1	22
F2	20
F3	15
F4	14
F5	12
Std (Marketed cream)	25

Figure no.11: Microbiological assay of Butenafine HCl medicated nail lacquer for F1,F2,F3,F4 ,F5 and marketed cream

Table no. 13: Ex vivo penetration data of the formulation F1 to F5

S.no.	Time(hrs)	Cumulative % drug release				
		F1	F2	F3	F4	F5
1	0	0	0	0	0	0
2	1	2.91	3.08	2.65	3.01	3.05

3	2	8.02	9.20	7.69	9.11	9.01
4	3	16.90	17.24	15.69	17.01	17.06
5	4	24.92	25.69	23.62	25.01	25.59
6	5	31.09	32.61	30.61	32.41	32.50
7	6	36.09	37.25	35.96	37.21	37.11
8	7	44.29	47.61	44.09	47.40	46.99
9	8	51.62	53.21	50.96	52.11	53.20
10	9	56.21	59.91	55.98	58.61	59.09
11	24	81.78	85.64	81.56	84.95	84.98

Table no.14: Ex vivo permeation data of formulated butenafine HCl from formulation F1

S.no.	Time (hrs)	√t	Log T	% Cumulative Drug release	% Cumulative Drug remain	Log % Cumulative Drug remain	Log % Cumulative Drug release
1	0	0	-	0	100	2	-
2	1	1	0	2.91	97.08	1.987	0.4647
3	2	1.4142	0.3010	8.02	91.97	1.963	0.9042
4	3	1.7320	0.4771	16.90	83.09	1.919	1.2285
5	4	2	0.6020	24.92	75.07	1.875	1.3965
6	5	2.2360	0.6989	31.09	68.90	1.838	1.4926
7	6	2.4494	0.7781	36.09	63.90	1.805	1.5574
8	7	2.6457	0.8450	44.29	55.70	1.745	1.6463
9	8	2.8284	0.9030	51.62	48.37	1.684	1.7128
10	9	3	0.9542	56.21	43.78	1.641	1.7498
11	24	4.8989	1.3802	81.78	18.22	1.260	1.9126

Table no.15: Ex vivo permeation data of formulated butenafine HCl from formulation F2

S.no.	Time (hrs)	√t	Log T	% Cumulative Drug release	% Cumulative Drug remain	Log % Cumulative Drug remain	Log % Cumulative Drug release
1	0	0	-	0	100	2	-
2	1	1	0	3.08	96.91	1.9863	0.4891
3	2	1.4142	0.3010	9.20	90.79	1.9580	0.9638
4	3	1.7320	0.4771	17.24	82.75	1.9177	1.2367
5	4	2	0.6020	25.69	74.31	1.8710	1.4098
6	5	2.2360	0.6989	32.61	67.38	1.8285	1.5133
7	6	2.4494	0.7781	37.25	63.74	1.7976	1.5711
8	7	2.6457	0.8450	47.61	52.89	1.7234	1.6777
9	8	2.8284	0.9030	53.21	46.78	1.6700	1.7260
10	9	3	0.9542	59.91	40.08	1.6029	1.7775
11	24	4.8989	1.3802	85.64	14.36	1.1571	1.9326

Table no. 16: Ex vivo permeation data of formulated butenafine HCl from formulation F3

S.no.	Time (hrs)	√t	Log T	% Cumulative Drug release	% Cumulative Drug remain	Log % Cumulative Drug remain	Log % Cumulative Drug release
1	0	0	-	0	100	2	-
2	1	1	0	2.65	97.34	1.9883	0.4234
3	2	1.4142	0.3010	7.69	92.30	1.9652	0.8862
4	3	1.7320	0.4771	15.69	84.30	1.9258	1.1956
5	4	2	0.6020	23.62	76.39	1.8830	1.3733
6	5	2.2360	0.6989	30.61	69.38	1.8412	1.4859
7	6	2.4494	0.7781	35.96	64.03	1.8064	1.5558
8	7	2.6457	0.8450	44.09	55.99	1.7481	1.6435
9	8	2.8284	0.9030	50.96	49.04	1.6905	1.7072
10	9	3	0.9542	55.98	44.10	1.6445	1.7480
11	24	4.8989	1.3802	81.56	18.44	1.2685	1.9114

Table no.17: Ex vivo permeation data of formulated butenafine HCl from formulation F4

