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FORMULATION, EVALUATION AND DEVELOPMENT OF CELLULOSE DERIVATIVES GEL CONTAINING ANTI-FUNGAL DRUG LOADED NANOSPONGES

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Abstract: The main objective of this study is to create and assess the properties of Gel containing BH Nanosponges that may function as efficient antifungal drug delivery systems (DDS) for the therapeutic treatment of fungal infections by delaying the medication release. Using a natural linear polymer and the solvent emulsion evaporation process, nano sponge was created (Cellulose and Polymethyl methacrylate). Butenafine Hydrochloride Nanosponges (F4) had a mean average particle size of 377.4 nm and a Z average of 341 nm. Zeta potential was found to be -27.7 and the polydispersity index was determined to be 0.152. The formulations of the Nanosponges were evaluated for their percentages of production yield (PY), entrapment efficiency (EE), and drug loading (%DL) (DL). The F4 formulation had the highest values at 70%w/w, 79.48% w/w, and 19.48% w/w, respectively. The drug release of the marketed formulation was found to be 100.5 in 150 minutes, while the in-vitro drug release of pure drug, drug containing nano sponges improved formulation (F4), and gel containing optimized nano sponges was found to be 33.35, 57.75, and 76.13, respectively. The butenafine hydrochloride loaded nano sponges Gel may have increased water solubility, percentage drug release, volume of drug loading, antifungal activity (significantly increased in Zone of Inhibition), and offer sustained impact after all results were seen.

Keywords: Nanosponges, Butenafine Hydrochloride, Solvent Evaporation Method, Carbopol Gel, In-vitro drug release, Activity Against Fungal Strain.

Introduction

Conventional topical solutions, like ointments and creams, are associated with adverse effects due to the uncontrolled release of the medication from the formulation, which makes them less effective as delivery vehicles. The development of particulate carrier systems, such as microspheres, liposomes, and nanoparticulate carriers, is now being focused on in order to control the delivery of medications to particular skin regions [1]. As they provide more precise control of drug release, nanoparticulate systems, such as Nanosponges (NS), have been under increased

attention in recent years. NS are a group of colloidal structures made of polymers that have nanoscale cavities. To benefit from these systems, a wide range of topical medications can be safely introduced into NS. Among the potential classes of medications that may be simply produced as topical NS based formulations include local anaesthetics, antifungals, and anti-acne agents [2].

Among the compounds whose inclusion into Nanosponges satisfies all conditions for topical application and localised medication delivery are local anaesthetics, antifungal, and antibiotic medicines. Because of its potential utility in regulated medication administration, nano sponges have become one of science's most promising disciplines. The trapping of substances by the use of nano sponges is thought to lessen adverse effects, improve stability, boost elegance, and increase formulation flexibility. The Nanosponges system is also non-toxic, non-allergenic, non-mutagenic, and non-irritating [3]. This technique is used to enhance the effectiveness of medications used topically [4].

These nano sponges can be successfully added to topical hydrogel drug delivery systems for prolonged drug release and retention of dosage form on skin, thereby lowering drug concentration variations, lowering medication toxicity, and enhancing patient compliance by extending dosage intervals [5]. In reaction to pressure, temperature, and solubility, nano sponges can be made to release a predetermined number of active substances over time. Diffusion, while taking into account the ingredient's partition coefficient between the nano-sponges and the external system, can also initiate the release.

Nano sponges with sustained release are also a possibility. The physical and chemical properties of the entrapped actives, the physical characteristics of the nano-sponges, and the characteristics of the vehicle in which the nano-sponges are ultimately dispersed are just a few of the variables that must be taken into account when developing such formulations. We chose hydrogel as the vehicle because it can be applied to the skin to create a thin, transparent film that can contain topical medications meant for prolonged release.

The skin covers and protects the body from environmental threats, and it is one of the largest organs, accounting for approximately 2 m2 of total body area. Skin is thought to be an impermeable membrane that acts as a barrier to external stimuli and toxins. As an outcome, developing successful topical dermal dosage forms, notably for treating dermal infections and disease states, is a challenge for formulation scientists. Fungal infections affect nearly 20- 25 % of the global population. Dermatophytes and candidiasis are cases of fungal infections that occur primarily in tropical regions and humid environments with an ambient temperature (25-28 0C) that promotes fungal germination [6].

A synthetic benzylamine derivative with a mechanism of action similar to that of the allylamine class of antifungal medications is butenafine hydrochloride, also known as N-(4- tert-butyl benzyl)-N-methyl-1-naphthalene methylamine hydrochloride. The fungal enzyme squalene epoxidase, which is necessary for the manufacture of ergosterol, which is a crucial component of fungal cell membranes, is inhibited by butenafine, much like it is by allylamines. It demonstrates

strong fungicidal activity, especially against dermatophytes, aspergilli, dimorphi, and dematiaceous fungi. (The liver and urine both break down butenafine hydrochloride. Methylation and dealkylation are examples of metabolic pathways. The entire amount that enters the systemic circulation through the skin has not been measured [7].

Materials and Methods

Materials

Butenafine Hydrochloride was purchased from Zeta Scientific LLP, Mumbai. Cellulose, Polymethyl methacrylate, Polyvinyl Alcohol, Dichloromethane, Carbopol 934, Triethanolamine, Propylene Glycol and Methyl paraben was obtained from S.D. fine chem. Ltd. Mumbai. All other reagents and chemicals utilized were of analytical grades.

Method [8]

Butanafine hydrochloride (100 mg) + Cellulose + Polymethyl methacrylate (PMMA)

(Organic Phase)

⇩ Dissolved in 20 ml Dichloromethane

PVA (0.3 % w/v) in 150 ml of water

(Aqueous Phase)

⇩

Organic phase emulsified dropwise into Aqueous phase (Stirrer at 1000 rpm for 2 hrs by using magnetic stirrer

⇩

Nanosponges collected, filtered and dried at 40 °C for 24 hr.

