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FORMULATION AND EVALUATION OF BUTENAFINE HYDROCHLORIDE LOADED CUBOSOMAL GEL

Ritik Chauhan and Nirmala

School of Pharmaceutical Sciences, Rayat and Bahra University, V.P.O. Sahauran, Tehsil Kharar, Mohali - 140104, Punjab, India.

Keywords:

Cubosomes, Butenafine Hydrochloride, Top down Approach, Cubosomal Gel

Correspondence to Author:
Ritik Chauhan

Research Scholar,
School of Pharmaceutical Sciences, Rayat and Bahra University, V.P.O. Sahauran, Tehsil Kharar, Mohali - 140104, Punjab, India.

E-mail: ritikchauhan836@gmail.com

ABSTRACT: The aim of this research was to develop and evaluate a cubosomal gel for the treatment of skin diseases such as athlete's foot (tineapedis), ringworm (tineacruris) and ringworm (tineacorporis). To increase the penetration of the drug and to provide longer duration of treatment this study was performed. Cubosomes are a novel nanoparticle system loaded with butenafine hydrochloride as an antifungal agent. Cubosomes were designed and approached using a top-down approach. Top-down approach was easy and repeatable also. Cubosomes loaded with Butenafine hydrochloride were prepared by a simple emulsification method using different concentrations of lipid phase GMO and poloxamer 407 enclosed in a cubic gel matrix. The prepared cubosomal dispersion was characterized by Drug Entrapment efficiency and particle size. Optimal formulation of cubosomes were incorporated into carbopol-based hydrogels to form cubosomes hydrogels (cubosomal-gels) characterized by physical morphology, drug release studies, pH, viscosity, and spreadability studies. Among all formulations (F7), was found to have the highest drug release at 24 h of 78.693±0.117%, entrapment efficiency (86.517±0.146) and particle size of 189.71nm.

INTRODUCTION: A synthetic antifungal drug called Butenafine Hydrochloride (BF) is used to treat a variety of fungal infections. BF used to treat of skin diseases such as athlete's foot (tineapedis), ringworm (tineacruris) and ringworm (tineacorporis). Tineacorporis occurs on body surfaces such as the hands and feet, especially exposed skin [1]. These superficial dermatophytes are easily spread by direct contact with infected people, and these infections occur in moist parts of the body, such as between the fingers and toes [2].

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Chemically, BF consists of benzylamine and naphthalene with a molecular weight (353.93 g/mol) and formula $C_{23}H_{27}NHCl$. It belongs to the class of broad-spectrum antifungal agents and inhibits the growth of fungi that produce ergosterol, an important mediator in the formation of fungal cell membranes. Terbinafine has a lower therapeutic effect than Butenafine Hydrochloride. It cannot be taken orally because it is heavily processed in the liver oral bioavailability (1.5-3%) and excreted in urine [1].

The objective of this study is to examine the potential of the cubosomal approach which is Nano-carrier to improve the drug release pattern. Cubosomes are free-form nanostructured particles with bi-continous cubic liquid crystalline phases with a hydration mixture of monoolein and poloxamer 407. Cubosome size is around 10-500

nm in diameter. They look like square dots, slightly spherical and each dot corresponds to a pore size of 5-10nm. In which the hydrophilic regions are separated by a bilayer.

Cubosomes have an excellent ability to build nano-sized particle systems for local drug delivery due to advantages such as high drug loading due to a larger internal surface area and cubic liquid structure, the ability to encapsulate hydrophilic, hydrophobic and amphiphilicparticles, which also have a relatively simple preparation method [3, 4].

MATERIALS AND METHODS:

Materials: Butenafine Hydrochloride was gift samples from Synergene Active Ingredients PVT. LTD. Glycerylmonooleate (GMO) was gifted by Manus Aktteva Biopharma LLP. Poloxamer 407 was gift sample from Mohini Organics PVT. LTD. All other reagents used were of analytical grade.

Method:

Formulation of Butenafine Hydrochloride loaded Cubosomes: Butenafine Hydrochloride cubosomes were prepared by a top-down method. Accurately weighed glycerylmonooleate (GMO) and poloxamer 407 were mixed and melted on a water bath (at 60°C). The drug Butenafine Hydrochloride was added to this mixture and mixed until it was completely dissolved, then this solution was added drop by drop in preheated distilled water (at 70ºC) with constant stirring for 2 hours. The cubosomal dispersion of cubosomes thus formed was kept at room temperature, avoiding direct sunlight, and used in further studies [5, 6].

TABLE 1: THE FORMULATION DESIGN OF CUBOSOMES

Name	Dispersion Phase (%)	GMO(g)	P407(g)	Drug(mg)	Water(up to) ml
F1	2.50	1.125	0.125	500	50
F2	5	2	0.5	500	50
F3	10	4.5	0.5	500	50
F4	5	2.12	0.38	500	50
F5	5	2.25	0.25	500	50
F6	5	2.31	0.19	500	50
F7	5	2.38	0.12	500	50
F8	5	2.44	0.06	500	50
F9	5	2.48	0.02	500	50

Formulation of Butenafine Hydrochloride loaded Cubosomal Gel: Cubosomal gel was formulated by Direct Dispersion method. Cubosomal gel was obtained by adding a weighed amount of carbopol 934 (2% w/w, 4% w/w) and carbopol 974 (2% w/w, 4% w/w) to distilled water and kept for half a day, not forgetting the swelling of carbopol, and then triethanolamine was added to adjust the pH. The resulting gel was then diluted with an appropriate amount of cubosomal dispersion at a 1:1 (w/w) ratio of dispersion togel [7].