S.no.	Time (hrs)	√t	Log T	% Cumulative Drug release	% Cumulative Drug remain	Log % Cumulative Drug remain	Log % Cumulative Drug release
1	0	0	-	0	100	2	-
2	1	1	0	3.01	96.99	1.9867	0.4772
3	2	1.4142	0.3010	9.11	90.88	1.9584	0.9598
4	3	1.7320	0.4771	17.01	82.98	1.9189	1.2309
5	4	2	0.6020	25.01	74.98	1.8749	1.3982
6	5	2.2360	0.6989	32.41	67.59	1.8298	1.5106
7	6	2.4494	0.7781	37.21	62.79	1.7978	1.5706
8	7	2.6457	0.8450	47.40	52.59	1.7209	1.6757
9	8	2.8284	0.9030	52.11	47.88	1.6801	1.7169
10	9	3	0.9542	58.61	41.38	1.6168	1.7680
11	24	4.8989	1.3802	84.95	15.02	1.1766	1.9293

Table no.18: Ex vivo permeation data of formulated butenafine HCl from formulation F5

| S.no.	Time (hrs)	√t	Log T	% Cumulative Drug release	% Cumulative Drug remain	Log % Cumulative Drug remain	Log % Cumulative Drug release
1	0	0	-	0	100	2	-
2	1	1	0	3.05	96.99	1.9867	0.4779
3	2	1.4142	0.3010	9.01	90.98	1.9589	0.9550
4	3	1.7320	0.4771	17.06	82.93	1.9187	1.2321
5	4	2	0.6020	25.59	74.40	1.8716	1.4080
6	5	2.2360	0.6989	32.50	67.49	1.8292	1.5118
7	6	2.4494	0.7781	37.11	62.88	1.7985	1.5695
8	7	2.6457	0.8450	46.99	53.00	1.7243	1.6720
9	8	2.8284	0.9030	53.20	46.79	1.6702	1.7259
10	9	3	0.9542	59.09	40.99	1.6126	1.770
11	24	4.8989	1.3802	84.98	15.02	1.1766	1.9293

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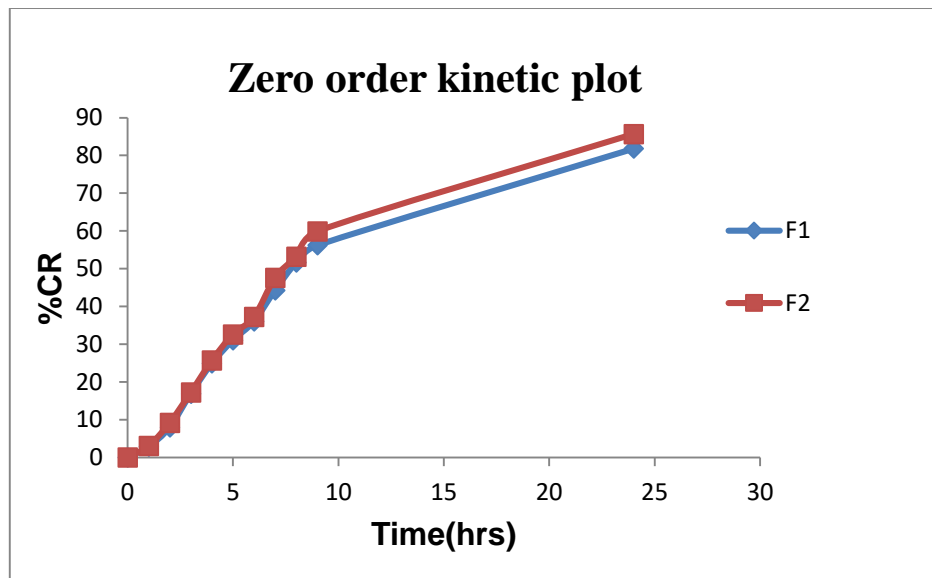
Figure no. 12: Zero order release kinetics of formulation F1&F2
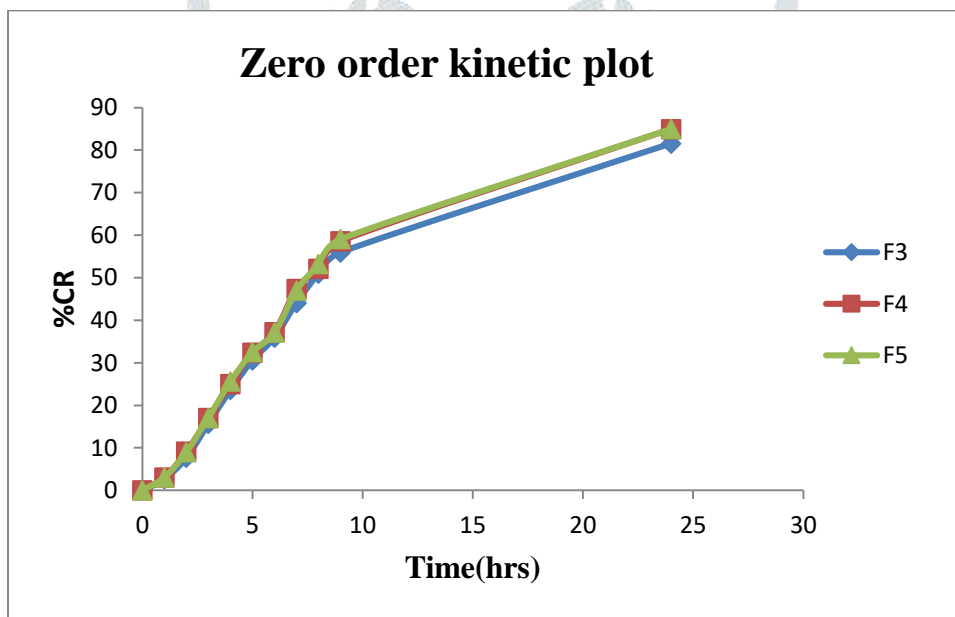