Table: Formulation of BH loaded Nanosponges

Ingredients	F1	F2	F3	F4	F5	F6
Butenafine Hydrochloride(mg)	100	100	100	100	100	100
Cellulose(mg)	75	100	125	150	200	200
Polymethyl Methacrylate (mg)	25	50	75	100	100	125

Polyvinyl Alcohol(%w/v)	0.03	0.03	0.03	0.03	0.03	0.03
Dichloromethane (ml)	20	20	20	20	20	20

Preformulation study of BHUV spectroscopy

Standard curve for BH

The stock solution was prepared by adding 10 mg of standard drug in 10 ml of methanol (1000µg/ml). The working solution (100 µg/ml) was prepared then withdraw 1ml of stock solution and diluted to 10 ml with Methanol. The maximum absorbance for the drug solution of 100 µg/ml was found to be at 278 nm wavelength. From the working solution of concentration 5, 10, 15, 20, 25 dilution was prepared. Methanol was used as the diluent solvent for the dilutions.

Compatibility Studies for BH And Excipients

To ensure there would be no interactions between the drug and recipients during the preparation of the formulation dosage form, reformulation tests were carried out. It offers guidance on choosing recipients for the drug's formulation in a nano sponge. The drug's compatibility with the recipients physically was tested. Through FT-IR spectrum analysis, the potential for drug recipients (Cellulose and Polymethyl methylcrylate) to interact was looked into. To ensure there would be no interactions between the drug and recipients during the preparation of the formulation dosage form, reformulation tests were carried out. It offers guidance on choosing recipients for the drug's formulation in a Nanosponges. The drug's compatibility with the recipients physically was tested. Through FT-IR spectrum analysis, the potential for drug recipients (Cellulose and Polymethyl methylcrylate) to interact was looked into.

Fourier Transformation Infrared Spectroscopy (FTIR)

For determination of presence of structure claiming functional groups of its analysis was done using FTIR spectrophotometer.

Evaluation of BH loaded Nanosponges

Entrapment Efficiency and Drug Loading Estimation [9]

An amount of Nanosponges (10 mg) was shaken with 5 mL of methanol for 1 min in a volumetric flask using a vortex mixer to accurately calculate the entrapment efficiency. The volume makes upto 10 ml. The solution was then filtered and diluted and the concentration of BH was measured spectrophotometrically at 278 nm.

% EE = (Amount of drug added - Drug amount in solution)/ Amount of drug added × 100

% DL = (Amount of drug added - Drug amount in solution)/ Total amount weight of Nanosponges × 100

% Production yield (PY) [10]

The Production yield (PY) can be determined by calculating the total weight of polymer and drug taken and the final weight of the Nanosponges.

Production yield = Practical mass of nano sponges / Theoretical mass (polymer + drug) × 100

Determination of particle size, PDI and Zeta Potential [11]

Butenafine Hydrochloride loaded particle length (z-averaged diameter) and polydispersity index (as a degree of particle length distribution width) Dynamic mild scattering, generally called photon correlation spectroscopy. To acquire the appropriate scattering intensity, all samples had been diluted with ultra–purified water previous to testing. The nano sponge dispersion become diluted and poured right into a disposable sizing cuvette, which become then located within side the instrument's cuvette holder and examined. Before measuring, air bubbles had been removed from the capillary.

Drug content Estimation [12]

The total drug content of Nanosponges was determined by UV Spectrophotometric analysis.10 mg of nano sponge's dissolve in 10 ml of Methanol. The resulting solution was filtered. The BH content in the methanolic extracts is analyzed by using a UV Visible spectrophotometer at a wavelength of 278 nm, against methanol as blank. From the absorbance drug content was calculated.

% Drug content = (WP/Wt) × 100 Where,
WP = Practical drug content
Wt = Theoretical drug content

Evaluation of optimize BH Nanosponges formulation

The optimized formulation, selection based on the results obtained from Entrapment Efficiency, Drug Loading, Particle Size, PDI And Zeta Potential.

Determination of Saturated Solubility of BH and drug loaded Nanosponges using UV Visible Spectrophotometer [13-15]

Determining the drug's solubility in distilled water was tested using 5 mL amber- colored glass vials. After adding an excessive amount of drug to each vial, the vials were capped with a stopper. These vials were attached to a shaking water bath to study their effects. Shaking was at a speed of 100 rpm for 24 hours and temperature maintenance was at approximately 37 ± 0.5 °C. The resulting test samples were then filtered using a 0.22 μm pore size syringe filter. The drug was diluted with distilled water, and its absorption at 278 nm was measured. The absorption was then converted into concentration using a standard curve of the drug.

Drug diffusion and In-vitro drug release kinetics [16-19]

A dialysis bag was used to conduct a drug diffusion study. Separately, the donor compartment contained the sample BH pure drug, optimized Nanosponges, Nanosponges containing gel, and marketed formulation. The receptor chamber was filled with phosphate buffer (pH 5.5), and it was kept on a thermostatically controlled magnetic stirrer at 37 ± 0.5 ℃ with magnetic bar stirring (100 rpm). At pre-determined intervals, 1 mL of drug-diffused solution was withdrawn and replaced with the equivalent volume of fresh release medium, and the aliquots were analysed by UV spectroscopy at 278 nm. The amount of drug released was calculated, and graphs of cumulative % drug released vs time for Nanosponges gel were plotted.

Kinetics of in-vitro drug release [20-22]

To evaluate the drug release mechanism, in-vitro release data were fitted into zero- order, first-order, Higuchi, and Korsmeyer-Peppas kinetics models, and regression analysis was performed. In zero order kinetics, the rate of drug release is independent of concentration. In first order kinetics, the drug release rate is proportional to the concentration. Higuchi defined drug release from porous, insoluble matrix as a time- dependent square root mechanism. The Korsmeyer-Peppas model illustrates how the proportion of drug release related to time exponentially.

Microscopic Study

Scanning electron microscopy is used to investigate the microscopically properties of the nano sponges, drug, and product.