TABLE 2: FORMULATION DESIGN OF CUBOSOMAL GEL

Sr. no.	Ingredients	Formulation Code			
		CG1	CG2	CG3	CG4
1	Butenafine Hydrochloride Cubosomal Dispersion(ml)	10	10	10	10
2	Carbopol 934 (%w/v)	2	4	-	-
3	Carbopol 974 (%w/v)	-	-	2	4
4	Triethanolamine (mL)	q.s	q.s	q.s	q.s
4	Distilled water (mL)	q.s	q.s	q.s	q.s

Evaluation of Cubosomes: Entrapment Efficiency- To evaluate the encapsulation efficiency of Cubosomes, the amount of unencapsulated Butenafine Hydrochloride in cubosomes was calculated. A predetermined amount of dispersion was transferred to a centrifuge tube. The dispersion was centrifuged for 30 minutes in a suitable diluent to estimate the percentage of drug entrapment. The following equation was used to determine the adhesion efficiency.

$$EE\ \% = W\ (\text{Added drug}) - W\ (\text{free drug}) / W\ (\text{Added drug}) \times 100$$

Where W (added drug) is the amount of drug added during preparation, W (free drug) is the amount of

free drug measured in the supernatant after centrifugation [8].

Particle Size Analysis and Zeta Potential: For the purposes of determining the Zeta potential and particle size, prepared Butenafine cubosomal dispersion, 1ml of dispersion diluted up to 10ml water before being added to the sample cell and placed in the sample holder unit. And the result was determined by Particle Zeta Analyser.

Transmission Electron Microscopy (TEM): The morphology and structure of Butenafine Hydrochloride Cubosomal Dispersion were studied by transmission electron microscopy. For TEM observations, the preparation was diluted 1:10 with water. A drop of the diluted mixture was then placed directly on a carbon-coated copper grid (200 mesh) and the drying process was observed. The shape and size of Butenafine Hydrochloride particles formed in Cubosomes were revealed using a combination of bright-field imaging with increasing magnification and diffraction mode.

Evaluation of Cubosomal Gel:

Appearance of Cubosomal Gel: The optical appearance of the dispersions was evaluated visually for things like colour, turbidity, uniformity, and the presence of macroscopic particles [9].

pH Determination: Using a digital pH meter, the pH of all formulations is measured by submerging the electrode in the gel [10].

Drug Content: 1 g of Cubosomal gel was mixed with 100 ml of suitable solvent (Methanol). The formulations were sonicated and then centrifuged. After that, solution was analyzed by UV [11].

Rheological Studies: A viscometer was used for rheological studies. The sample (30 g) was placed in a beaker and allowed to equilibrate for five minutes before the reading was taken on a T-spindlerrotating at five revolutions per minute. A corresponding viscometer reading was observed at speed. A reading was recorded for each decrease in spindle speed. Measurements were performed three times [12].

Spreadability Study: The spreadability of Cubosomal Gel was determined by the following method- 0.1 g of gel was placed in 1 cm diameter circles on a glass slide, which was then covered with another glass slide. A 250 g weight was allowed to rest on the top glass plate of for 5 minutes to compress the sample to a uniform thickness. Weight (250 g) was added to the pan. The time in seconds required to separate the two slides was taken as a measure of spreadability [13].

$S = m * l/t$

m-- Weight tied on upper slide

l- Length of glass slide

t- Time in sec

Homogeneity and Grittiness: The thumb and index finger were used to press a little amount of Cubosomal gel. If any coarse particles showed up on fingers, the Cubosomal Gel's consistency (homogeneous or not) was noted. In a similar way, the prepared Cubosomal Gel gritty texture was also noted [14, 15].

FTIR Spectra of Formulation: FTIR provides quantitative and qualitative analysis of organic and inorganic samples. Fourier transform infrared spectroscopy (FTIR) identifies chemical bonds within molecules by producing infrared absorption spectra. The spectrum creates a sample profile. This is a unique molecular fingerprint that can be used to screen and screen the samples for many different components.

***In-vitro* Drug Release Studies:** A Franz diffusion cell was used to study the drug release profile of Butenafine Hydrochloride Cubosomal gels and a control gel. The cells have a cellophane diffusion barrier that separates the donor and receptor compartments. The volume of the receiver chamber was 23 ml. The receiver chamber was filled with a magnetic bead. The diffusion medium was phosphate-buffered saline (PBS), pH 7.4. The entire assembly was placed on a magnetic stirrer at a movement speed of 100 rpm maintaining the temperature at 37.0 ± 0.5 °C. In the donation chamber, 1 g of samples corresponding to 0.5 mg of drug were kept on top of the film and rotated. 1 mL samples were taken from the receiver chamber at regular intervals and the volume was then filled with the same volume of diffusion medium. When

adding the diffusion medium to the receiver chamber, care was taken to ensure that no air remained under the diffusion membrane. After appropriate dilution, the samples were subjected to spectrophotometric analysis. Drug release was calculated and a graph showing drug release over time was prepared [16].

