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Formulation and Evaluation of Solid Lipid Microparticle Loaded Terbinafine HCl Gel for Topical Delivery

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ABSTRACT

The purpose of the present research work was to formulate the antifungal solid lipid microparticle gel of Terbinafine hydrochloride with the aim of prolonged drug action to evaluate its physicochemical and the pharmacodynamics properties. In this research work, SLM gel was formulated by using Terbinafine hydrochloride as an antifungal drug, steric acid and comprised 888 as lipid, span 80 and Tween 80 as a surfactant, ethanol, and DMF as an organic solvent and water as a solvent. A total of sixteen formulations of SLM were prepared. This is prepared by a solvent evaporation method. After SLM were soaked in different concentrations of Carbopol- 934P for 24 hrs. The formulated SLM gel was evaluated for the different parameters such as physical characterization, pH, solubility, entrapment efficiency, in-vitro drug release, and stability. The formulation F2 out of sixteen formulations was selected as an optimized formulation, which showed the highest % entrapment efficiency (92.77±0.49%), prolonged drug release (62.8±0) in 24 hrs. The vesicles formed were spherically identified by optical microscopy. The optimized formulation (F2) was stable for six months of the period. FTIR results showed that there was no interaction between the drug and the excipients. Out of four formulations, F18 is best in SLM gel. SLM gel can be used for enhanced permeation and sustained release of drugs.

INTRODUCTION

Fungal infection of the skin can be treated by antifungal drugs. Terbinafine hydrochloride is a synthetic allylamine antifungal that is fungicidal against dermatophyte, molds, fungi and some yeast. It is the agent of choice for the treatment of dermatophyte nail infection. [1] It acts as a competitive inhibitor of "squalene epoxidase". An early step enzyme in ergosterol biosynthesis by fungi. Accumulation of squalene within fungal cells appears to be responsible for the fungicidal action. Side effects of oral Terbinafine are gastric upset, rashes, taste disturbance. [2]

In the topical administration of antifungal, the drug substances should pass the stratum corneum, which is the outer most layer of skin, to reach a lower layer of the skin, particularly into viable epidermis. In this context, the formulation may play a major role in the penetration of the drug into the skin. The development of alternative approaches for topical treatment of fungal infection of skin encompasses new carriers systems for an approved and investigational compound. Delivery of antifungal compounds into the skin can be enhanced with the carriers including colloidal systems, vesicular carriers, and nanoparticles. [3,4]

To enhance the efficacy and to improve the safety formulation of solid lipid microparticles is carried out. Solid lipid microparticles are having a size between in the range of 1-1000 µm with the drug being dissolved, entrapped and encapsulated in the microparticle matrix. [5] The drug entrapment got up to 80% which is easily compatible with living systems since the SLMs system based on biomaterials. In SLMs drug is protected from degradation as it is sealed in the biomaterial matrix. The leaching of the drug is a passive mechanism and is independent of the concentration of the drug. As the microparticle continues to get dissolved leading to slow sustained release of the drug in the stomach. The suitability of solid lipid microparticles for sustained release has been established by several authors [6-8]. SLMs can be prepared by Spray-drying, Spray congealing, O/W melt dispersion technique, Double-emulsion solvent evaporation, solvent evaporation, High-pressure homogenization, w/o melt dispersion technique. [9]

The gel can resist the physiological stress caused by skin flexion, mucociliary movement, adapting the shape of the applied area and controlling drug release.

The purpose of topical and dermatological dosage form development is to conveniently deliver drug molecules at a localized area of the skin. [10]

MATERIALS AND METHODS

MATERIALS

The following chemicals were purchased: Terbinafine hydrochloride (Hetero labs, Hyderabad, India), Stearic acid (Gattefosse, France), Tween80 (Molychem, Mumbai), Ethanol (Molychem, Mumbai), carbazole 934P.

METHOD

Preformulation Studies

Preformulation studies are the first step in the rational development of dosage forms. It can be defined as an investigation of the physical and chemical property of a drug substance alone and combined with excipients. Preformulation studies not only help to guide dosages form selection but also provide knowledge that how drug products should be processed and stored to ensure their quality. [11,12]

Organoleptic Properties of Drug:

The drug sample (Terbinafine hydrochloride) was noted for its organoleptic properties such as color, odor, taste, and appearance. [13]

Melting Point:

The melting point of the drug sample (Terbinafine hydrochloride) was determined using a capillary tube method. A small amount of powdered drug was filled inside the thin capillary tube and sealed from one side by melting. The capillary was placed into the melting point apparatus. The thermometer was also placed in the apparatus. After some time at a specific temperature, drugs were melted which was the melting point of the drug. The melting point range of the Terbinafine hydrochloride is 195- 197ºC. [13]

Partition Coefficient of Drug:

For determination of the partition coefficient of the drug, an equal ratio of n-octanol and water, 5-5ml of each was taken. In this mixture excess amount of drug was added and shake properly in separating funnel for mixing the drug with both phases and leave the mixture of solution for 24 hr for proper separation into two phases such as chloroform and water. After

24 hrs chloroform and water phases were separated individually in beakers. Sonicate the obtained filtrate for better clearance of the solution for 15 minutes at 80 Hz. Perform the dilution and check the absorbance at 224 nm. Repeat the same procedure in triplicate for better accuracy. [14]

The solubility of Drug:

About 5mg Terbinafine hydrochloride was added to 10 ml of various solvent and sonicated for 10 minutes and inspected visually for solubility and compared with standard. [15]

Determination of Wave Length (λmax): Wavelength maxima (λmax) of terbinafine HCl was determine as follows.