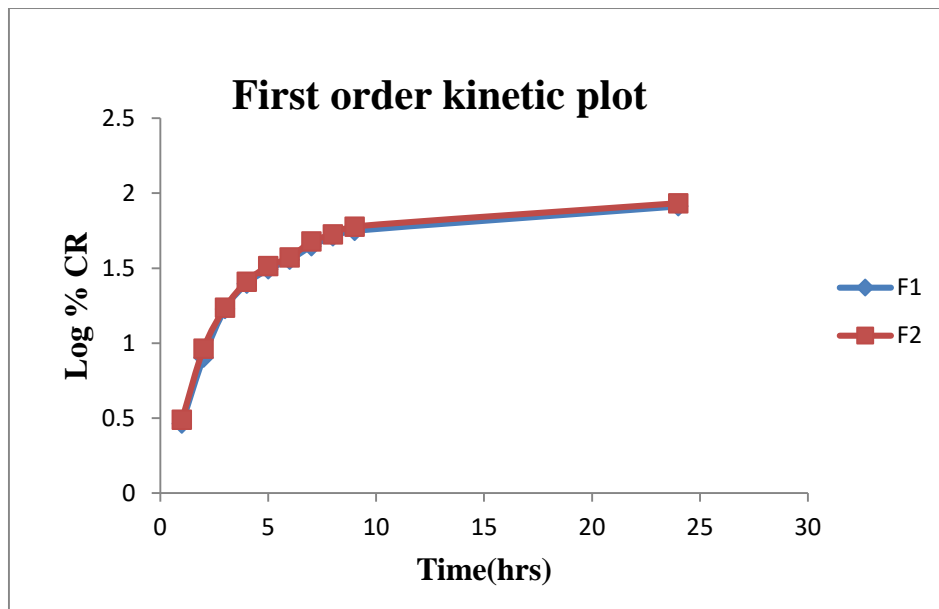**Figure no. 13: Zero order release kinetics of formulation F3, F4&F5**