Drug Release Kinetics: *In-vitro* release studies were performed using a two-chamber donor-recipient compartment model (vertical Franz diffusion cell). *In-vitro* release studies were performed using an artificial membrane (molecular weight 12000) in a diffusion cell. The receiving chamber contains phosphate butter (pH 6.8), whose temperature is maintained at 37°±2°C and is continuously stirred using a magnetic stirrer. A predetermined amount of 1g Cubosomal gel was placed on the donor site.

At regular time intervals, 1 ml samples were withdrawn from the receptor compartment and replaced with an equal volume of fresh receptor fluid. Aliquots were diluted appropriately with receptor medium and analyzed with a UV spectrophotometer [17].

RESULT AND DISCUSSION:

Determination of absorption maxima by UV spectroscopy in Methanol:

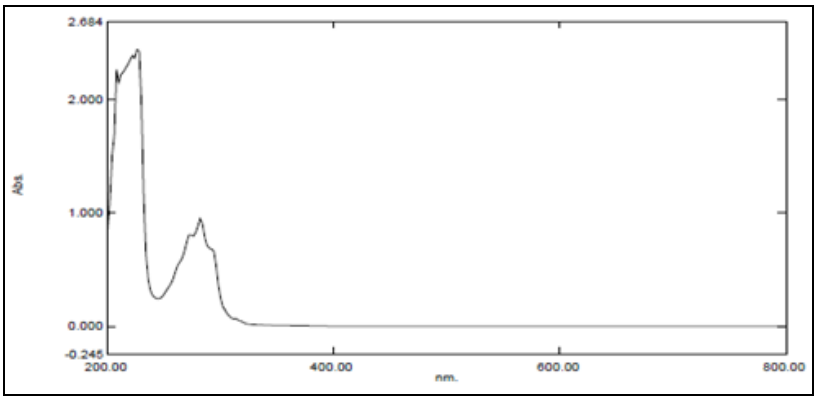

FIG. 1: THE MAXIMUM WAVELENGTH OF BUTENAFINE HYDROCHLORIDE WAS OBSERVED AT 282nm IN METHANOL WHICH IS FOUND TO BE NEAR WITH REFERENCE STANDARDS I.E. 280nm [18]

TABLE 3: PREPARATION OF CALIBRATION CURVE OF BUTENAFINE HYDROCHLORIDE IN METHANOL

S. no.	Conc. (µg/ml)	Abs
1	5	0.118±0.003
2	10	0.239±0.003
3	15	0.324±0.002
4	20	0.451±0.003
5	25	0.532±0.003
6	30	0.636±0.002
7	35	0.739±0.002
8	40	0.843±0.003
9	45	0.949±0.002

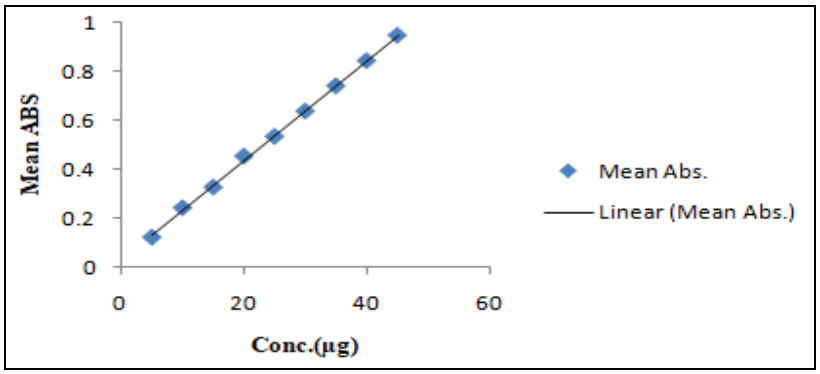

FIG. 2: CALIBRATION CURVE OF BUTENAFINE HYDROCHLORIDE IN METHANOL

DISCUSSION: The calibration curve for Butenafine Hyrochloride was obtained by using the 5 to 45µg/ml concentration of Butenafine Hydrochloride in Methanol. The absorbance was measured at 282nm. The standard curve of Butenafine Hydrochloride as shown in graph indicated the regression equation y = 0.0205x - 0.0246 and R^2 value is 0.9991, which shows good linearity.

Evaluation of Butenafine Hydrochloride Loaded Cubosomes:

Percentage Drug Entrapment:

TABLE 4: ENTRAPMENT EFFICIENCY OF ALL THE FORMULATIONS

Sr. no.	Formulation Code	% Entrapment Efficiency
1	F1	58.517±0.146
2	F2	60.956±0.146
3	F3	53.037±0.122
4	F4	70.354±0.122
5	F5	76.468±0.146
6	F6	81.769±0.171
7	F7	86.517±0.146
8	F8	83.736±0.146
9	F9	79.460±0.122

Value is expressed as mean ± SD.