Preparation of standard curve of Terbinafine HCL in methanol:

10 mg of Terbinafine HCl was weighed accurately and transferred into a 10 ml volumetric flask then the volume was made up with methanol to get 1000 µg/ml primary solution of Terbinafine HCl. The solution was sonicated for 5 min. This solution was further diluted with methanol by taking 0.5 ml from the primary solution in 50 ml volumetric flask and volume make up by methanol to get a 10 µg/ml stock solution. Further dilution will be done by the stock solution of 10 µg/ml of Terbinafine HCLby serial dilution method and samples are analyzed by UV spectrophotometer using methanol as blank. [16]

FTIR spectral analysis of Terbinafine HCL:

FTIR spectrophotometry is used for structural and functional group analysis of drugs. The analysis was carried out using potassium bromide (KBr) pellet method. The KBr and drugs (Terbinafine HCL) were mixed separately and carefully in a mortar while grinding with the pestle and dried completely. The powdered sample was placed just enough to cover the bottom in pellet die and pressure of 5000-7000 psi was applied to make the pellets. Then the pellets were placed in the sample holder of FTIR spectrophotometer. FTIR spectra were recorded in the 4000-400 cm^{-1} regions. [17]

Solubility studies of Terbinafine HCl in lipids:

1000 mg of several types of lipids (Dyansan 116, Dyansan 114, Compritol 888, Stearic acid) were taken in a different culture tube and placed them in a water bath shaker at 80°C and kept

shaking until they melt. An excess amount of drug was added while shaking meanwhile 10 ml of methanol solution was added and allowed their shaking for 72 h at 80°C. After 72 h. centrifuge the sample at 15000 rpm for 30 min followed by taking the supernatant and diluted with methanol if required. Scan the sample in UV spectroscopy between 200-400 nm. [18]

Preparation of SLMs

Solvent evaporation method widely used for the preparation of solid lipid microparticles. Firstly weigh an accurate amount of substance. Then, in this method drug (TerbinafineHCl) and lipid (stearic acid) were dissolved in an organic solvent, this mixture was kept on a magnetic stirrer at the above the melting point of lipid with the help of thermometer. Aqueous solutions of Tween 80 containing as emulsifiers were stirred with the help of magnetic stirrer. Then, both the mixtures were added and stirred at 1000 rpm at 70˚C. Microparticles were filtered, washed with acetone and vacuum dried overnight at room temperature. [19]

Table No. 1: Formulation quantity used

Drug	TerbinafineHCl	250mg
Lipid	Stearic acid	1500mg
Surfactants	Tween 80	100mg
Organic solvent	Ethanol	5ml
Solvent	Water	100ml

Preparation of gel

The Terbinafine HCl solid lipid microparticle was generated by solvent evaporation method Take 300 mg solid lipid microparticle and added different gelling agent 50 mg (1%), 75 mg (1.5%), 100 mg (2%) of Carbopol- 934 and kept aside for 1 hour for swelling continuous stirring at a speed of 800 rpm using a mechanical agitator. The dispersion was neutralized using diluted NaOH until pH 6.0 to 8.0. The gel could stand overnight to remove entrapped air. [20]

Evaluation of SLMs formulation

Percentage practical yield [21]:

SLMs obtained after filtration were dried overnight in vacuum desiccators and weighed; the weight obtained was the practical yield of SLMs. The total amount of lipids plus the amount of drugs gives the theoretical yield.

$$\textbf{Percentage practical yield} = \frac{\text{Practical mass of SLMs}}{\text{Theoretical mass}} \times 100$$

Micrometrics property [21]

Angle of repose

The angle of repose is the angle formed by the horizontal base of the bench surface and the edge of a cone-like pile of granules. Funnel used was a stainless-steel funnel and the size of the orifice was 10 mm and the height from the beginning of funnel to the end of the orifice was 111 mm. The funnel was fixed in place, 4 cm above the bench surface. After the cone from 5 g of sample was built, the height of the granules forming the cone (h) and the radius (r) of the base was measured. The angle of repose (θ) was calculated as follows:

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$$\theta = \tan^{-1}\frac{h}{r}$$

Results were only considered valid when a symmetrical cone of powder was formed.

Bulk density & Tapped density

Bulk density (BD) and tapped densities (TD) were determined using the methods outlined in the USP (2). SLMs were passed through a no. 18 sieve into a pre-weighed 25 ml graduated cylinder with 0.5 ml markings. The bulk volume was measured after manually tapping the cylinder two times on a flat tabletop surface. The tapped volume was measured with the Electrolab ETD-1020 Tap Density Tester (Globe- Pharma) after tapping of 500 drops per minute. Followed by using the formula to calculate bulk and tapped density.

$$\text{BD} = \frac{\text{amount of SLMs taken}}{\text{Bulk volume}}$$

$$TD = \frac{\text{amount of SLMs taken}}{\text{Tapped volume}}$$

Hausner's ratio & Carr's index

Hausner's ratio of microparticles was determined by comparing the tapped density to the bulk density using the equation. Carr's index value of microparticles was computed according to the following equation:

$$\text{Hausner's ratio} = \frac{TD}{BD}$$

$$\text{Carr's Index } (\%) = \frac{(TD - BD)}{TD} \times 100$$

Particle size [22, 23]

The particle size of the drug-loaded SLMs was measured by a digital microscope. The average particle size of SLMswas determined with a micrometer and calculated as the average value of the size of 100 particles.

Determination of % EE [24]

SLMs entrapped Terbinafine HCl was estimated by the centrifugation method. The prepared 10 mg SLMs were dispersed in 10 ml volumetric flask then volume makes up with methanol and then vortex. After that prepared solution was centrifuged at 15000 rpm for 15 minutes. The supernatant (1 ml) was withdrawn and diluted with methanol. The unentrappedTerbinafineHCl was determined by UV spectrophotometer at $\lambda_{max}$of a drug. The samples from the supernatant were diluted before going for absorbance measurement. The free Terbinafine HCl in the supernatant gives us the total amount of unentrapped drug. Encapsulation efficiency is expressed as the percent of drug trapped.

The %EE was calculated as:

$$EE = \frac{\text{Amount of drug entraped}}{\text{Amount of drug added}} \times 100$$

Scanning electron microscopy [25]

Scanning electron microscopic (SEM) studies: For SEM analysis, the sample was mounted onto an aluminum stub and sputter-coated with platinum particles in the inert atmosphere. Particles were analyzed at an operation voltage of 5.00 kV. As can be evidenced from the SEM image, SLMs were spherical with a regular surface profile. No indentations were observed on their surface.

Evaluation of Terbinafine HCl loaded solid lipid microparticle gel: [26, 27, 28]

The appearance of gel

The prepared solid lipid microparticlegel visually observed by placed in the beaker.

Percentage detection of pH

The pH of solid lipid microparticle gel was determined by using a digital pH meter at room temperature. Take gel in a beaker and then, the electrode was dipped into gel formulation and constant reading was noted in triplicate.

