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FORMULATION AND EVALUATION OF TERBINAFINE HYDROCHLORIDE AS A CUBOSOMAL TOPICAL GEL TO TREAT DERMATOLOGICAL INFECTIONS

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ABSTRACT

The purposes of current research work were to develope and evaluate cubosomal gel to treat dermatological infections like athlete's foot (tineapedis), jock itch (tineacruris) and ringworm (tineacorporis. To solve problems of frequent administration and longer duration of treatment. Cubosomes are novel nanoparticle system loaded with Terbinafine Hydrochloride as Antifungal agent. Hydrating surfactant which forms cubic phase dispersing solid phase into nanoparticles forms a cubosomes .They have three dimensional bilayers therefore allows greater loading ability. Cubosomes were developed and approach by top-down method. Drug release from commercial available formulation is lower than prepared cubosomal based gel .Terbinafine Hydrochloride loaded cubosomes were prepared by simple emulsification technique using different concentrations of a lipid phase monooleinand Poloxamer 407enclosing in cubic gel matrix .The prepared cubosomal dispersion were characterized through dimensional distribution (light microscopy), entrapment efficiency and particle size. The optimal cubosomal formulae were incorporated in a carbopolbased hydrogels, to form cubosomal hydrogels (cubogels) which characterized through physical morphology, vitro drug release studies, pH, viscosity, spreadability studies. Optimized cubogel was microbiologically evaluated *against A. niger* and *C. albicans* using agar cup diffusion method which showed superior anti-dermatomycosis activity as compared to the marketed formulation. Among all the preparation (F4)was found to show maximum drug release of 81.95±0.25% in 6 hours, entrapment efficiency 92.76±0.42% and particle size of 231± 5.3nm.

INTRODUCTION

Terbinafine hydrochloride is acts as an antifungal drug which inhibits fungal infection and also enzyme inhibitor .Terbinafine (TB), a synthetic allylamine, exerts potent broad-spectrum fungicidal activity Now a day's fungal infection is common skin problem. This drug is most commonly used for dermatophyte infection. (1) Fungi that colonize the nail, hair and outer layer of epidermis i.e. stratum corneum called dermatophytes. Tinea infections are apparent and superficial fungal infections caused by three species of fungi known as dermatophytes. Usually these infections are named for the body part affected, including *Tineacorporis* (general skin), *Tineacruris* (groin or Jock itch), and *Tineapedis* (feet) and therefore can be often treated with topical antifungal medications. Accurate diagnosis is necessary for effective treatment. *Trichophytonrubrum*is the most likely agent in these dermatophytes. *T.*

*rubrum*accounted for76.2 % of all superficial fungal diseasesin a representative sample of the U.S. population with exception of tineacapitis which is ringworm of scalp. Tineapedis or ringworm of the feet orathlet's foot infection which is a common skin disease and upto 15 % of the population may have this disorder.*Tineacruris* or ringworm of groin or jock itch caused by susceptible fungi which rapidly grow in dead keratinized layer of skin .Tineacorporis occurs on the body surfaces such as arms and legs particularly on glabrous skin.These superficialdermatophytes spreads easily by direct contact with infected people and these infection because of moist part of body such as between fingers and toes.(2)Terbinafine administered orally as well as topically which well tolerated and about 40% of drug is undergoes first pass metabolism therefore topical dosage form may be more easily achieved for antifungal activity.To achieve similar local drug concentrations, oral dose needs to be allocated with more quantity, which increases the risk of adverse effects and topical administration results in reducing the possible toxicity of the drug. Terbinafine Hydrochloride is poorly water soluble drug so solubility is important straint for bioavailability. The objective of this study is to examine the potential of the cubosomal approach which is Nano-carrier to improve the solubility of drug and also to sustain the drug release.(1,3,4). Cubosomes are nanostructured particles which are in free form having bicontinuous cubic liquid crystalline phases by hydrating mixture of monoolein and poloxamer 407(5-7) Its size ranges from 10-500 nm in diameter. They appear like dots square shaped, slightly spherical, each dot matches to the presence of pore size 5-10 nm. In which hydrophilic regions separated by the bilayer.(8) Cubosomes have great capability in formulating nano sized particulate systems for topical drug delivery owed to advantages such as high drug loading due to more internal surface area and cubic liquid structure, encapsulating ability of hydrophilic, hydrophobic and amphiphilic particles also having relatively simple method of preparation these are bioactive agents with controlled and targeted drug release .(9)

MATERIAL AND METHODS:

Material: Terbinafine Hydrochloride was gift samples from Sava Health Care-Research CenterChinchwad, Pune and Nulife Pharmaceuticals, Pimpri-Chinchwad, India. Glycerylmonooleate (GMO) was gifted by GATTEFOSSE SAS ,Frace .Poloxamer 407 and Carbopol 934 were kind of gift sample fromANALAB FINE CHEMICALS , Mumbai. Triethanolamine and tween 80 were gift samples from LobaChemie, Mumbai, India. All otherreagents used were of analytical grade.