It was found that Percentage drug entrapment of all formulation was found to be in a range 53.037±0.122 to 86.517±0.146. These results explain that there is a significant effect on percent drug entrapment was observed with lipid concentration. Maximum percentage drug entrapment was found of formulation F7 that was 86.517±0.146.On the bases of entrapment efficiency percentage; F7 was taken for further evaluation.

Particle Size: The result shows that the final formulation particle size was 189.71 nm, with a PDI of 19 percent.

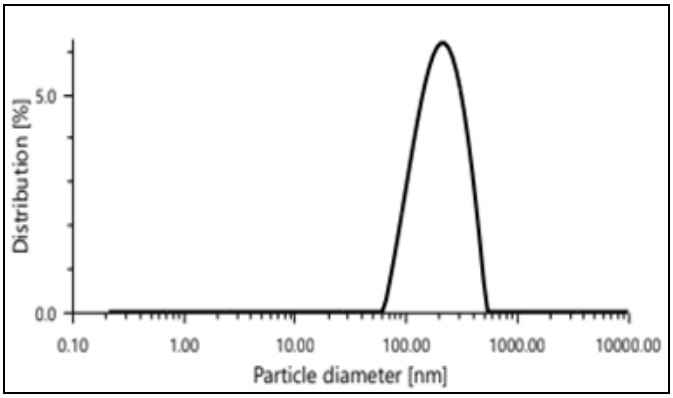

FIG. 3: PARTICLE SIZE PEAK OF F7

Zeta Potential: The result demonstrated zeta potential of F7 formulation was -24.9mV represents stability of formulation.

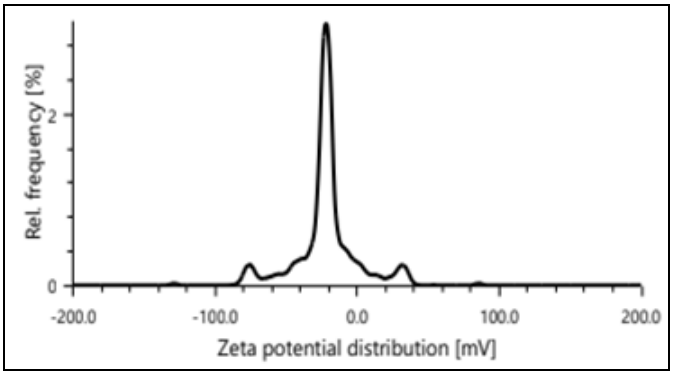

FIG. 4: ZETA POTENTIAL GRAPH OF F7 FORMULATION

TEM of Butenafine Hydrochloride Loaded Cubosomes:

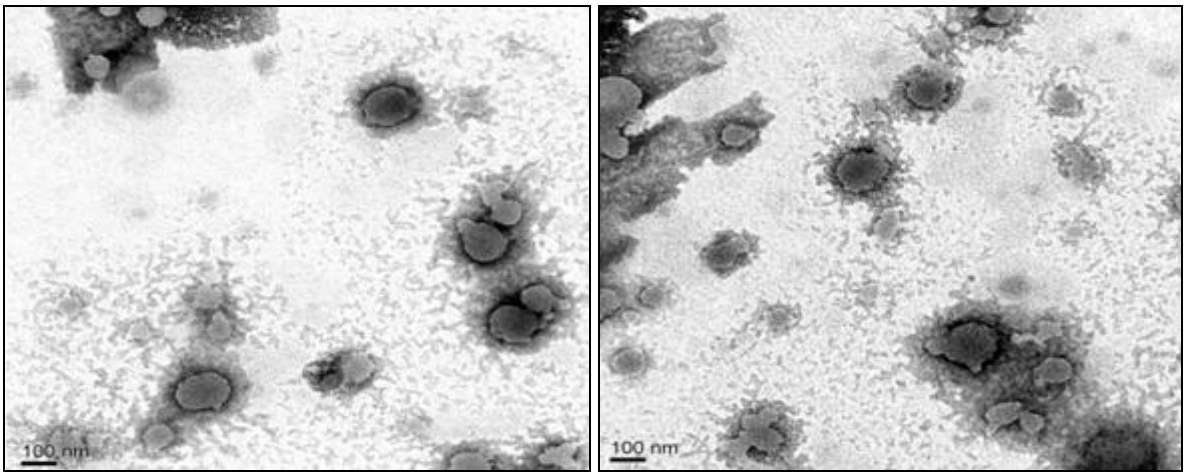

FIG. 5: TEM OF CUBOSOMES (F7)

Physical Appearance of Cubosomal Gel: Evaluation of Butenafine Hydrochloride Loaded Cubosomal Gel:

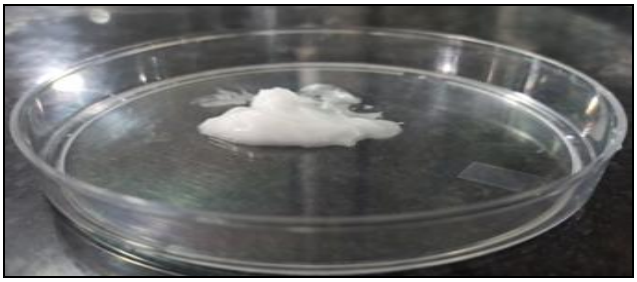

FIG. 6: VISUAL APPEARANCE OF BUTENAFINE HYDROCHLORIDE LOADED CUBOSOMAL GEL (G3)