Percentage drug content

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The drug content of the gels was determined by dissolving an accurately weighed quantity of gel (about 1 gm) and diluted in 25 ml methanol, sonicate for 10 mins and fill it into Eppendorf, centrifuged for 15 mins. After that 1 ml supernatant layer taken and makeup volume up to 10 ml with methanol. Then further and further diluted and analyzed under UV spectrophotometry analysis for terbinafine at 224 nm. Drug content was determined from the standard curve of Terbinafine. [15]

In-vitro permeation studies

The in vitro permeation studies were performed using Franz diffusion cells for studying the dissolution release of various formulation of gel through a dialysis membrane-70 with an effective diffusion area of 1.77 cm^2 and receptor volume of 20 ml.1g of gel sample was taken in the dialysis membrane. The diffusion studies carried out at 37 ± 1°C using 250 ml of phosphate buffer saline (pH 7.4) as the dissolution medium. A standard dialysis membrane (soaked in 20% ethanol for 24 hours before use) was fixed to one end of the cylinder with the aid of an adhesive to result in permeation cell. One gram of gel was taken in the cell

(acceptor compartment) and the phosphate buffer saline 7.4 filled in the donor compartment in a beaker. Sample (1 ml) of the donor compartment was taken at a various interval of time (0.25, 0.5, 1, 2, 3, 4, 6, 8, 10, 12, 24 hr) and assayed for terbinafineHClsolid lipid microparticle gel at 224 nm in UV apparatus. The volume withdrawn at each time was replaced with drug-free phosphate buffer. The amount of Terbinafine HCl released at various intervals of time was calculated and plotted against time.

Drug release kinetics [29, 30]

Model dependent methods are based on different mathematical functions, which describe the release profile. Once a suitable function has been selected, the release profiles are evaluated depending on the derived model parameters. The data obtained from in vitro permeation studies were plotted in different models of the data treatment as follows;

- Zero Order model
- First Order model
- Higuchi's Model
- Korsmeyer-Peppas model

Zero-order kinetics

It can be used to describe the drug dissolution of several types of modified release pharmaceutical dosage forms, as in the case of some transdermal systems, as well as matrix tablets with low soluble drugs in coated forms, osmotic systems, etc. In its simplest form, zero-order release can be represented as:

$$Q0 - Qt = K0t$$

Where, Qt is the amount of drug dissolved in time t, Q0 is the initial amount of drug in the solution (most times, Q0 = 0) and K0 is the zero-order release constant expressed in units of concentration/time. To study the release kinetics, data obtained from in vitro drug permeation studies were plotted as the cumulative amount of drug released versus time.

First-order kinetics

It can be used to describe the drug dissolution in pharmaceutical dosage forms such as those containing water-soluble drugs in porous matrices. The release of the drug which followed first-order kinetics can be expressed by the equation:

$$\log C = \log C0\ n\ Kt / 2.303$$

Where C0 is the initial concentration of the drug, k is the first-order rate constant, and t is the time. The data obtained are plotted as log cumulative percentage of drug remaining vs. time which would yield a straight line with a slope of nK/2.303.

Higuchi's Model

This model expected to pronounce drug release from a matrix system. Primarily regarded for planar systems, it was then extended to different geometrics and porous systems. This model is based on the hypotheses that (i) initial drug concentration in the matrix is much higher than drug solubility; (ii) drug diffusion takes place only in one dimension (edge effect must be negligible), (iii) drug particles are much smaller than system thickness, (iv) matrix swelling and dissolution are negligible, (v) drug diffusivity is constant, and (vi) perfect sink conditions are always attained in the release environment.

Higuchi was the first to derive an equation to describe the release of a drug from an insoluble matrix as the square root of a time-dependent process based on Fickian diffusion. Simplified Higuchi equation is following;

$$Qt = KH\ (t)\ 0.5$$

Where Qt is the amount of drug released in time t and KH is the release rate constant for the Higuchi model. When the data is plotted as a cumulative drug released versus square root of time, it yields a straight line, indicating that the drug was released by diffusion mechanism. The slope is equal to "KH".

Korsmeyer-Peppas Model

Korsmeyer derived a simple relationship that described drug release from a polymeric system. The release rates from controlled release polymeric matrices can be described by the equation proposed by Korsmeyer et al.

$$Q = Kt^n$$

Where Q is the percentage of drug released at time "t" K is a kinetic constant incorporating structural and geometric characteristic of the tablets and "n" is the diffusional exponent indicative of the release mechanism.

For Fickian release, n=0.45 while for anomalous (Non-Fickian) transport, n ranges between 0.45 and 0.89 and for zero-order release, n = 0.89. The Korsmeyer-Peppas model was plotted between log cumulative % drug releases versus log time.

RESULTS AND DISCUSSION

Preformulation studies

1. Organoleptic Properties

Table No. 2: Organoleptic Properties of Terbinafine HCl

S. No.	Properties	Inferences
1.	Colour	Offwhite
2.	Odor	Odorless
3.	Form	Fluffy powder
4.	Taste	Bitter

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2. UV Spectroscopy

UV-visible spectroscopy

UV absorption maxima (λ_{max}) of Terbinafine HClin methanol was determined by using a UV-visible spectrophotometer and shown in **Figure. 1** The drug exhibited maxima at 224 nm.