METHOD:

Formulation of Terbinafine HCL cubosomes: Cubosomes were prepared by Top Down Method which requires two immiscible phases internal and external phase with an emulsifier which helps formation of an emulsion by reducing the interfacial tension.

Method of Preparation of Terbinafine HCL Loaded Cubosomes: TBF cubosomes were prepared by Top Down Method. The organic internal phase containing poloxamer 407 and GMOwere mixed (internal phase) and melted in a water bath until emulsifier completely dissolves in surfactant .Drug was added in mixture then itadded slowly by drop by drop in into distilled water (external phase) of suitable quantity by continuous stirring and subjected to bath sonicationfor period of 15 to 45 minutes with intermittent shaking and stirring. The end result will be a white opaque dispersion without presence of any aggregates .The prepared dispersions were stored in closed glass vials at room temperature protected from direct sunlight for 72 hrs and later evaluation was carried out.(7,9,10)

Preparation of Terbinafine Hydrochloride Cubosomal Topical Gel: The topical gels are prepared with similar manner to cubosomaldispersions using the optimized concentration of GlycerylMonooleateand poloxamer from the above study as lipid phase & aqueous solution of gelling agent (1% Carbopol 934, 0.5ml Tween 80, 0.1ml Triethanolamine) as aqueous phase.(9,11)

METHODS FOR OPTIMIZATION OFFORMULATION VARIABLES OF CUBOSOMES

1. Optimization of formulation variables: The effect of GMO concentration and Poloxamer 407 concentration on formation of cubosomes were characterized using optical lightmicroscopy.

CHARACTERIZATION OF CUBOSOMES

1. Vesicle shape and size analysis of cubosomes: Size and shape of the cubosomes were determined using optical microscopy and Surface methodology of particle was studied scanning electron microscopy (SEM).

2. Particle size measurement: Particle size was determined using an optical light microscope with software (Pixel Pro).The average particle size was expressed in terms um. Cubosomes were mounted on slide and placed over stage of micrometre the software (Pixel Pro) for image analysis of microparticles. Each determination was carried out on a minimum of 100 particles and mean was reported. (12)

3. Powder X-ray diffraction: The powder X-ray diffraction (PXRD) pattern was recorded using X-ray diffractometer for pure drug.

4. Entrapment Efficiency (EE): Entrapment efficiency is defined as the percentage amount of drug which is entrapped by the cubosomes. For the determination of entrapment efficiency, the cubosomes from the resulting dispersions were first separated by centrifugation.The separation of the free (nonentrapped) drug from the entrapped drug in the cubosome dispersion was achieved by centrifugation at 15000 rpm for 30 minutes. The resulting solution wasthen separated and supernatant liquid was collected. The collected supernatant was then diluted appropriately and estimated using UV visible spectrophotometer at 283 nm. The percent of encapsulation efficiency (EE %) was determined by the following equation:

$$\% \text{ of EE} = Ct - Cf/Ct \times 100$$

Where,

Ct is equal to total drug concentration and **Cf**is equal to free drug concentration. (9)

EVALUATION OF TOPICAL GELS

A. FTIR: Spectra of drug along with gelling agents (excipients) is taken and analyzed for presence of any incompatibility.

B. pH: The pH of formulations is determined by a digital pH meter (Equip-Tronics model EQ-614). The cubogel (1gm) was weighed and dispersed in 100 ml of purified water. It is standardized using pH 7 Buffer. The measurement of pH of each formulation was done in triplicate and mean values were calculated.

C. Spreadaility : Spreadability was determined by glass slide apparatus. It consist of two slides upper movable slide and lower non movable slide. 1gm quantity of gel was placed on lower slide and upper slide was placed on it and diameter of spreaded gel was measured.(13)

D. Viscosity: Viscosity of prepared gel was measured by Brookfield viscometer (DV-II + Viscometer) at room temperature. Selected formulation were poured in beaker, the spindle should not touch the bottom of beaker. Viscosity was measured at 25ºC.