TABLE 5: VISUAL EXAMINATION

Sr. no.	Formulation code	Visual Appearance
1	G1 (C934-2%)	Gel not formed
2	G2 (C934-4%)	Milky white gel formed
3	G3 (C974-2%)	Milky white gel formed
4	G4 (C974-4%)	Milky white viscous gel formed

The prepared gel were examined visually for their consistency and found to smooth appearance. Out of four developed gel formulations batches G2 and G3 were showed good homogeneity with absence of lumps. So those batches were used in further study.

pH Determination: pH of both formulations (G2 and G3) was found to be 6.54±124 and 6.87±0.53 which is within the physiologically acceptable range for gel.

Drug Content: The drug content gels were found to 91.577±0.745 and 94.829±0.975 respectively. The percentage drug content of both formulations was found to be satisfactory. Hence, the method adopted for gel formulations was found to be suitable.

Rheological Studies: The viscosity of both the formulation (G2 and G3) was 13941±6.55cps and 12521±5.56cps.

Spreadability Study: The Spreadability of both formulations (G2 and G3) was found to be (18.741 ± 0.728g.cm/sec and 16.854 ± 0.917g.cm/sec).

Homogeneity and Grittiness:

TABLE 6: OBSERVATION OF HOMOGENEITY AND GRITTINESS

S. no.	Formulation Code	Homogeneity	Grittiness
1	G2	Homogeneous	No
2	G3	Homogeneous	No

FTIR Studies:

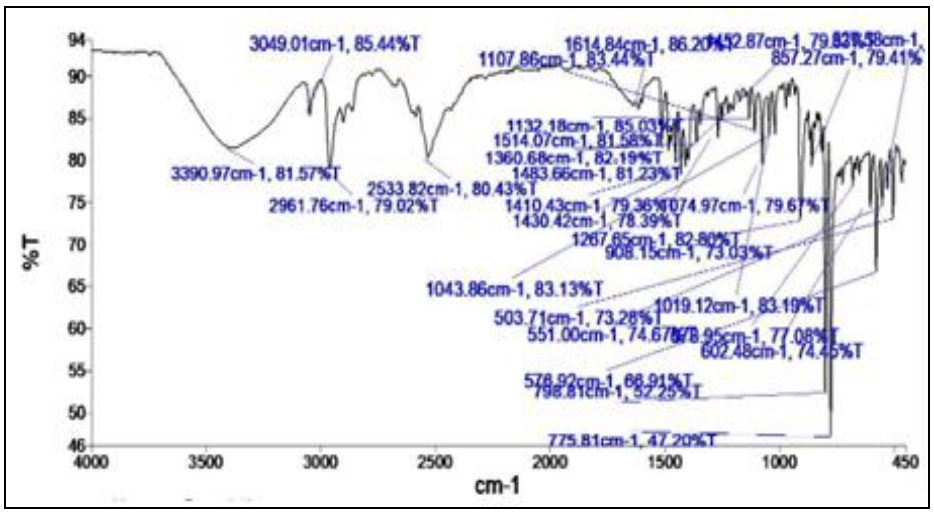

FIG. 7: FTIR SPECTRA OF BUTENAFINE HYDROCHLORIDE

TABLE 7: INTERPRETATION OF FTIR SPECTRUM OF BUTENAFINE HYDROCHLORIDE

S. no.	Standard peak (cm^{-1})	Observed peak (cm^{-1})	Functional group
1	690-900cm^{-1}	857.27	-C-H aromatic, out of plane
2	2850-3000cm^{-1}	2961.76	-C-H Alkane
3	1000-1350cm^{-1}	1074.97	C-N Amines
4	1475-1600cm^{-1}	1483.66	C=C aromatic
5	1375-1450cm^{-1}	1410.43	CH3 ,bending