Formulation and evaluation of Carbapol gel loaded with optimize Nanosponges Formulation of carbapol gel

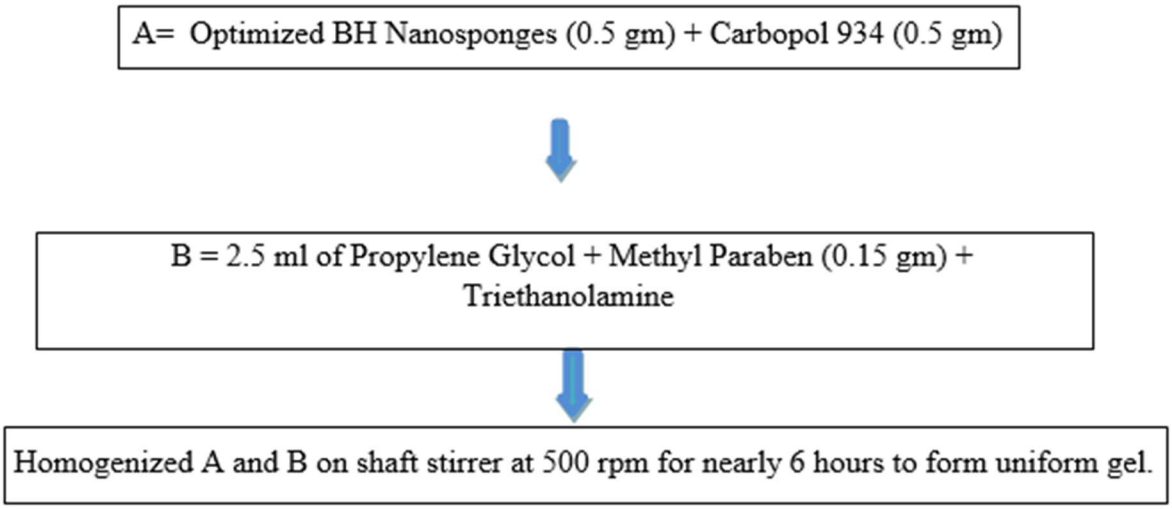

Table: Formulation for gel

Sr. No	Ingredients	Quantity taken
1	Nanosponges	0.5 gm
2	Carbopol 934	0.5 gm
3	Methyl Paraben	0.15 gm
4	Propylene Glycol	2.5 ml
5	Triethanolamine	0.6 ml
6	Distilled Water	q.s.50 ml

Physical Appearance

The prepared gel was inspected for clarity, colour, homogeneity, and foreign particle presence.

pH

2.5g of gel was precisely weighed and distributed in 25 mL of purified water. The pH of the dispersion was determined using a digital pH meter.

Drug Content

In nano sponge loaded gel, the percentage of drug content was evaluated. The drug was extracted by dissolving 5 gm of gel in 10 ml of methanol and sonicating for 30 minutes, then adding 3 ml of phosphate buffer pH 5.5 to make a solution up to 10 ml. UV spectrometer at 278 nm was used to filter and assess the drug content.

Spreadability

1gm of gel was weighed and placed on the spreadability apparatus, which had one glass slide on the lower side and another on the top side. After applying gel to the lower slide, the higher slide was placed on top of the lower slide, and the time necessary to glide across both slides from gel was calculated using a formula (Length of slide = 7.5 cm).

$$S=M*L/T$$

Where,

S= Spreadability

L= Length of glass slide

M=Weight tied to upper slide

T= Time taken to separate two slides (sec)

Antifungal activity of the BH loaded Nanosponges Gel

An antifungal investigation was conducted to test the effectiveness of the NG gel against Candida albicans, Aspergillus niger, and Fusarium Oxysporum fungus strains. This study made use of potato dextrose agar (PDA) substrate and sanitized Petri plates. PDA (20 mL), treated with the test organism (0.5 mL), was allowed to harden in a sterile Petri-plate. BH, Nanosponges (F4), NG Gel, and commercialized Butenafine gel (1 percent, w/w cream). The Petri plates were incubated at 27 0C for 48 hours. The sizes of the zones of inhibition (ZI) were determined in mm based on the observation of transparent zones surrounding the wells.

Result and Discussion

Preformulation results

API characterization

Table: Organoleptic properties of Butenafine hydrochloride

Sr. No.	Name of property	Specification
1.	Colour	White
2.	Odour	Unpleasant
3.	Nature	Amorphous

Identification of pure drug

a) Melting Point

Table: Melting point of Butenafine hydrochloride

Sr. No.	Obtained range (ºC)	Mean value (ºC)	Reference value
1.	209	209.33℃	208-210℃
2.	211		
3.	208		

Melting point of Butenafine hydrochloride was found to be 209.33℃, which is in range as given in literature (208-210˚C). Hence the drug can be stated as pure.

b) UV Spectroscopy

1) Determination of λ max in water

Accurately weighed 1 mg of drug was transferred to 100 ml of volumetric flask add dissolved in methanol and volume was made up to 100 ml and the solution was scanned on UV spectrometer in the range 200-400 nm.

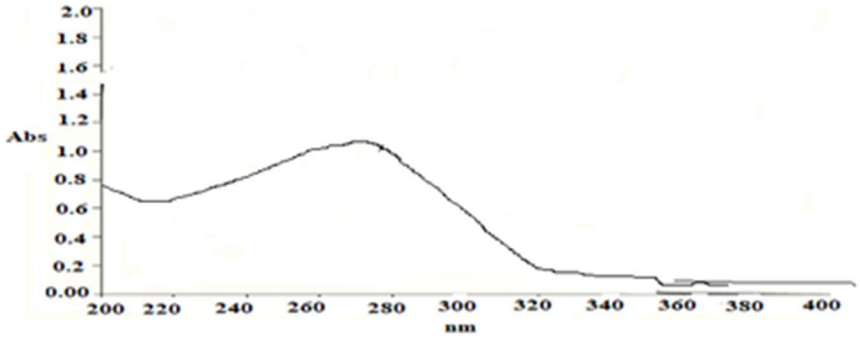

Fig. UV Spectrum of Butanafine hydrochloride

An absorption maximum was found to be at 278 nm. Hence 278 nm was selected as λ max for further studies

2) Calibration curve of Butenafine hydrochloride in water

The stock solution for the standard drug of 1 mg in was prepared using 100 ml of water. The maximum absorbance for the drug solution of 10 mcg/ml was found to be at 278 nm. The linearity was found between the concentration range of 10-35 mcg/ml for UV spectroscopy.