E. Drug content: 1 g of the prepared gel is mixed with 100ml of suitable solvent. Aliquots of different concentration are prepared by suitable dilutions after filtering the stock solution and absorbance is measured.

F. *In-vitro* release studies:

Studies were performed for all the formulations. *In vitro* release studies were carried out using bichambered donor- receiver compartment model (a vertical Franz diffusion cell) In-vitro release studies were performed using artificial cellophane membrane (Molecular weight 12000).. The artificial membrane was securely placed between the two halves of the diffusion cell. The receptor compartment contains phosphate butter (pH 6.8), its temperature maintained at 37º± 2C and stirred continuously using magnetic stirrer. A predetermined amount of 1g of TerbinafineHCI gel was placed on the donor side. One ml of the sample was withdrawn from the receptor compartment at definite time intervals and replaced with equal volume of fresh receptor fluid. The aliquots were suitably diluted with the receptor medium and analyzed by UV spectrophotometer. (9).

Table 1: Formulation of cubosomes using GMO and poloxamer 407 concentration for optimization

Formulation code	Glyceryl Monooleate (%w/v)	Poloxamer 407 (%w/w)	Drug (mg)	Water upto (100%)
F1	5	3	50	100
F2	15	0.5	50	100
F3	5	1	50	100
F4	25	1	50	100
F5	15	2	50	100
F6	25	3	50	100
F7	15	3.4	50	100
F8	29.14	2	50	100
F9	0.85	2	50	100

Table2: Analytical data for calibration curve of terbinafine hydrochloride.