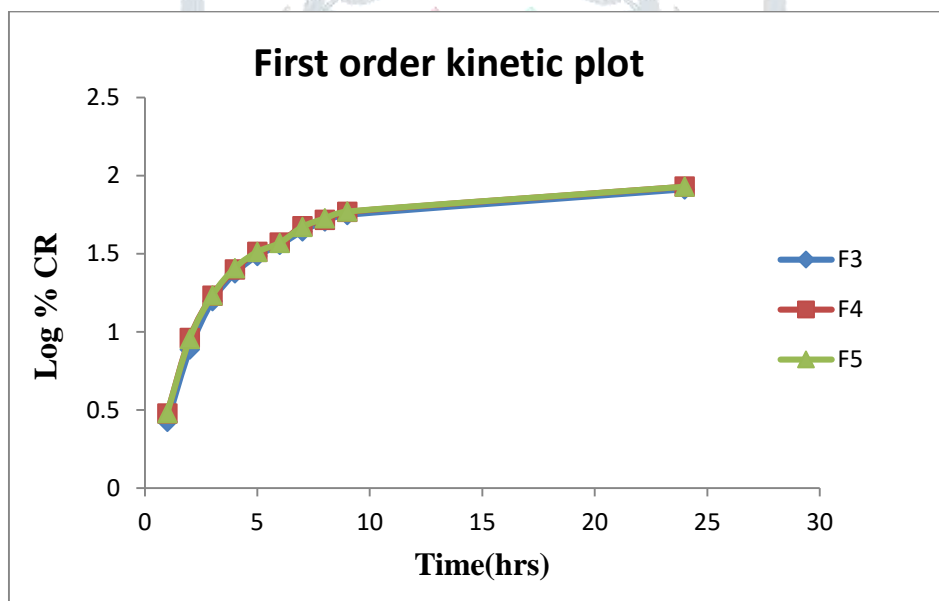**Figure no.14: First order release kinetics of formulation F1&F2**

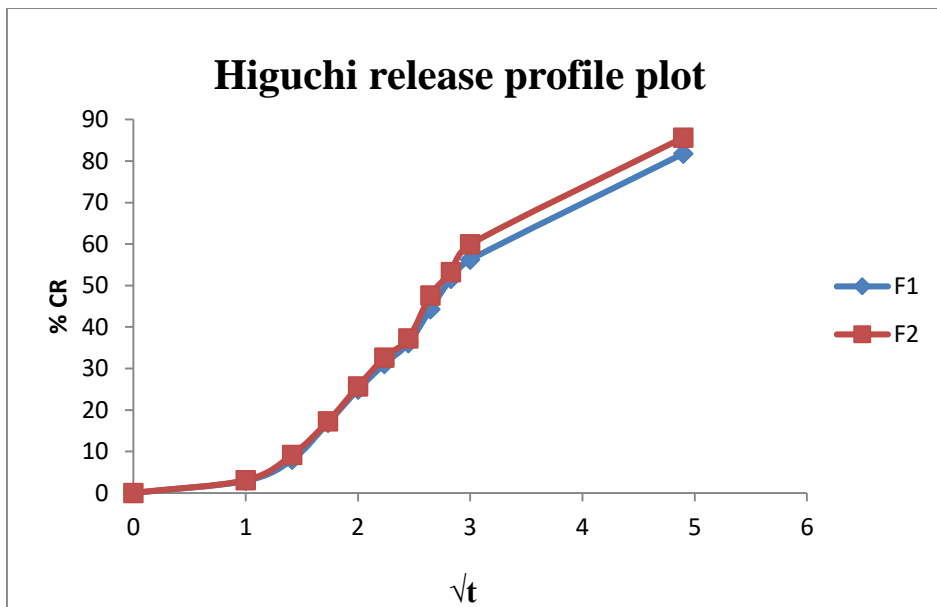**Figure no.15: First order release kinetics of formulation F3, F4&F5**

Higuchi release profile plot

Figure no.16: Higuchi release kinetics of formulation F1&F2
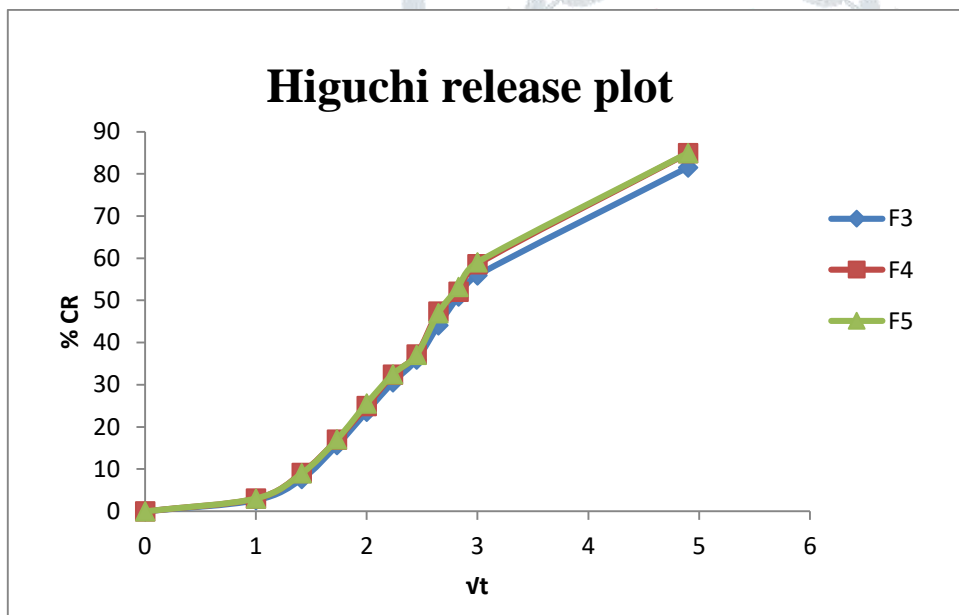