Table: Different concentration & absorbance of Butenafine hydrochloride

Sr.No.	Concentration (µg/ml)	Absorbance
1	0	0
2	10	0.123
3	15	0.199
4	20	0.276
5	25	0.345
6	30	0.432
7	35	0.551

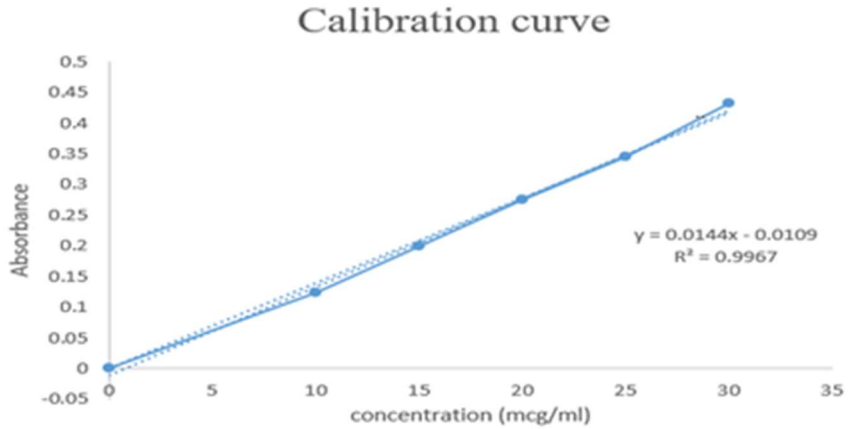

Fig. Calibration curve of Butenafine hydrochloride in water.

Table: Parameters found in calibration curve

Sr.No.	Parameter	Finding
1	Wavelength detection	278 nm
2	Regression equation	y = 0.0144x – 0.0109
3	Correlation coefficient	R^2 = 0.9967

Formulation and Evaluation of Nanosponges containing BH

Fig. Nanosponges formulation

Determination of Particle size, PDI and Zeta Potential

Table: PS, PDI, ZP, EE and DL data of Nanosponges

Formulation code	PS (nm)		PDI	ZP (mV)	EE (% w/w)	DL (% w/w)
	Mean	Z-average				
F1	391	3026	1.26	-17.9	65.98	7.6
F2	386	2957	1.66	-18.5	64.49	7.8
F3	388	4083.4	1.33	-19.96	78.66	14.16
F4	**377.4**	**341**	**0.152**	**-27.7**	**79.48**	**19.48**

F5	747.1	2842	0.582	-18.9	75.28	15.6
F6	895.5	2513	1.22	-20.86	70.82	14.9

PS (Particle size), PDI (Polydispersity index), ZP (zeta-potential), EE (Entrapment efficiency), DL (Drug loading).

Formulation F4 was optimized based on the % EE, % DL, particle size, and zeta potential. This formulation was used in further research.

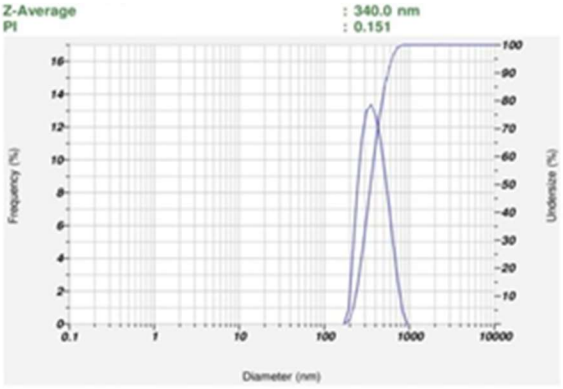

Fig. PS And PDI of F4

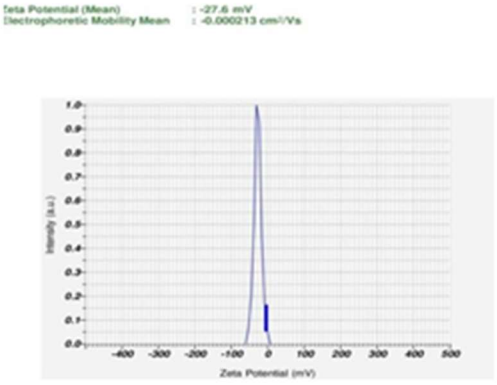

Fig. Zeta potential of F4

Drug and excipient interaction study

A. Fourier Transformation Infrared Spectroscopy (FTIR)

FTIR spectrum of Butenafine hydrochloride was shown in following Fig. revealed that the characteristic peaks representing the presence of functional groups claim by its chemical structure. From this we can consider that the Butenafine hydrochloride was of pure quality.