Concentration (µg/ml)	Absorbance
10	0.213
20	0.480
30	0.747
40	0.959
50	1.261

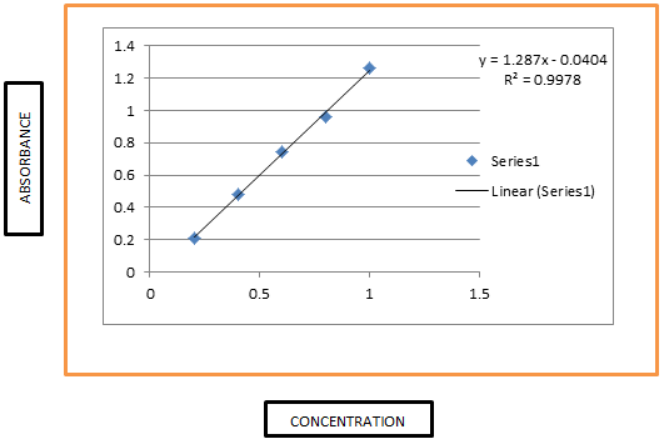


Figure 1. Calibration curve of Terbinafine Hydrochloride

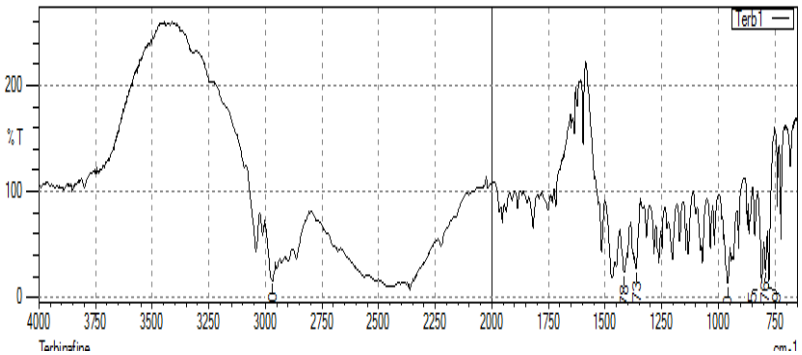


Figure 2 : FTIR spectrum of Terbinafine HCL

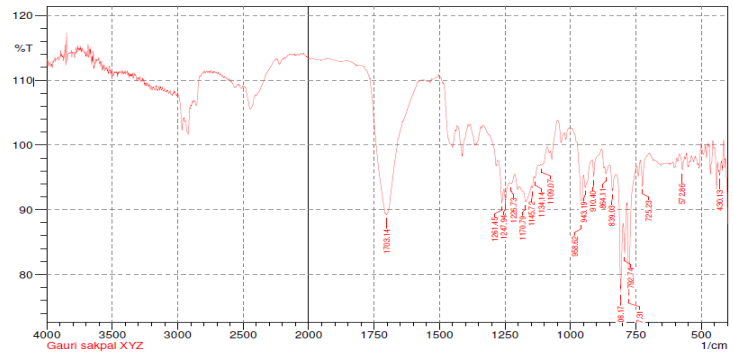


Figure 3 : FTIR spectrum of Terbinafine HCL with carbopol 934

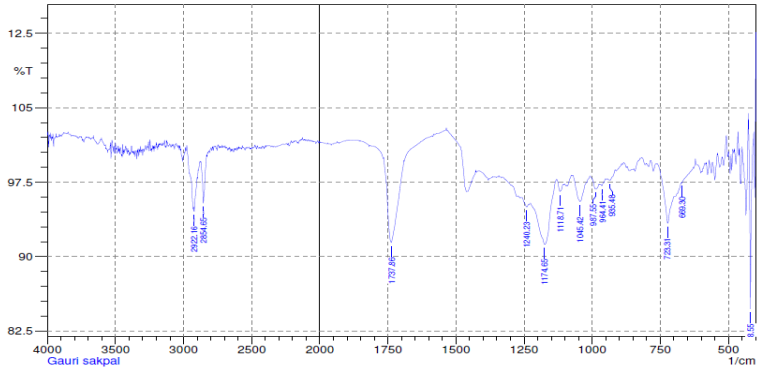


Figure 4: FTIR Spectrum of drug+ GMO+ Poloxamer 407

Table 3: FTIR spectrum of Terbinafine HCL

Reported value	Absorpton peak	Attributed to
850-550	778.29	C- Cl stretching
3000-2840	2968.50	C-H stretching
1372-1266	1362.73	C-N stretching
840-790	809.15	C=C bending

Table 4 : FTIR spectrum of Terbinafine HCL with carbopol 934

Reported value	Absorpton peak	Attributed to
850-550	777.31	C- Cl stretching
840-790	808.17	C=C bending
1720-1700	1703.14	C=O stretching
1210-1163	1179.65	C-O
3000-2840	2922.16	C-H stretching

Table 5 : FTIR Spectrum of drug+ GMO+ Poloxamer 407

Reported value	Absorpton peak	Attributed to
1740-1720	1737.86	C=O stretching
3000-2840	2922.16 2854.65	C-H stretching
850-550	723.31	C- Cl stretching
2050-1020	1174.65	C-N Stretching

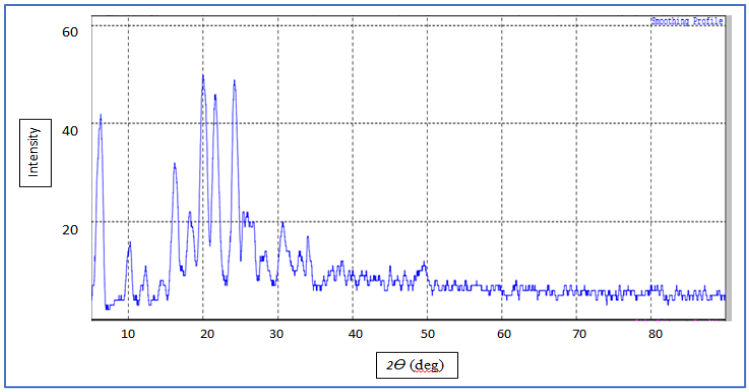


Figure 5 : Powder X-Ray diffraction of pure Terbinafine Hydrochloride drug

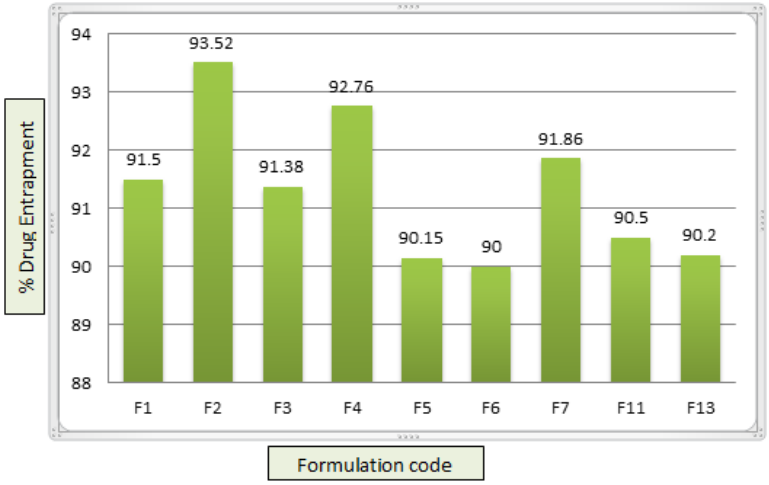


Figure 6. Percentage entrapment efficiency

Table 6: Viscosities in cps of TerbinafineHclcubosomal topical gel F4 formulation at different rpm