Higuchi release plot

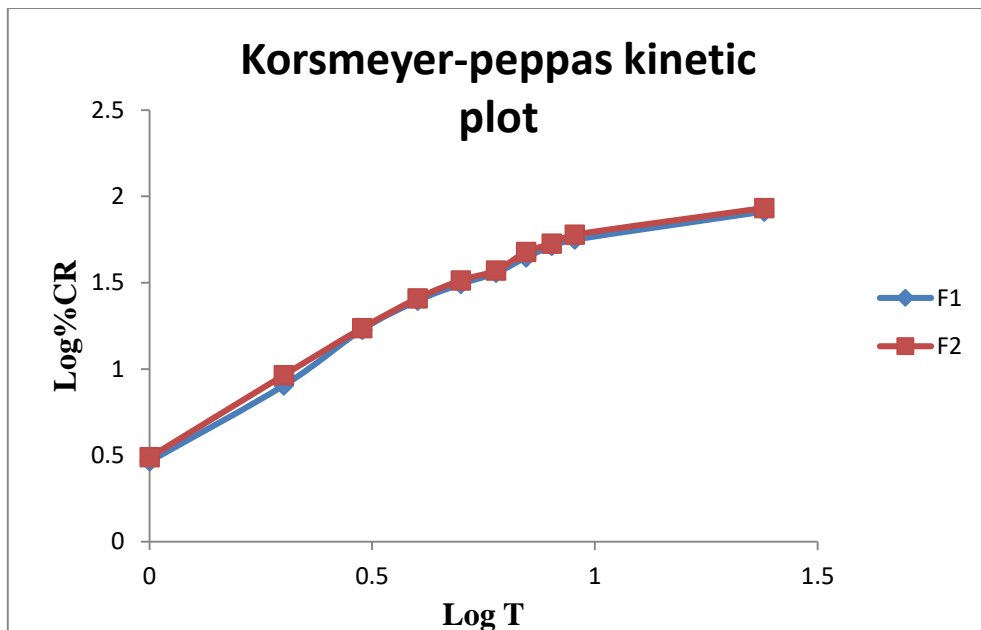**Figure no.17: Higuchi release kinetics of formulation F3, F4&F5**

Figure no. 18: korsmeyer-peppas release kinetics of formulation F1&F2
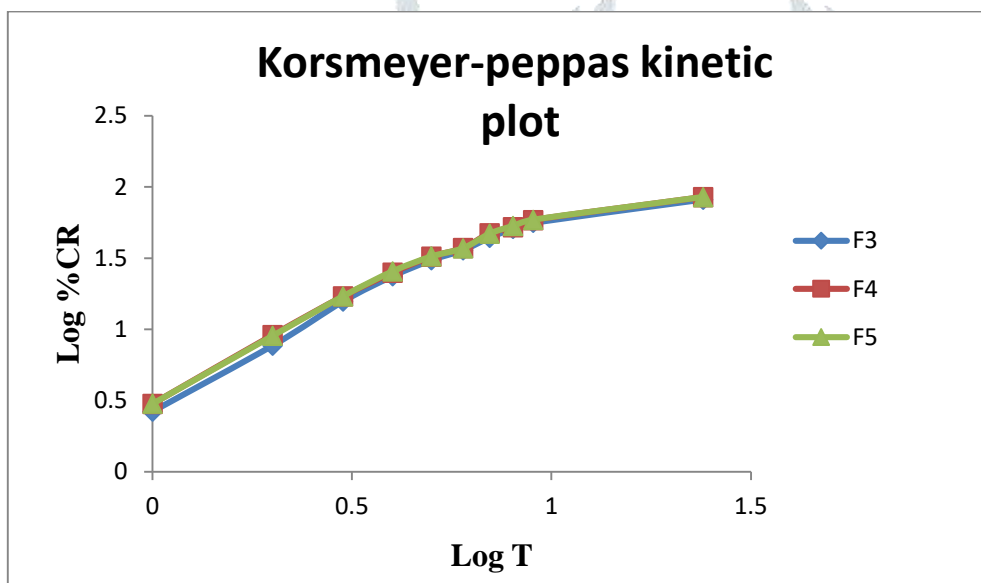