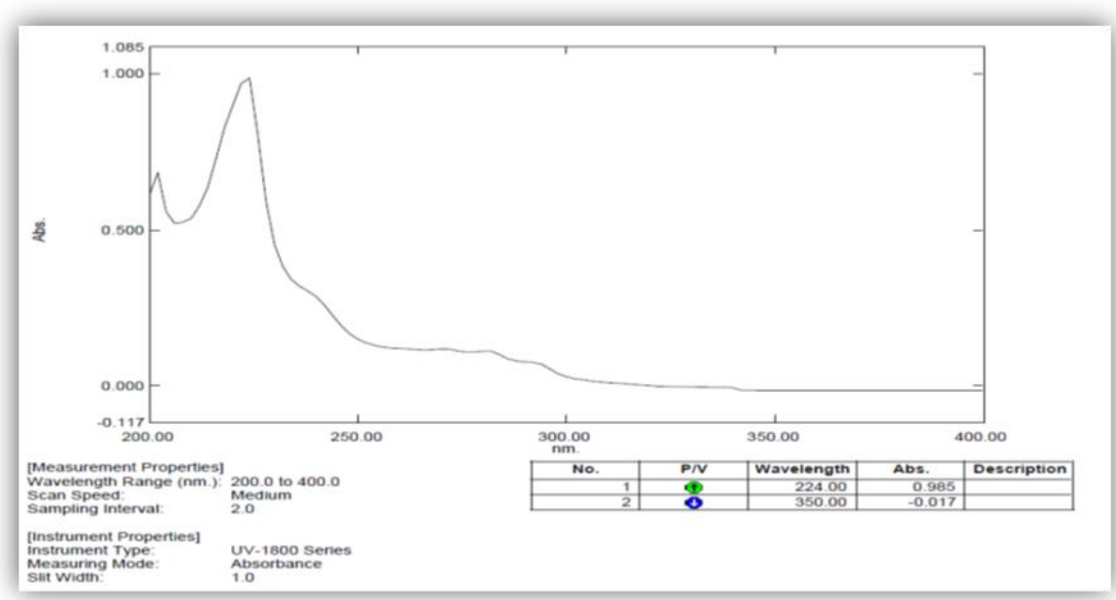

Figure 1: UV-visible spectrum of Terbinafine HCl in methanol

Table 3: Absorption maxima (λ_{max}) of Terbinafine HCl

Observed absorption maxima	Reported absorption maxima
224 nm or 282	224nm

Preparation of standard curve of Terbinafine HCl in methanol

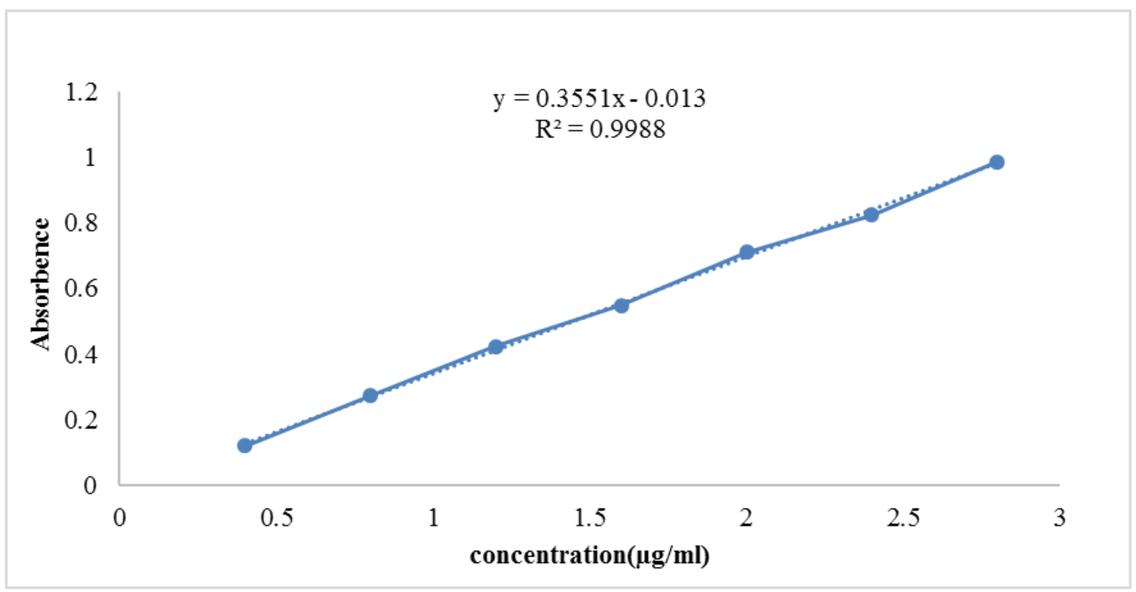

Figure No. 2: Graph of standard calibration curve of Terbinafine HCl in methanol

Table No. 4: Result of regression analysis of the UV method for the estimation of Terbinafine HCl

Statistical parameters	Results
λ max	224 nm
Regression equation ** Y=mx+C	y = 0.3551x - 0.013
Slope (b)	0.3551
Intercept (C)	-0.013
The correlation coefficient (r^2)	0.998

Melting point determination

Table No. 5: Melting point of Terbinafine HCl

Drug	Reference M.P.	Observed M.P.
Terbinafine HCl	195-197°C,	194-198°C

Partition coefficient determination

Table No. 6: Partition coefficient determination of Terbinafine HCl

The partition coefficient of drug	Solvent system	Log p Values
Terbinafine HCl	n-octanol: water	2.07± 0.005

The partition coefficient of Terbinafine HCl in n- Octanol: Water was found to be 2.07±0.005 this indicates that the drug is lipophilic.

FT-IR spectral analysis

FT-IR analysis measures the selective absorption of light by the vibration modes of specific chemical bonds in the sample.