Rpm	Viscosity (cps)
10	9231±2.3
20	8563±5.4
50	4436±0.6
100	3120±2.8

Data are mean %Viscosity ± SD(n=3)

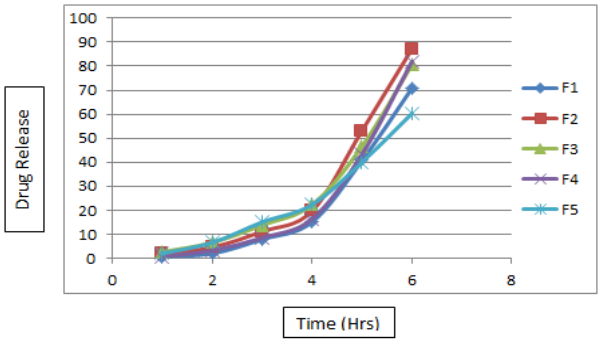


Figure 7 :*In Vitro* diffusion profile of Terbinafine Hydrochloride Cubosomal Topical Gel using Carbopol 934 F1 to F5 in 6.8 pH phosphate buffer

Table 7:*In vitro* drug release of Terbiafine HCL from cubosome loaded carbopol gel

Time (Hrs)					Formulation Code			
F1			F2		F3		F4	
% DR		± SD	% DR	± SD	% DR	± SD	% DR	± SD
1	0.65	0.51	1.96	0.21	2.62	0.23	0.65	0.15
2	1.96	0.65	4.59	0.12	6.55	0.22	3.27	0.14
3	7.86	0.24	11.14	0.11	13.77	0.29	8.52	0.12
4	15.08	0.31	19.67	0.23	22.2	0.31	16.39	0.22
5	40.65	0.20	53.11	0.24	46.55	0.26	43.27	0.23
6	70.4	0.53	87.31	0.43	80.4	0.31	81.95	0.25

Time (Hrs)					Formulation Code					
F5			F6		F7		F8		F9	
% DR		± SD	% DR	± SD	% DR	± SD	% DR	± SD	% DR	± SD
1	1.96	0.31	1.31	0.2	1.96	0.13	1.55	0.21	0.77	0.31
2	6.55	0.35	6.55	0.3	4.59	0.54	3.48	0.26	2.71	0.56
3	15.08	0.41	8.52	0.21	12.45	0.13	6.20	0.42	6.20	0.41
4	22.29	0.51	17.04	0.15	22.2	0.23	16.66	0.51	15.1	0.21
5	40	0.31	40.65	0.18	38.68	0.26	31.78	0.21	30.23	0.31
6	72.96	0.36	60.09	0.28	58.29	0.34	76.99	0.31	73.8	0.15

Data are mean %DR ± SD (n=3)

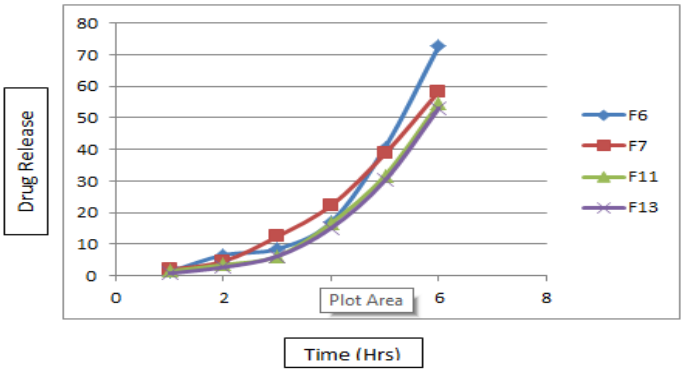


Figure 8 :*In Vitro* diffusion profile of Terbinafine Hydrochloride Cubosomal Topical Gel using Carbopol 934 F6 to F13 in 6.8 pH phosphate buffer

Table 9: Stability studies of optimized gel F4 formulation

Evaluation Paramater	Before	1 Month	2 Month	3 Month
Physical Appearance	**Transparent**	**Transparent**	**Transparent**	**Transparent**
pH	7.1	7.1	7.0	7.0
Drug content	92.76±0.42%	91.95±1.02%	91.14±0.56%	89.88±0.65%
Drug release (%)	81.95±0.25%	81.02±0.35%	80.19±1.25%	79.68±0.89%