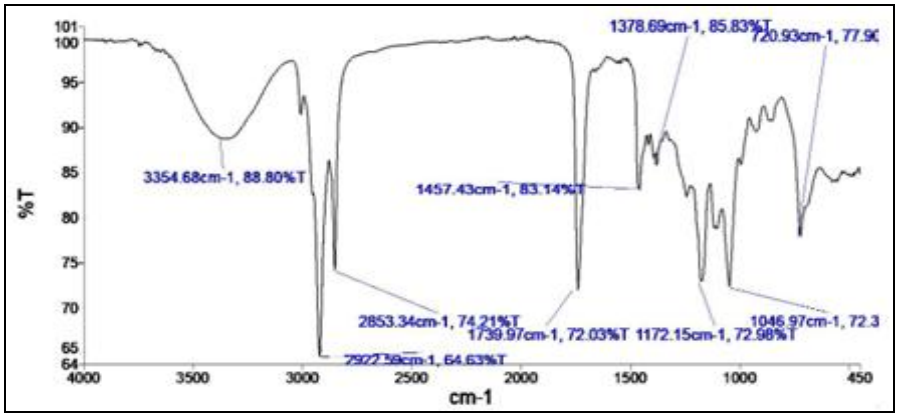

FIG. 8: FTIR SPECTRA OF GMO

TABLE 8: INTERPRETATION OF FTIR SPECTRUM OF GMO

S. no.	Standard peak (cm^{-1})	Observed peak (cm^{-1})	Functional group
1	1738cm^{-1}	1739.97cm^{-1}	C=O

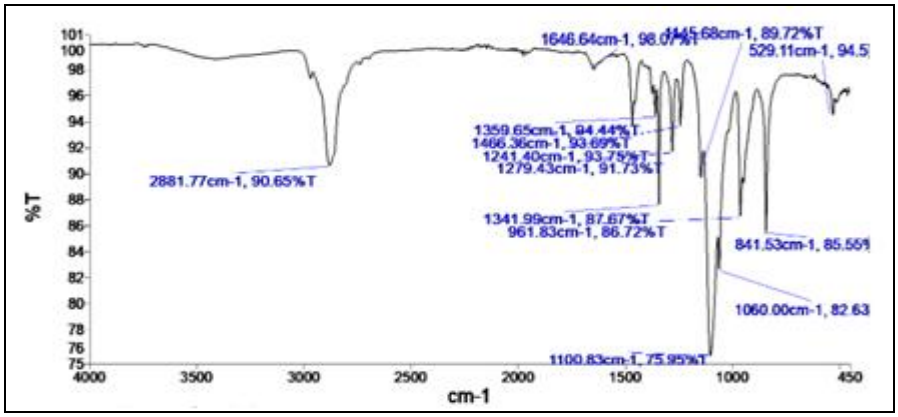

FIG. 9: FTIR SPECTRA OF P407

TABLE 9: INTERPRETATION OF FTIR SPECTRUM OF P407

S. no.	Standard peak (cm^{-1})	Observed peak (cm^{-1})	Functional group
1	2881.11cm^{-1}	2881.77cm^{-1}	Carbon Chain
2	1365.12 cm^{-1}	1359.65 cm^{-1}	O-H Bend
3	1096.99cm^{-1}	1060.00 cm^{-1}	C-O Stretch
4	840.6 cm^{-1}	841.53 cm^{-1}	$CH=CR_2$

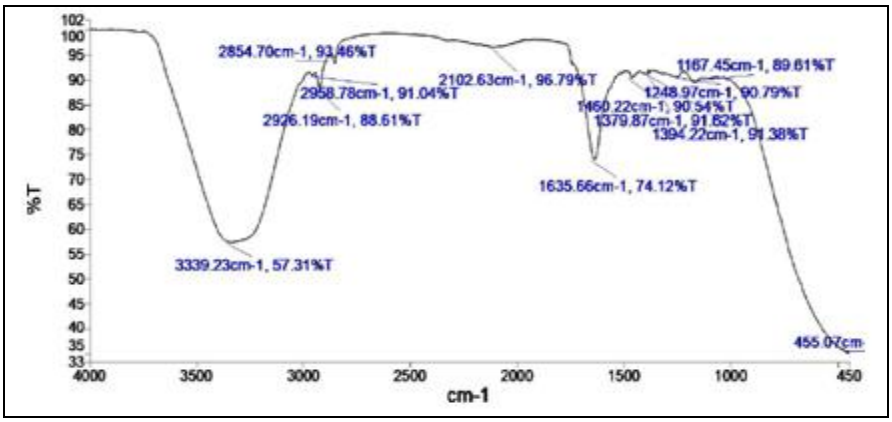

FIG. 10: FTIR SPECTRA OF FINAL FORMULATION

TABLE 10: INTERPRETATION OF FTIR SPECTRUM OF FINAL FORMULATION

S. no.	Standard peak (cm^{-1})	Observed peak (cm^{-1})	Functional group
1	2917.32	2926.19	C-H Alkane
2	1453.77	1460.22	C=C aromatic

3	2853.09	2854.70	Carbon chain
4	1342.65	1379.87	O-H Stretch
5	1104.88	1167.45	C-N Amine

In-vitro Drug Release:

TABLE 11: *IN-VITRO* DRUG RELEASE

S. no.	Time (hr)	Percentage Drug Release of Pure Drug Gel (Mean±SD)	Percentage Drug Release of G3 (Mean±SD)
1	0	0	0
2	0.25	7.293±0.469	7.703±0.354
3	0.5	8.625±0.354	18.254±0.307
4	1	8.727±0.614	21.737±0.639
5	2	14.771±0.639	30.035±0.469
6	4	26.859±0.097	41.303±0.532
7	6	33.903±0.773	48.269±0.709
8	8	27.986±0.469	54.313±0.938
9	24	62.098±0.002	78.693±0.177

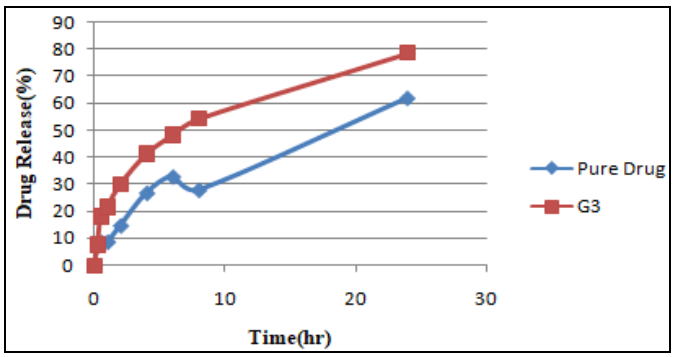

FIG. 11: PERCENTAGE DRUG RELEASE OF BUTENAFINE HYDROCHLORIDE LOADED CUBOSOMAL GEL & PURE DRUG GEL FORMULATION

Zero order Kinetics:

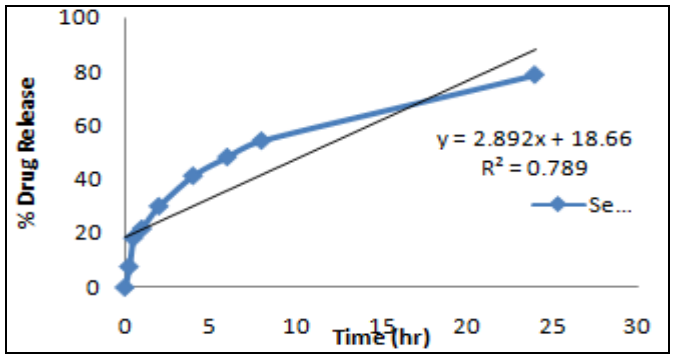

FIG. 12: ZERO ORDER KINETICS

First Order Kinetics:

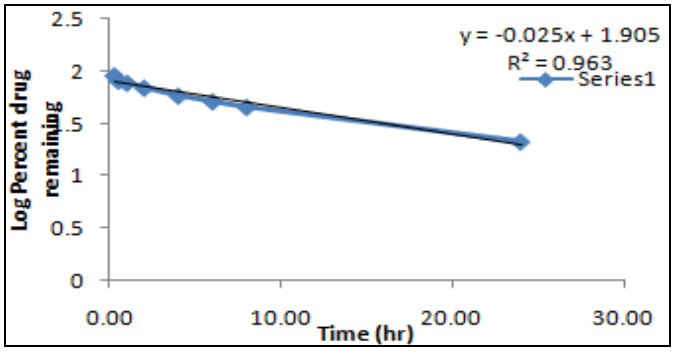

FIG. 13: FIRST ORDER KINETICS

Higuchi's Model:

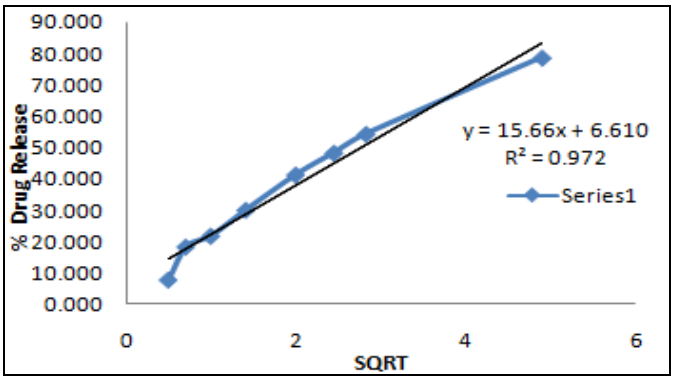

FIG. 14: HIGUCHI'S MODEL

Korsmeyer-Peppas Model:

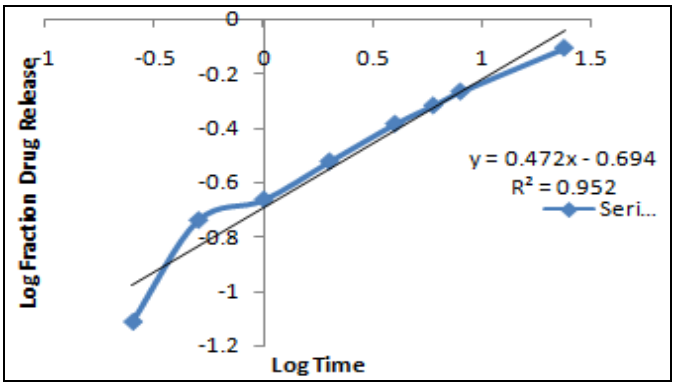

FIG. 15: KORSMEYER-PEPPAS MODEL

TABLE 12: KINETIC EQUATION PARAMETER OF G3

Formulation Code	Zero order		First order		Higuchi		K. Peppas	
	K_0	R^2	K_0	R^2	K_0	R^2	K_0	R^2
G3	2.8924	0.7895	-0.0253	0.963	15.662	0.972	0.4726	0.9524