Figure no. 19: korsmeyer-peppas release kinetics of formulation F3, F4 &F5

Table no.19: Model fitting release profile of prepared butenafine HCl nail lacquer formulations F1 to F5

Formulation code	Zero order	First order	Higuchi model	Peppas model(n)	Mechanism of release	Best fitting release Mechanism

F1	0.8436	0.9755	0.9151	0.9218	Supercase II transport	First order
F2	0.8416	0.9838	0.9147	1.0948	Supercase II transport	First order
F3	0.8453	0.9751	0.9159	1.1375	Supercase II transport	First order
F4	0.8454	0.9828	0.9144	1.0977	Supercase II transport	First order
F5	0.8389	0.9830	0.9153	1.0979	Supercase II transport	First order

4. Conclusion:

In the current research mainly focus on formulation & evalution of medicated nail lacquer for effective drug delivery into the nail.

In this study it is clearly indicated that transport of Butenafine HCl can successfully done via the nail by prepared medicated nail lacquer & in this research it was found that the nail lacquer is non-irritating and transport via the nail which help to deliver the drug in a controlled rate which decreases frequency of dosing of dosing of the drug which better ups the patient compliance.

These formulation are also having lesser chances of drug -drug interaction & also used for those substances having poor oral bioavailability.

In this work different ratio of drug and polymer in formulation F1 to F5 was successfully prepared & with different concentration of polymer, showing desired pH, gloss, smoothness of flow, drying time, water resistance, non volatile content , In vitro transungual permeability study & some other tests are accomplish to get appropriate formulation mainly to attain successful nail drug delivery.

The melting point were performed into the drug & it was conforming that drug was Butenafine HCl.

The FTIR study was performed into the drug and for the drug identification it was done by using functional group detection method,which showing that obtained peaks are matched with standard peaks of the drug.The FTIR of drug and polymer was also done ,which showing that no possible interaction is there.

The other parameter UV spectroscopy was accomplished to check the linearity in equation.

The analysis of solubility was done in various solvents & phosphate buffer,it was demonstrating that butenafine is soluble in methanol,ethanol and phosphate buffer 7.4.

The pH study decleard that nail lacquer formed within the range.

The water resistance test showing that increase in the concentration of polymer water resistance increases simultaneously.

The drug content study showing that the nail lacquer formulations are not influencing the stability of drug.

The non-volatile content showing that as increase in polymer concentration from 1 to 1.5 gm showing the nonvolatile content higher.

The viscosity of the nail lacquer decreases as rising in the RPM that reveals that formulation is pseudoplastic in nature.

The antifungal activity was performed on nail lacquer and compares it with marketed formulation& it will showing that zone of inhibition is nearer to the marketed formulation.

The transungual permeation study was performed on hooves membrane, using phosphate buffer 7.4 for 24 hours. By performing in vitro permeation study it was showing that the formulation F2(85.64),F4 (84.95) and F5(84.98) showing highest release as compared to F1 (81.78) and F3(81.56).So it was observed that as the concentration of penetration of penetration increases ,the release of the drug also increases.By comparing the different penetration enhancers used in the formulation it was also predicted that the TGA having better activity as compared to 2-mercaptoethanol and urea in respect of release of drug.

From the in-vitro permeation study in different medicated nail lacquer formulations the collected data were analysed for several mathematical models which are- zero order, first order, Higuchi model, Peppas model and Hixon crowel model, for determination of release mechanism from the developed butenafine HCl nail lacquer.

From the above observed data it was showing first order kinetics and all the prepared formulations from F1 to F5 follows supercase II transport mechanism.

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