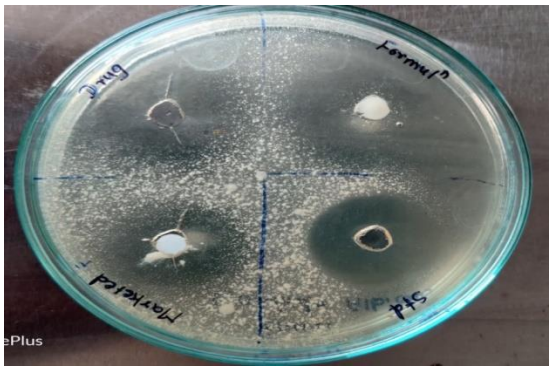
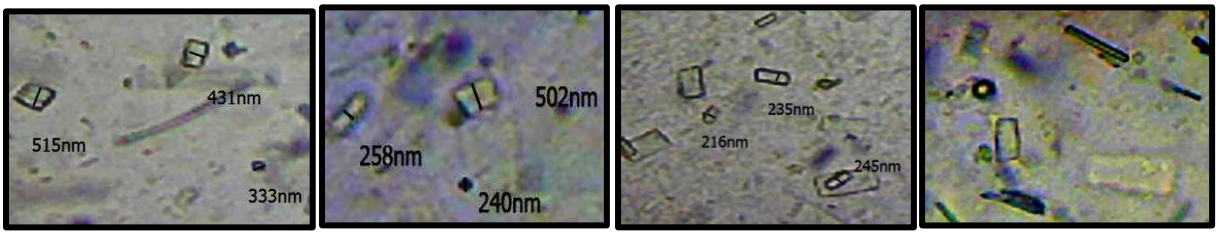


Figure 9: Antifungal activity on *Aspergillusniger*by cup plate method

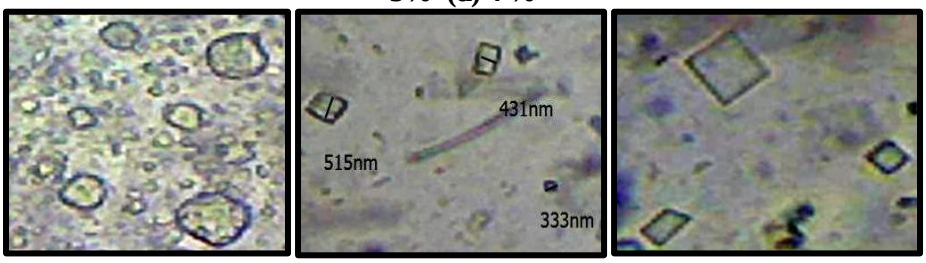
Table 8: Zone of Inhibition

Parameters	Zone of inhibition (Diameter in cm)
TH Pure drug	2.8cm
Std drug	2.8cm
Marketed formulation	2.7cm
Cubogel formulation	3.1cm



(a) C (d)

Figure 10: Different types of cubosomes formed using poloxomer 407 (a)1% poloxamer 407 (b) 2% (c) 3% (d) 4 %



(a) (b) (c)

Figure 11 :Structure of cubosomes (a) below 5% GMO concentration, (b) 5-25% GMO concentration, (c) above 25%GMO concentration

Figure 12 :cubosomal topical gel of optimized formulation F4

G.Antifungal activity: Antimicrobial efficiency studies were carried out to ascertain the biological activity of gel systems against microorganisms .Optimized formulation was evaluated for antifungal activity. The activity was tested against the *Aspergillusniger*and *Candida albicans*by cup plate technique. Fungal culture was inoculated to agar medium and uniformly poured into sterile petri dish. The agar medium was left to solidify. Under aseptic condition the optimized formulation gel, marketed gel, pure drug and standard were placed on Sabourd dextrose agar plate at 25 °C for 48 hrs after which zone of inhibition was compared and measured.(9,12)

H. Accelerated Stability Studies: Chemical and physical stability study of optimized batch of formulation was carried. Batch of Terbinafinecubosomal gel were monitored at sampling intervals of 0, 30,60 and 90 days respectively at 40 ±2 and 5±5% Room temperature and RH as per ICH Guidelines. At the interval of 1, 2, 3 hrs samples were withdrawn tested for physical appearance, Ph, viscosity. Stability necessary to predict the long term stability of formulation.(14)

RESULTS AND DISCUSSION

The key objective of the study is to develop Terbinafine Hydrochloride cubosomal gels using various concentrations of GMO, poloxamer, distilled water and same formula for gelling agent(Carbopol 934, Tween 80, Triethanolamine) using Top Down Approach. Benefit of the method is simple technique and easy availability of raw materials.