CONCLUSION: Cubosomes can be created by a simple combination of biologically compatible lipids (GMO) and water and are thus well appropriate for pharmaceutical and body tissue. The ability to form cubosomes during manufacture offers superior flexibility for product improvement. The cubosomal topical gels deserve consideration due to its unique liquid crystalline structure and ease of preparation. Cubosomes are unique dosage forms formed by GMO when added to water. Since it is a lipid that tends to detach in the aqueous phase P407 is used as a stabilizer to avoid aggregation. Butenafine Hydrochloride drug has low solubility and formulated into cubosomes to check the drug release it was formulated to topical gels. Cubosomes formulation prepared by GMO (4.76%), P407 (0.24%) was considered as an optimized formulation that shows adequate Entrapment Efficiency (This is a sub-heading of Evaluation of Cubosomes) (86.517±0.146), and drug release (78.693%). As GMO concentration increases entrapment efficiency and drug release are increased but the prepared formulations are not steady, the phase separation has occurred. To check the drug release the optimized cubosomal formulation F7 was formulated into cubosomal gel using carbopol 974P. Dealing with other aspects, Preparations containing Carbopol 974P show higher drug release (78.693%) at closing stages of 24 hours in pH 7.4 buffer and stable than other formulations. The formulation G3 follows the Higuchi release mechanism. The above research specifies cubosomes effectiveness as a sustain release drug carrier. The sustained-release is achieved when they are formulated as topical gels maintaining the cubosomes structure. Although they possess advantageous characteristics, there is still an extensive way to go before their clinical relevance.

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CONFLICTS OF INTEREST: No Conflicts of Interest.

REFERENCES:

1. Maeda T, Takase M, Ishibashi A, Yamamoto T, Sasaki K, Arika T, Yokoo M and Amemiya K: Synthesis and antifungal activity of butenafine hydrochloride (KP-363), a new benzylamine antifungal agent. Yakugaku Zasshi: Journal of the Pharmaceutical Society of Japan 1991; 111(2): 126-37.
2. Marcel Dekker: Common skin disorders and their topical treatment. dermatological and transdermal formulations. Drugs and the Pharmaceutical Sciences 2002; 1-12: 53-54.
3. Ramya Sri: A. Madhusudhanreddy, A review on: cubosomes drug delivery system. Indian Journal of Drugs 2017; 5(3): 104-108.
4. Venkatesh S: Indira, Formulation and Evaluation of Miconazole Nitrate as a Cubosomal Topical Gel. J of Global Trends in Pharma Sciences 2014; 5(4): 2037-2047.
5. Beena P, Varghese SA, Alexander JA, Raju SP, Koshy S, Mathew FE and Abraham E: Formulation and evaluation of cubosomal gel of an anti-inflammatory agent. Research Journal of Pharmacy and Technology 2021; 14(2): 857-62.
6. Elnaggar YS, Etman SM, Abdelmonsif DA and Abdallah OY: Novel piperine-loaded Tween-integrated monoolein

cubosomes as brain-targeted oral nanomedicine in Alzheimer's disease: pharmaceutical, biological, and toxicological studies. Int J of Nanomed 2015; 10: 5459.
7. Maha KaKhalifa: Miconazole Nitrate Based Cubosome Hydrogels for Topical Application. International Journal of Drug Delivery 2015; 7: 01-12.
8. Omar S, Ismail A, Hassanin K and Hamdy S: Formulation and evaluation of cubosomes as skin retentive system for topical delivery of clotrimazole. Journal of Advanced Pharmacy Research 2019; 3(2): 68-82.
9. Ramani R, Rao CB and Ayanampudi A: Formulation and evaluation of mephenesin topical gel. World J Pharma Res 2013; 2: 1475-1489.
10. Morsi NM, Abdelbary GA and Ahmed MA: Silver sulfadiazine based cubosome hydrogels for topical treatment of burns: development and *in-vitro/in-vivo* characterization. Eur J Pharm Bioph 2014; 86(2): 178-89.
11. Ben JB: Characterisation of drug release fromcubosomes using the pressure ultrafiltrationmethod. Int J Pharm 2003; 260: 239-247.
12. Mitkari BV, Korde SA, Mahadik KR and Kokare CR: Formulation and evaluation of topical liposomal gel for fluconazole. Indian J Pharm Educ Res 2010; 44: 324-333.
13. Sabale V, Kunjwani H and Sabale P: Formulation and *in-vitro* evalua-tion of the topical antiageing preparation of the fruit of *Beninca sahispida*. JAIM 2011; 2(3): 124-8.
14. Archana A, Vijayasri K, Madhurim M and Kumar CA: Curcumin loaded nano cubosomal hydrogel: Preparation, *in-vitro* characteri-zation and antibacterial activity. ChemSci Trans 2015; 4(1): 75-80.
15. Venkatesh B, Indira S and Srinivas P: Formulation and evaluation of miconazole nitrate as a cubosomal topical gel. J Glob Trends Pharm Sci 2014; 5(4): 2037-47.
16. Ahmed MM, Fatima F, Anwer MK, Ibnouf EO, Kalam MA, Alshamsan A, Aldawsari MF, Alalaiwe A and Ansari MJ: Formulation and *in-vitro* evaluation of topical nanosponge-based gel containing butenafine for the treatment of fungal skin infection. Saudi Pharmaceutical Journal 2021; 29(5): 467-77.
17. Baboota S, Al-azaki A and Kohli K: *In-vivo* assessment of enhanced topical delivery of econazole nitrate to human stratum corneum. J Pharma Sci Technol 2007; 58: 1-10.
18. Kumar G, Lohani B and Khotiyal P: Formulation and Evaluation of Medicated Nail Lacquer of Butenafine Hydrochloride Hcl for Effective Treatment of Paronychia. 2018; 5(7): 25.

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