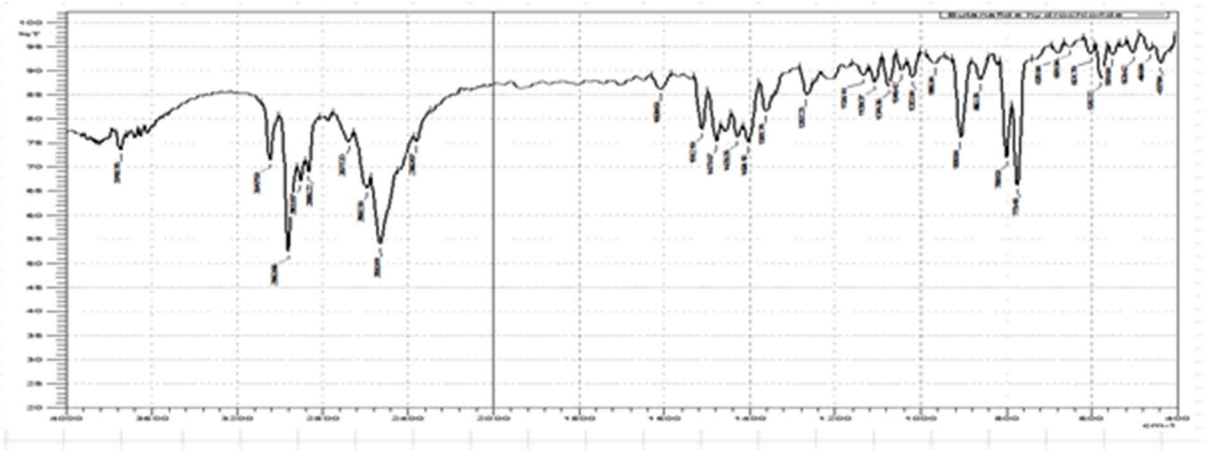

Fig. FTIR spectra of Butenafine hydrochloride

Table: Interpretation data of Butenafine hydrochloride

Material	**Functional group**	**Standard IR Ranges (cm^{-1})**	**Observed IR Ranges (cm^{-1})**
Butenafine hydrochloride	C-N Stretching C=C Stretching C-H Stretching	1200-1350 1500-1650 2900-2954	1268.24 1513.18, 1609.67 2903.88

After interpretation of FT-IR Spectrum of Butenafine hydrochloride, it was concluded that the characteristic peak corresponding to the functional group present in the molecular structure of Butenafine hydrochloride were found within the reference range and confirming its identity.

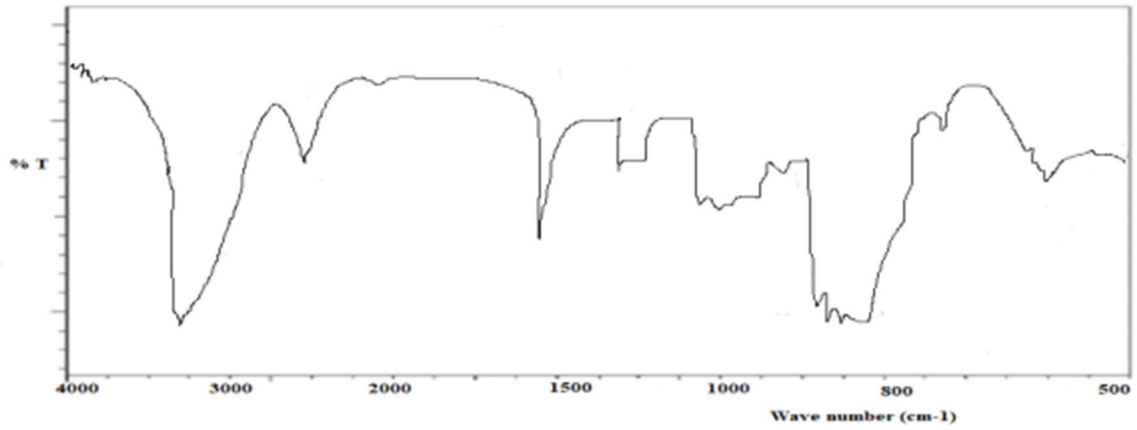

Fig. FTIR Spectra of Cellulose

After interpretation of FT-IR Spectrum of polymer, it was concluded that all the characteristic peaks corresponding to the functional group present in molecular structure of Cellulose were found within the reference range, confirming its identity.

FTIR spectrum of Butanafine hydrochloride loaded Nanosponges was shown in following Fig., revealed characteristic peaks representing the presence of functional groups claim by its chemical structure.

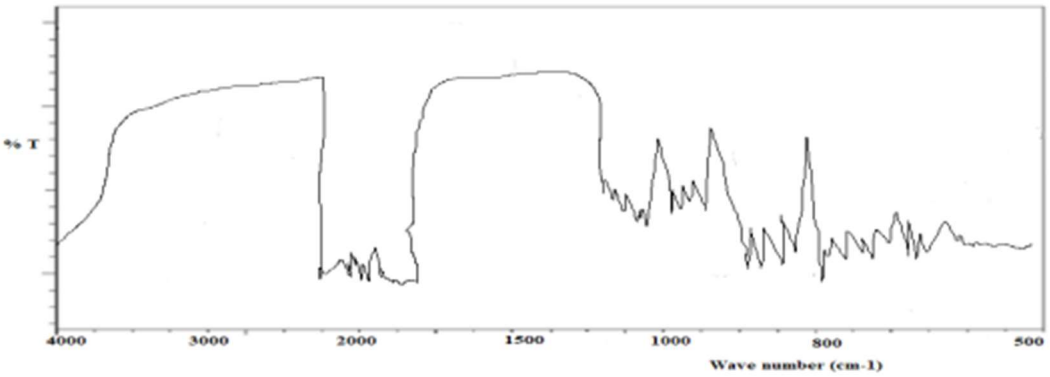

Fig. FTIR spectra of Butanafine hydrochloride loaded optimized nano sponges

There was no considerable change in the positions of characteristic absorption bands and bonds of various functional groups present in the Butanafine hydrochloride. This observation clearly suggests that the Butanafine hydrochloride shows no prominent change in its characteristics even in its physical mixture. The results of FTIR spectra indicated the interaction between drug and polymer. It showed that Butanafine hydrochloride was compatible with Cellulose.