A. Calibration curve of TH: Solution of Terbinafine Hydrochloride (500µg/ml) was prepared by appropriate dilution of standard working solution. The solution was scanned in the spectrum mode from 200 nm to 400 nm

Preparation of Calibration curves:

- Appropriate dilutions of the standard working solution were done separately to get 10, 20, 30, 40, 50µg/ml of Terbinafine Hydrochloride. The absorption spectra of all solutions were recorded between 200-400 nm.
- The absorbances were measured at 283.0 nm max of TerbinafineHydrochloride and calibration curve of the drug was plotted separately.
- The standard calibration curve of Terbinafine Hydrochloride was obtained by plotting Absorbance vs. Concentration. Table shows the absorbance values of Terbinafine Hydrochloride. The standard curve is shown in figure.

B. FTIR Studies: The interaction study between the drug and excipients as well as optimized formulation was evaluated using IR spectrophotometer. Terbinafine Hydrochloride has characteristic absorption peaks C-Cl at 778.29cm^{-1},C-H at 2968.50 cm^{-1},C-N at 1362.73cm^{-1} and C=C at 808.95 cm^{-1} . Similar peaks were observed in spectra of different combinations of excipients, along with absence of interfering peaks indicating there is no unwanted reaction between TerbinafineHcl and other excipients used in the study. From the Figures2,3 and 4 also from Tables no. 3,4 and 5 it can be inferred that there was no appearance or disappearance of any characteristic peaks. This shows that there was no interaction between the drug and excipients used in cubosomal topical gel preparation.

C. Optimization of formulation variables

(A)Effect of surfactant (Poloxamer 407) concentration on entrapment efficiency and Drug release:

Poloxamer 407 is hydrophilic non-ionic surfactant consisting of central hydrophilic block of polypropylene glycol. It was found that 1% conc. Of poloxamer 407 was the optimum concentration for cubosome formation and it shows highest drug release about 81.95± 0.25% and highest drug entrapment about 92.76±0.42% . As poloxamer concentration increases there will be change in structure of cubosome from cubic shape to rod like shape and also there will be decrease in entrapment efficiency and drug release of cubosomes formulation. The result showed that the increase in concentration of surfactant is inversely proportional to the entrapment efficiency and Drug release.

(B)Effect of Emulsifier (Glyceryl Monooleate) concentration on entrapment efficiency and Drug release: GlycerylMonooleate is oil soluble gives particular desirable property as an emulsion. It is synthetic surface active chemical widely used as emulsant and non ionic surfactant. It serve to stabilize emulsion through their ability to thicken the emulsion. It was observed that cubosomes were obtained in cubic shape by using concentration of Glycerylmonooleate in range of 5% to 25%. Below 5% and above 25% GMO spherical structures were obtained instead of cubic structure and also large size structure were obtained. The result showed that the increase in concentration of Glycerylmonooleate is directly proportional to the Entrapment efficiency and Drug release.

CHARACTERIZATION OF CUBOSOMES

1. Particle size of cubosomes: Particle size of cubosome dispersion was analysed byOptical lightmicroscopy.From the Figure10 and 11it was found that the diameter (nm) of cubosomes was found to be in the range of 10 to 500 nm and the average particle size was found to be 231±5.3nm.

Particle size cubosomes depends on concentration of emulsifier and surfactant and also on sonication time. If concentration of surfactant increases the shape of particle changes into rod like shape . Increase in the emulsifier concentration can be attributed to an apparent viscosity. Such increased viscosity would result in larger emulsion droplets and finally in greater cubosome size. If lower the concentration or volume of emulsifier decreases the viscosity of the formed emulsion so globues could easily divide into smaller droplets and particle size decreases.

2. Powder XrayDiffraction :

A Ray powder diffractogram for pure drug Terbinafine Hydrochloride showed in Figure No 5. A Ray powder diffractogram for pure drug Terbinafine Hydrochloride showed in Figure No.4 . The X-Ray diffraction patterns of pure Terbinafine hydrochloride were illustrated in Figure. For the crystalline nature of drug powder the sharp intensity peaks were observed around 6^0, 20^0, $21^0$and 24^0. The characteristic peaks of drug appeared at a diffraction angle of 24.2600, maximum intensity of 27 and maximum integrated count 1157 .Pure drug Showed sharp peak indicating crystalline state .