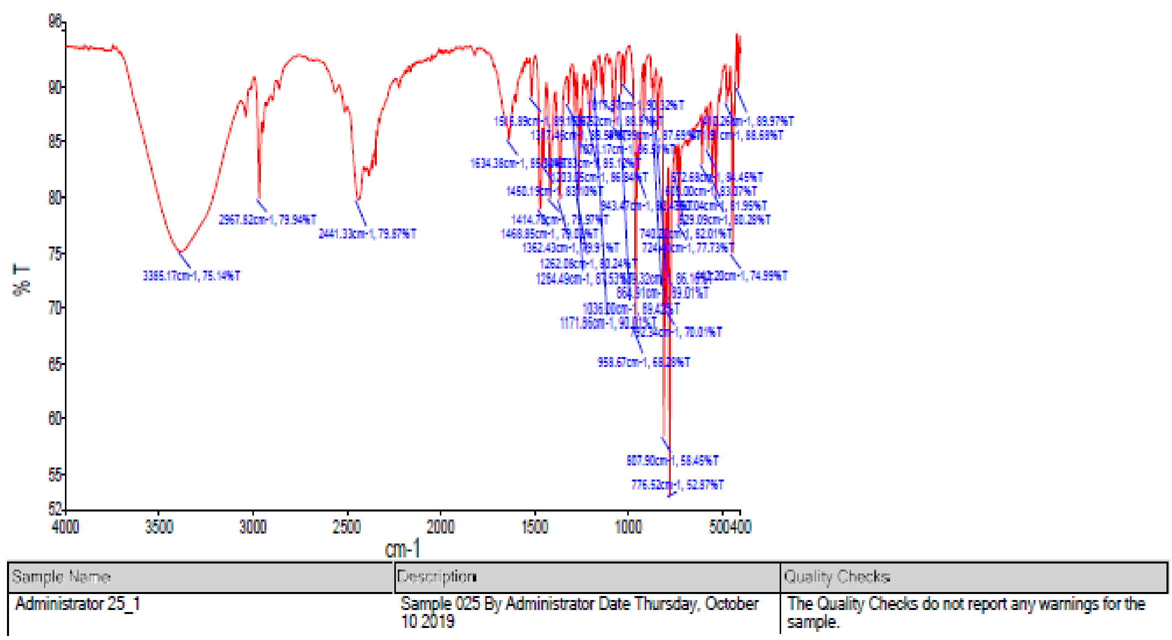

Figure 3: FTIR Spectrum of Terbinafine HCl Drug

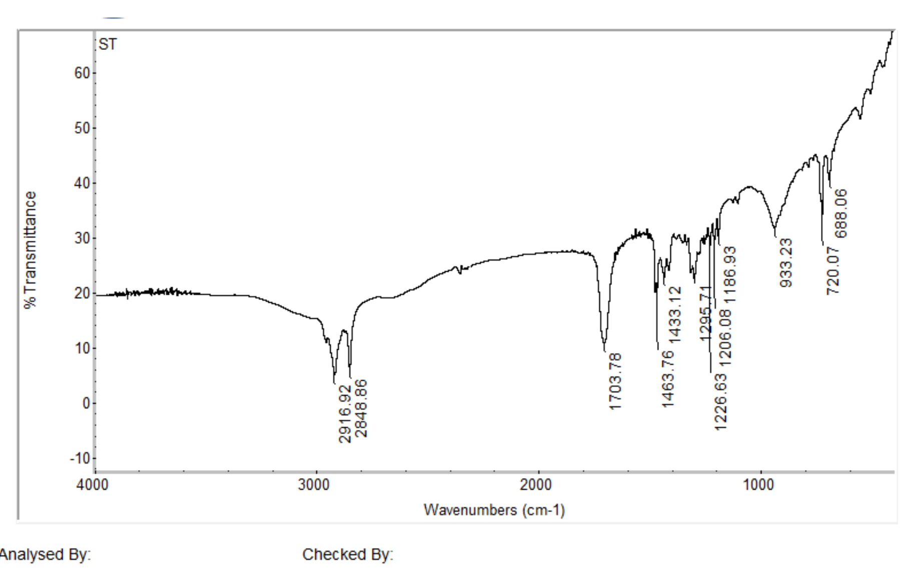

Figure 4: FTIR Spectrum of stearic acid

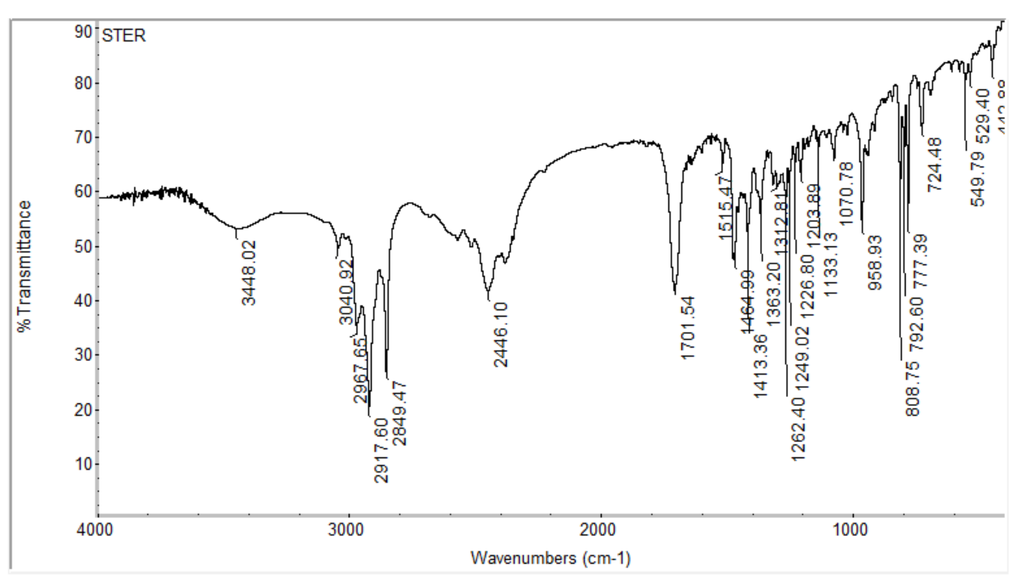

Figure 5: FTIR Spectrum of Terbinafine HCl + excipient

Solubility studies

The solubility of the drug in various types of solvents and was carried out to screen for the components to be used for formulation development. Analysis of the drug was carried out on UV Spectrophotometer at 224 nm.

Table 7: Solubility of Terbinafine Hydrochloride

S.No.	Solvent	Solubility
1	Water	Slightly soluble
2	Methanol	Freely Soluble
3	Ethanol	Freely Soluble
4	Acetone	Freely Soluble
5	DCM	Freely soluble
6	Ph 6.8	Slightly soluble

Terbinafine HCl highly soluble in organic solvent and drug is less soluble in inorganic solvents.

Lipid solubility study

Table 8: Solubility studies of Terbinafine HCl for different lipids

S. no.	Lipids	Solubility (mean±SD)*
1	Stearic acid	1.02±0.022
2	Compritol 888	0.76±0.083
3	Dyansan 116	0.66±0.054
4	Dyanasan 114	0.96±0.074

* Each value is average of three independent determinations

Discussion: Solubility studies indicated that amongst Dyansan 116, Dyansan 114, Compritol 888, Stearic acid. Terbinafine HCl had more affinity toward comprital 888 and stearic acid as compare to another lipid.