Morphology Study (SEM)

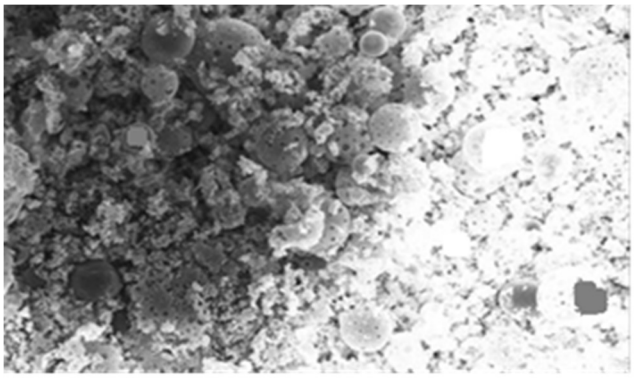

Fig. Scanning electron microscopical image of Nanosponges

As shown in the figure, a scanning electron microscopy (SEM) image of the optimized nano sponges depicted the spherical, porous, and nano-size range of F4. The porous, spongy existence of nano sponges was revealed by the SEM image.

Saturated solubility study

Table: Solubility in Water

Sr. No	Sample	Solubility(mg/ml)
1	Pure drug	0.095

2	Nanospong es	1.140

The solubility of Butenafine Hydrochloride in water was 0.095 mg/ml and Nanosponges loaded with Butenafine Hydrochloride drug solubility in water was 1.140 mg/ml. The solubility of drug in water was enhanced by 12.30 folds after converting into Nanosponges.

Formulation And Evaluation of BH loaded Nanosponges Gel

Fig. Gel containing Nanosponges of BH

Evaluation of gel

Physical Qualities- The gel was consistent and milky white in colour. It was revealed to be smooth and greasy.

Table: Evaluation of gel

Sr.No.	Formulation	% Drug content	Spreadability	pH	%Drug release
1	NG	98.87 % w/w	16 ± 1.23 gm.cm/sec	5.85 ± 0.09	58.79 %w/v

Morphology of Gel

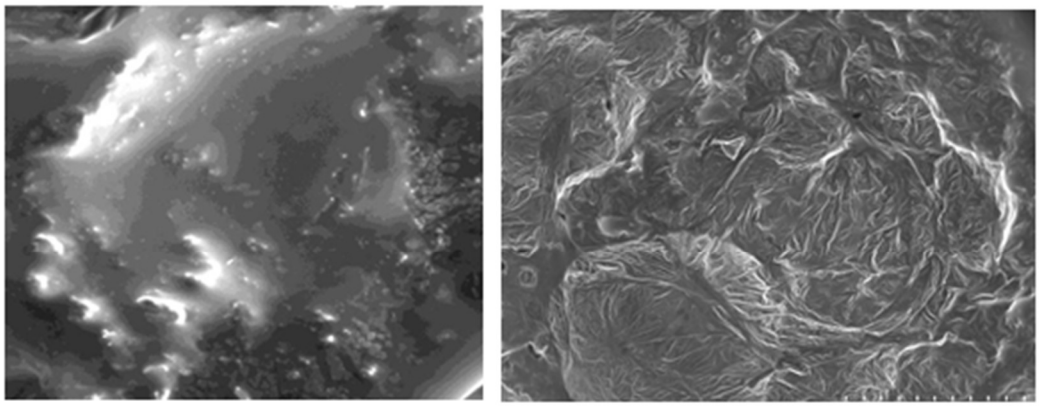

Fig. SEM of gel containing Nanosponges

Morphology of gel under microscope

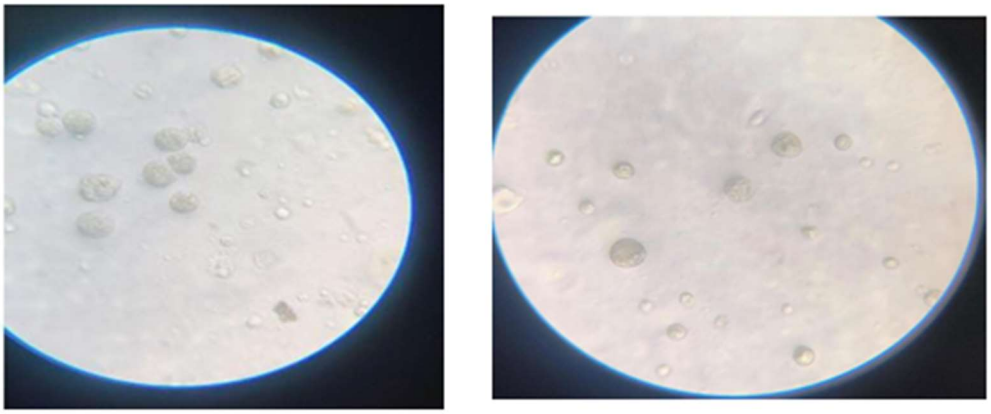

Fig. Morphology of gel under microscope

Inference

The SEM image showed that nano sponges are porous, spongy, and gel-like in nature. Under an electronic microscope, a porous, spherical structure comprising Nanosponges and a carbopol layer was evident.

In-vitro drug release

Table: Data for in - vitro drug release

Time in Minutes	Pure Drug	Nanosponges (F4)	NG	Marketed Formulation
30	0.879	18.04	4.52	34.84
60	1.76	19.36	13.76	55.48
90	3.52	21.94	28.92	79.13

120	7.02	23.21	34.28	82.98
150	11.5	27.08	38.50	100.5
180	17.55	50.32	42.04	
210	24.57	65.80	50.3	
240	33.34	76.13	57.74	