3. Entrapment Efficiency :

From fig. no.6Entrapment efficiency of all cubosomes was found to be 90.00±0.5 % to 93.52±0.8% .Drug content of optimized F4 cubosomal formulation was found to be 92.76± 0.42%

EVALUATION OF CUBOSOMAL TOPICAL GELS

Physical parameters

A. Homogeneity: It was evaluated by visual observations. All formulations were found to be homogenous and clear.

B. pH: The pH of all the formulations were observed in the range of 6.8 to 7.1, which indicated prepared formulation were compatible with skin pH.

C. Viscosity: The result of viscosity showed that with increasing concentration of Carbopol 934 from 0.5 to 1 % viscosity was found to be increased. The viscosity of optimized formulation (F4) was shown in Table no. 6.

D. Spreadability: It was observed that increasing the concentration of the Carbopol 934 was associated with a decrease in the spreadability. As the carbopol concentration increased viscosity and gel Strength of formulation was found to be increased and spreadability was decreased. Spreadability plays an important role in patient compliance and help in unifom application of gel to the skin. A good gel takes less time to spread and will have good spreadability.

E. *In vitro* drug release of Terbiafine HCL from cubosome loaded carbopolgel :Diffusion studies were performed for all formulations and formulation F4 was optimized. The drug release profiles of various formulations are given in Figure no.7 and 8. From the Figure; drug release was found to increase by increasing GMO concentration from 5 to 25 % (w/w), as the lipid concentration was increased, drug release was increased but phase separation was observed as seen in the remaining formulations. So Formulation F4 was optimized and it was formulated into topical gels. From the Figure

no.6 it was showed that at the end of 8 hours the optimized Terbinafine Hydrochloride loaded cubosome formulation F4 was sustained over a period of 6hours in 6.8pH phosphate buffer.The optimized cubosome formulation releases 81.95±0.25 % in 6 hours and it was observed that Terbinafine Hydrochloride highly soluble in GMO. The in vitro release characteristics of percutaneous cubosomes showed that the drug release is directly proportional to the concentration of GMO i.e. the cubosomes showed decrease in percent drug release when using of lower concentration of GMO. It was found that in the presence of less poloxamer 407 concentration, cubic particles observed.

F. Antifungal activity: Optimized formulation inhibits growth of fungus and zone of inhibition was observed From fig.9 and Table no.8.The diameter of zone of inhibition was measured of pure drug , Standard drug (Nystatin), Marketed formulation of TH , Cubogel formulation.

G. Stability study: The optimized formulation was subjected to accelerated stability studies . There were no changes in physical appearance. There was some decrease in drug content and Drug releaseof gel after storage shown in table no.9

SUMMARY

Cubosomes containing Terbinafine HCL were prepared by Top-down method .Terbinafine HCL is very slightly soluble in water so because of its hydrophobicity, cubosomal dispersion (emulsion) can formulate. Cubogel is stable one and better vehicle for hydrophobic or water insoluble drugs. Thus it is increasingly administered via topical route may increase the bioavailability. Dispersion were produced by emulsifiifation and homogenization of cubic lipid phases (contains GMO ,Poloxamer 407) in water .Sustained Release cubosomal development is accomplished when they are formulated as topical gels keeping the cubosome structure. To sustain the drug release the optimized cubosome formulation F4 was formulated into gel carbopol 934.Terbinafine Hydrochloride drug has low solubility and formulated into cubosomes in order to sustain the drug release it was formulated to topical gels. Cubosome formulation prepared by GMO (25%), poloxamer407 (1%) shows good cubic structure, satisfactory entrapment efficiency (92.76±0.42%) and drug release (81.95± 0.25%) at end of 6 hours in pH 6.8 buffer and stable than other formulations. As poloxamer concentration increases there will be decrease in intrapment efficiency and drug release of cubosomes formulation. Below 5% and above 25% GMO spherical structures were obtained instead of cubic structure and also large size structure was obtained. The result showed that the increase in concentration of Glycerylmonooleate is directly proportional to the Entrapment efficiency and Drug release. The nature of cubosome dispersion andtopical gel formulation is observed microscopically.

CONCLUSION

Cubosomes containing Terbinafine HCL were prepared by Top-down method. Dispersion were produced by emulsification and homogenization of cubic lipid phases (contains GMO , Poloxamer 407) in water .The cubosomal topical gels earn attentiondue to its distinctive liquid crystalline structure and simple method of preparation. Cubosomes can be designed by simplepreparation of biologically compatible lipids (GMO) ,Poloxamer , water and are thus well suitable for pharmaceutical and also for body tissues. The manufacturing ability of cubosomes offers enhanced flexibility for product development and through the research cubosomal development specifies efficiency as controlled release drug carrier

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