Characterization of SLMs

Appearance of SLMs

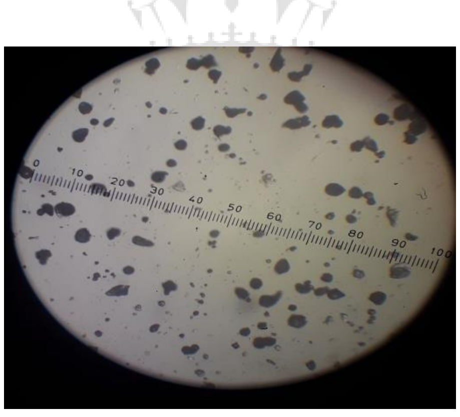

Figure 6: Microscopically view of Terbinafine HCl loaded SLMs of formulation

Micrometrics property

Table 9: Micrometric property of F2

FORMULATION CODE	BULK DENSITY (G/ML)	TAPPED DENSITY (G/ML)	CARR'S INDEX	HAUSER'S RATIO	ANGLE OF REPOSE
F2	0.533±0.02	0.571±0.003	6.71±0.005	1.07±0.001	28.8±0.78

Percentage yield, particle size and % drug entrapment

The percentage yield, particle size and % drug entrapment of SLM was given a **Table 10**.

Table No. 10: Percentage yield of SLMs formulation

S. No.	Formulation Code	Percentage Yield	Particle size	%drug entrapment efficacy
1	F2	92.77±0.49	5.36±0.04	96.45±0.014

Discussion: Out of 16 formulation f2 formulation has a high percentage yield, particle size and % drug entrapment. Formulation F2 was the optimized formulation among all Terbinafine HCl loaded SLMs formulations. F2 showed good entrapment of drug and compatibility with lipid.

Analysis of SEM

Scanning Electron Microscope (Model: JSM 5200, Japan) was used to characterize the surface morphology of optimized SLMs. The samples were prepared by absorbing the lipospheres suspension on double side adhesive tape which stuck to aluminum stab and gold-coated under vacuum using a sputter coater. Samples were exposed to a vacuum for 5-10 min. at 40 mA and investigated at an accelerating voltage of 15 kV and 10 kV12.

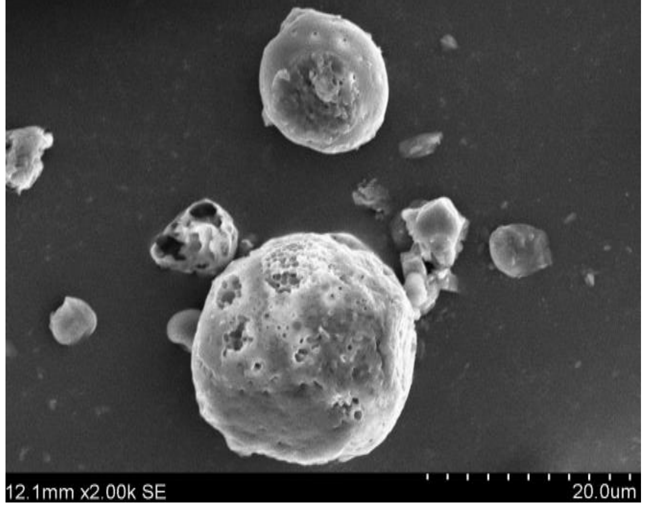

Figure 7: SEM of SLMs

Evaluation of SLM loaded Terbinafine HCl gel

Appearance: All gel is viewed and record its appearance.

Table 11: Appearance of SLMs Gel formulation

S. No.	Appearance	F17	F18	F19	F20
1	Colour	White	White	White	White
2	Odor	Odorless	Odorless	Odorless	Odorless
3	Smoothness	Smooth	Smooth	Smooth	Smooth
4	Irritation	Non-irritant	Non-irritant	Non-irritant	Non-irritant

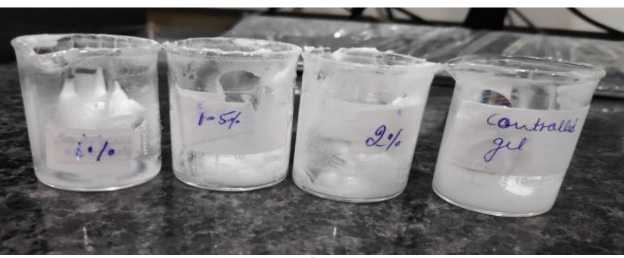

Figure 8: Appearance of all gel

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Determination of pH, % Drug content

All the formulation ph. was recorded by pH. Meter and drug content of the formulation.

Table 12: pH. and % Drug content of SLMs Gel formulation

S. No.	Formulation	pH. Determination	% Drug content
1	F17	7.1±0.057	94.76±0.24
2	F18	7.2±0.020	90.33±0.15
3	F19	6.5±0.005	80.98±0.08
4	F20	6.8±0	80.13±0

Discussion: Formulation F17 and F18 have high drug content and good pH as according to nearby pH of skin**.** F18 will proceed for in vitro studies.

In-vitro permeation studies

This study was done by Franz diffusion method in the various time intervals in the following table.

Table 13: In-vitro release of SLMs Gel formulation

Time in hrs	F17	F18	F19	F20
0	0±0	0±0	0±0	0±0
0.25	25.7±0.23	6.4±0.2	7±0.001	4.5±0.12
0.5	46.2±0.002	14.3±0.5	11.10±0.12	9.9±0
1	60.3±0.02	21.2±0.01	18.8±0.56	11.9±0.02
2	72.1±0.11	26±0.002	21.9±0	16.9±0.25
3	87.2±0.12	30±0.01	23.8±1.4	19.1±0
4	98.2±0.13	36±0.12	26.5±0.03	20.5±0.12
6		40.3±0.12	28.5±0	22.8±0
8		44.1±0.01	30.8±0.02	25.4±0.03
10		48.6±0.12	32±0.01	25.9±0
12		54.5±0	36±0	27.2±0.11
24		62.8±0	45±0	31.5±0.96