NG- Nanosponges gel

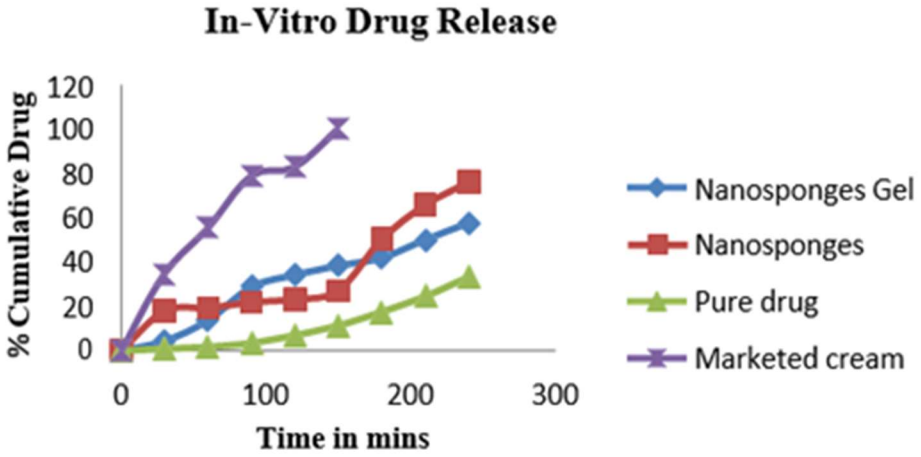

Fig. In- Vitro drug release

Table: kinetics of Gel containing nano sponges drug release

Sr. No	Release Kinetics	X-axis	Y-axis	R^2	Linear Equation
1.	Zero order equation	Time in hours	Cumulative % Drug release	0.974	y = 0.241x + 1.048R^2 = 0.974
2.	First order equation	Time in hours	Log % cumulative drug release	**0.979**	y = -0.001x + 2.02R^2 = 0.979

3.	Higuchi release kinetic	Square rootof time	Cumulative % Drug release	**0.984**	y = 5.129x - 23.52R^2 = 0.984
4.	Hixon Crowell equation	Time in hours	Cube root of % drug release	0.977	y = -0.004x + 4.672R^2 = 0.977
5	KorsmeyerPeppas equation	Log time	Log % cumulative drug release	**0.982**	y = -0.001x + 2.012 R^2 = 0.982

Formulation Gel aligned to first order kinetics, with an R2 value of 0.982 signifying the release was dosage dependent.

The drug release was proportionate to the square root of time, demonstrating that BH release from Nanosponges gel was diffusion regulated.

Antifungal activity of the Butenafine Hydrochloride loaded Nanosponges Gel

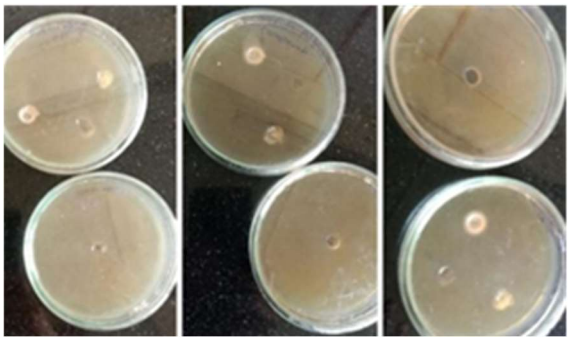

Fig. After inoculation, 0 min growth

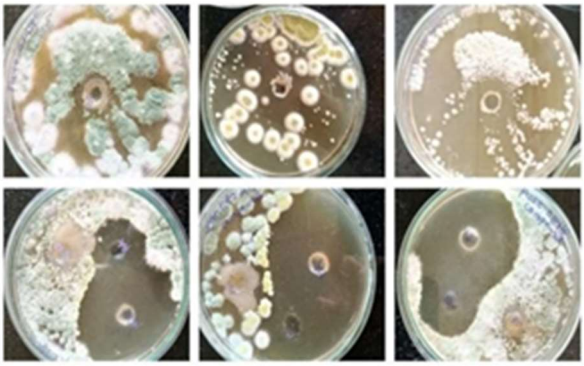

Fig. After 72 hrs of inoculation for Marketed cream, Pure drug, Nanosponges and Nanogel

Table: Data for Antifungal activity study (ZI- zone of inhibition)

Sr. no.	Fungal strain	Marketed Cream ZI in mm	Pure drug ZI in mm	Nanosponges (F4)ZI in mm	Nano Gel ZI in mm
1	**Aspergillus niger**	17	15	21	39.5
2	**Candida Albicans**	14.5	17.5	26	30.05
3	**Fusarium Oxysporum**	20	8.5	16.5	38.5

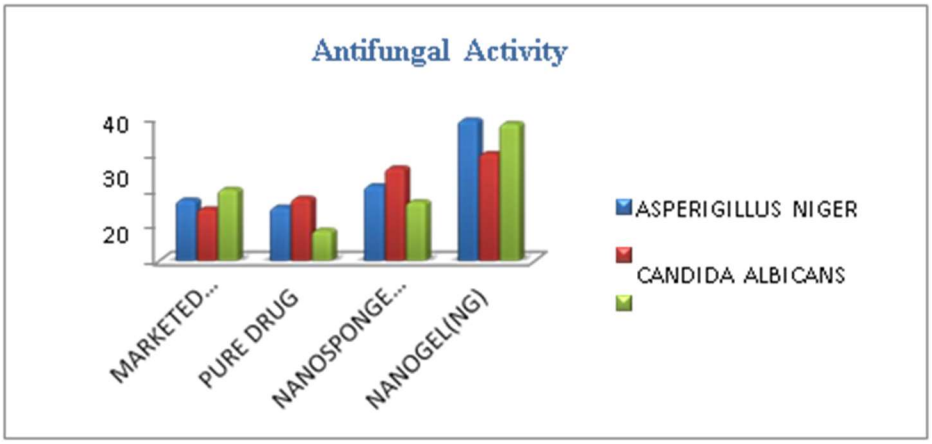

Fig. Antifungal activity study

The antifungal activity against Candida albicans for BH Pure drug, Nanosponges, Nanogel and marketed cream Zone of Inhibition was 17.6 mm, 27 mm, 30.06 mm and 14.6 mm.
The antifungal activity against Aspergillus niger for BH Pure drug, Nanosponges, Nanogel and marketed cream Zone of Inhibition was 16 mm, 22 mm, 39.6 mm and 18 mm.
The antifungal activity against Candida albicans for BH Pure drug, Nanosponges, Nanogel and marketed cream Zone of Inhibition was 8.6 mm, 16.6 mm, 38.6 mm and 21 mm.
The antifungal activity of the Nanosponges gel showed enhancement of antifungal effects of BH.

Conclusion

Because the nanocarrier in nano-based gel formulations can carry the drug deeper into the skin layer than other topical semisolid preparations may be able to, fungus infections can be efficiently treated with them. Nanocarriers improve treatment efficacy by transporting medications to the target site deeper into the epidermal layers for complete eradication of fungal infections. Natural linear polymers were used in the solvent emulsion evaporation process to create nano sponges (Cellulose and Polymethyl methacrylate). The butenafine hydrochloride loaded nano sponges Gel may have increased water solubility, percentage drug release, volume of drug loading, antifungal activity (significantly increased in Zone of Inhibition), and offer sustained impact after all results were seen.

References

1. Ghanbarzadeh S., Arami S. Enhanced transdermal delivery of diclofenac sodium via conventional liposomes, ethosomes, and transferosomes. BioMed research international. 2013; 67:778.
2. Sharma R., Pathak K. Polymeric Nanosponges as an alternative carrier for improved retention of econazole nitrate onto the skin through topical hydrogel formulation. Pharmaceutical development and technology. 2011;16(4):367-76.
3. Nacht S., Kantz M. The Microsponge: A Novel Topical Programmable Delivery System, In: Topical Drug Delivery Systems. David WO, Anfon H A editors. New York: Marcel Dekker; 1992. 42: 299-325.
4. Delattre L., Delneuville I. Biopharmaceutical aspects of the formulation of dermatological vehicles. J Eur Acad Derm Vener. 1995; 5: S70- 76.
5. Jenning V., Schafer-Korting M., Gohla S. Vitamin A loaded solid lipid nanoparticles for topical use: drug release properties. J Control Release. 1999; 66: 115-126.
6. Mohammed Muqtader Ahmed, Farhat Fatima , Md. Khalid Anwer , Elmutasim Osman Ibnouf , Mohd Abul Kalam , Aws Alshamsan , et al. Formulation and in vitro evaluation of topical nano sponge-based gel containing butenafine for the treatment of fungal skin infection. Saudi Pharmaceutical Journal. 2021;6: 1-11.

7. Shruti Rao, Tularam Barot, K. S. Rajesh & Lalit Lata Jha . Formulation, optimization and evaluation of microemulsion based gel of Butenafine Hydrochloride for topical delivery by using simplex lattice mixture design. Journal of Pharmaceutical Investigation. 2016; 46: 1–12.
8. Salunkhe A., Kadam S., Magar S., Dongare K. Nanosponges: a modern formulation approach in drug delivery system. World J Pharm Sci. 2018; 7:575-92.
9. Swaminathan S., Vavia PR., Trotta F., Torne S. Formulation of B-cyclodextrin based nano sponges of itraconazole. J Incl Phenom Macrocycl Chem. 2007; 57:89–94.
10. Swetha A., Gopal Rao M., Venkata Ramana K., Niyaz Basha B., Koti Reddy V. Formulation and in vitro evaluation of etodolac entrapped in microsponge based drug delivery system. Int J Pharma. 2011; 1:73-90.
11. Swetha A., Gopal Rao M., Venkata Ramana K., Niyaz Basha B., Koti Reddy V. Formulation and in vitro evaluation of etodolac entrapped in microsponge based drug delivery system. Int J Pharma. 2011;1: 73-90.
12. Ahmed, Mohammad Muqtader, Fatima, F., Mohammed, A.B., Olive Oil Based Organogels for Effective Topical Delivery of Fluconazole: In-vitro Antifungal Study. Journal of pharmaceutical research international.2020; 32, 29–36.
13. Controlled release approach to novel multiparticulate drug delivery system , SL Patwekar, MK Baramade, Int J Pharm Pharm Sci 4 (3), 757-63
14. Dissolution and Stability Enhancement of Poorly Water Soluble Drug – Lovastatin by Preparing Solid Dispersions, JDS Khayyam Shaikh , Shailesh Patwekar , Santosh Payghan, Asian Journal of Biomedical and Pharmaceutical Sciences 1 (4), 24-31
15. Polymer nanocomposites: An overview, PP Sambarkar, SL Patwekar, BM Dudhgaonkar, International Journal of Pharmacy and Pharmaceutical Sciences 4 (2), 60-65
16. Review on preparation and evaluation of oral disintegrating films, PM Dhere, SL Patwekar, IJPT 3 (4), 1572-1585
17. Plant profile, phytochemistry and pharmacology of Cordia dichotoma (Indian cherry): A review, PG Jamkhande, SR Barde, SL Patwekar, PS Tidke, Asian Pacific journal of tropical biomedicine 3 (12), 1009-1012
18. Needle free injection system: A review, SL Patwekar, SG Gattani, MM Pande, Int J Pharm Pharm Sci 5, 14-19
19. Review on nanoparticles used in cosmetics and dermal products, S Patwekar, S Gattani, R Giri, A Bade, B Sangewar, V Raut, World J Pharm Pharm Sci 3 (8), 1407-21
20. Biological activities of leaves of ethnomedicinal plant, Borassus flabellifer Linn.(Palmyra palm): An antibacterial, antifungal and antioxidant evaluation, PG Jamkhande, VA Suryawanshi, TM Kaylankar, SL Patwekar, Bulletin of Faculty of Pharmacy, Cairo University 54 (1), 59-66
21. Plant profile, phytochemistry and pharmacology of Cordia Prasad Jamkhande, SR Barde, SL Patwekar, ST Priti, Asian Pac J Trop Biomed 3 (12), 1009-1012
22. Prescribing Patterns of Antibiotics and Sensitivity Patterns of Microorganisms 23] towards Different Antibiotics in multidisciplinary Health Care Hospital, PSAPS Khavane K., Addepalli V., Bhusare K., International Journal of Pharmaceutical and Biological Archieves 1 (02), 1-8