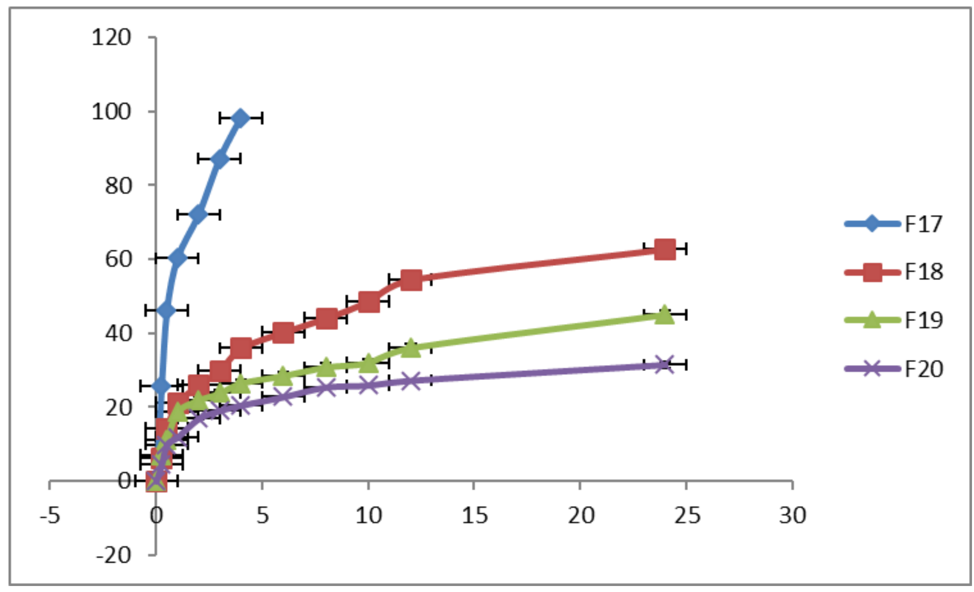

Figure 9: In-vitro drug release of SLM gel

Discussion: The best release of the gel was recorded in the F18 formulation. So as this result the drug release kinetics will be recorded for F18 formulation.

FTIR spectral analysis

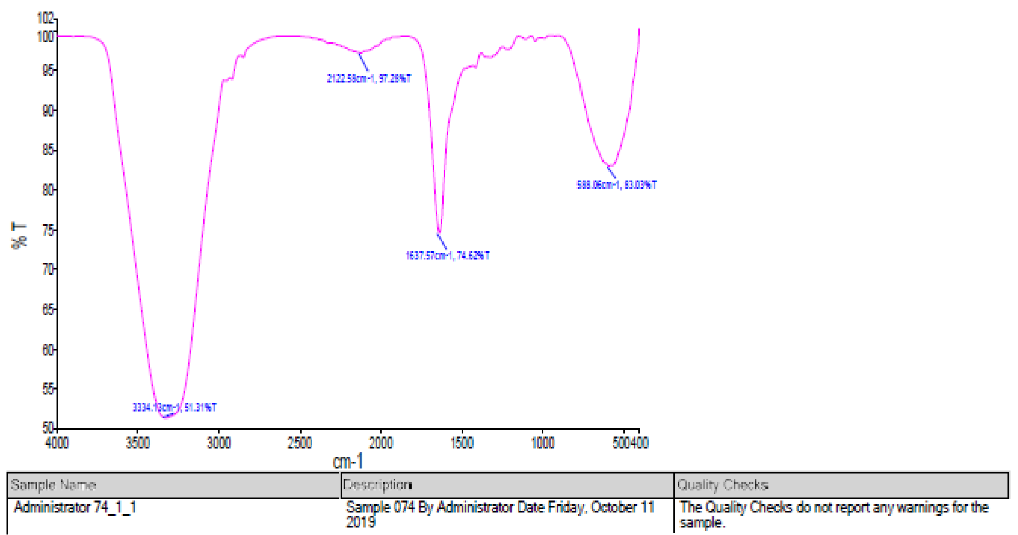

Figure 10: FTIR of SLMs gel

Discussion: The absence and low peak intensity of drug show entrapment of drug in developed SLMs gel. No interaction is shown in their chemical bonding.

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Drug release kinetics

In-vitro drug release kinetic study data of formulation F 18 was given below.

Zero-order

Zero-order graph % drug release vs. Time

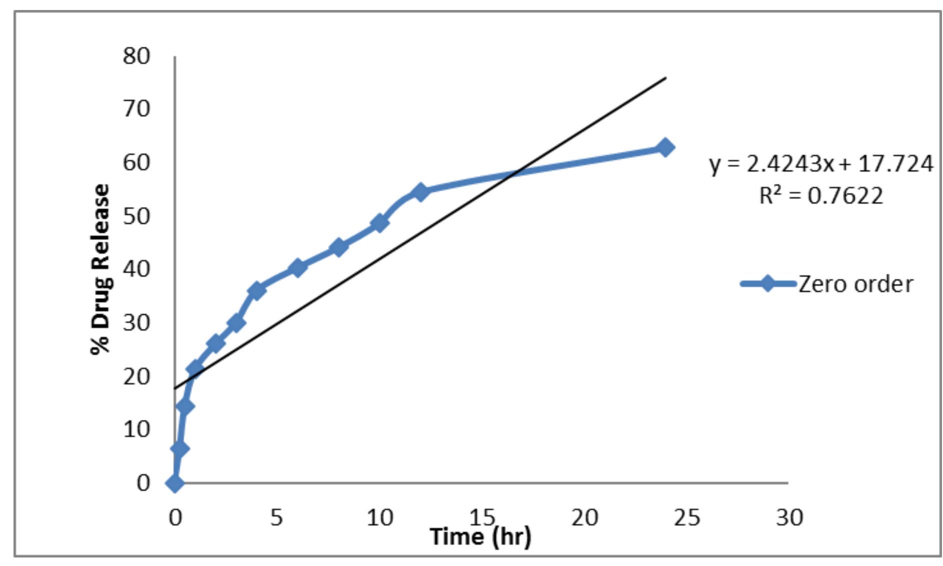

Figure 11: Zero-order kinetics of F18 formulation

First-order

First-order graph Log % drug remaining vs. time

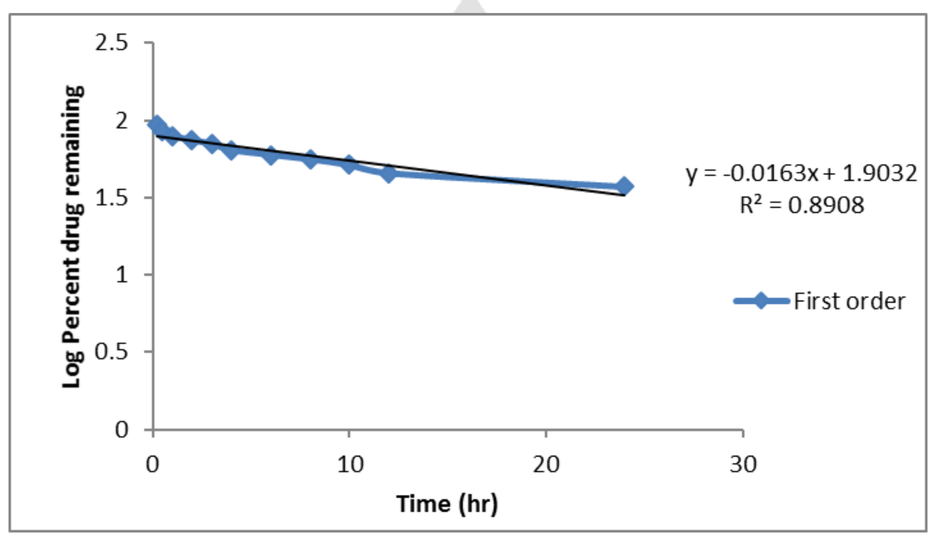

Figure 12: First-order kinetics of F18 formulation

Higuchi kinetics

Higuchi release kinetics log %drug release vs. Square root of time

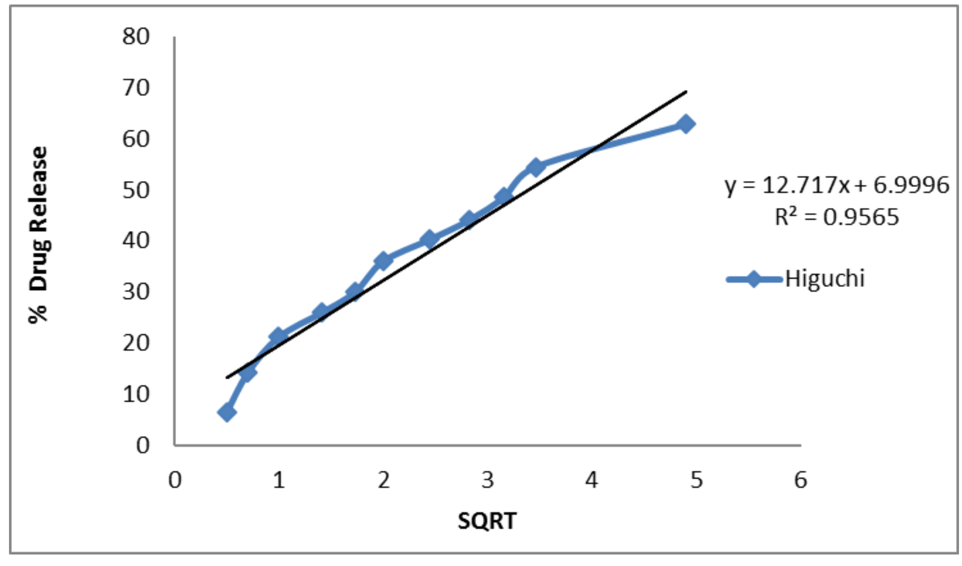

Figure 13: Higuchi kinetics of F18 formulation

Korsmeyer-peppas

Korsmeyer-Peppas release kinetics Log % drug release vs Log time

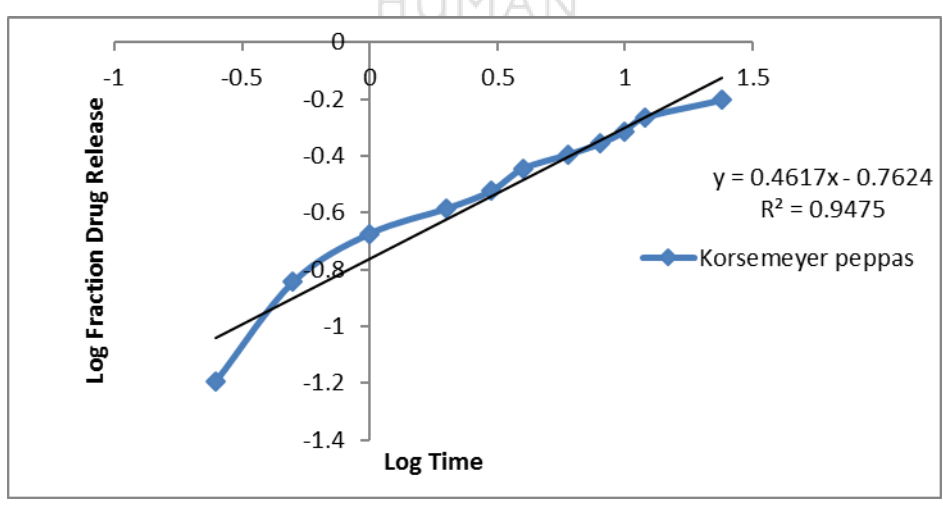

Figure 14: Korsmeyer-Peppas Model of F18 formulation

Table No. 14: Kinetic equation parameter of F18 formulation

Formulation Name	Zero-order		First-order		Higuchi		Korsymer-peppas	
	R^2	K_0	R^2	K_0	R^2	K_0	R^2	K_0
F18	0.762	2.4243	0.890	-0.0163	**0.956**	12.717	0.947	0.4617

Discussion: Considering the determination coefficients i.e. R^2, Higuchi order was found (R^2=0.956) to fit the release data best. It could be concluded from the results that the drug was released from the SLM gel of Terbinafine HCl by a sustained mechanism.

Stability study analysis [31]

Stability studies of formulation f18 were examined over 6 months period by storing samples at three different temperatures and relative humidity for ph and drug content.

Table No. 15: Stability study data of F18 Formulation

Period (6 months)	5°C±2°C		25°C±5°C/60% RH		40°C±5°C/75% RH	
	ph	Drug content	ph	Drug content	Ph	Drug content
Before	7.21± 0.001	95.26± 0.149	7.21± 0.001	95.26± 0.149	7.21± 0.001	95.26± 0.149
After	7.16± 0.04	94.61± 0.086	7.01± 0.08	90.58± 0.212	6.8± 0.005	87.58± 0.175

CONCLUSION

This research has proved that Terbinafine HCl could be formulated as SLMs and then SLMs loaded gel. SLMs were prepared by solvent evaporation method and then SLMs was soaked in different concentration of Carbopol 934P. The aim of this research work was that we have to make the sustained release gel and enhance permeation through the skin. The Terbinafine HCl loaded SLMs gel was successfully made and evaluated through a different parameter. The evaluation parameter is best for this formulation. SLMs gel formulation is presented as an alternative with improved permeability and decreased dosage frequency (hence improving compliance) and also decrease the side effects.

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