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Research Article

Investigation of Microemulsion System for Topical Delivery of Halobetasol Propionate

Bansi Zalavadia[1*], Khushbu Patel[2]

[1]*Faculty of Pharmacy, Nootan Pharmacy College, Sankalchand Patel University, Visnagar, India.*
[2]*Department of Pharmaceutics, Faculty of Pharmacy, Nootan Pharmacy College, Sankalchand Patel University, Visnagar, India.*

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ABSTRACT

Halobetasol propionate (HBT) is a topical corticosteroid used to manage psoriasis. The current studies investigate the microemulsion-based gel of halobetasol propionate in the management of psoriasis. Based on solubility studies, the oil, surfactant, and co-surfactant were determined first. The pseudo-ternary phase diagram was then developed using the phase titration method to optimize the surfactant and co-surfactant (Smix) ratio. After the determination of the concentration range, the microemulsion was optimized by simplex lattice design. Independent factors amount of oil- capmul MCM C8 (X1), amount of Smix- Acrysol EL 135:Transcutol HP (X2) and amount of water (X3) were selected and assessed for globule size, %transmittance, zeta potential, PDI and *in-vitro* diffusion study. Optimized microemulsion containing HBT was converted into a gel by using a gelling agent, HPMC K100M to enhance viscosity and maintain the drug's activity by extending residence duration. Optimized HBT-loaded microemulgel evaluated for spreadability, viscosity, pH, *in-vitro* diffusion study, *ex-vivo* permeation study and stability study. The globule size of the optimized HBT-loaded ME batch was found (119.3 ± 0.58 nm) confirming the micron size of the formulation, %T (98.8 ± 0.02%). The TEM image confirmed the uniform droplet size of the microemulsion and the proper incorporation of drug molecules into the system. The optimized HP-loaded ME batch's zeta potential and polydispersity index (PDI) were determined to be -11.2 mV and 0.203, respectively, demonstrating the stability and even distribution of dispersed systems. The finalized formulation of HBT-loaded microemulgel showed viscosity value (9862 ± 15.28 cps), spreadability value (3.58 ± 0.08 gm.cm/sec), pH (5.2 ± 0.08), drug content was found to be 96.35 ± 0.21%. The *ex-vivo* permeability of HBT emulgel within 12 hours was 91.92 ± 0.48% which is a 2-fold increase in permeability as compared to HBT marketed gel. Improvement of drug penetration may enhance therapeutic efficacy, reduce dosing frequency, and augment patient compliance in topical medication delivery.

Introduction

Psoriasis is a chronic skin condition, distinguished by excessive epidermal proliferation, recurrent episodes of potentially debilitating inflammatory lesions, and abnormal hyperkeratotic plaque formation.[1]

The microemulsion was first described by Hoar and Schulman as an isotropic mixture of water, oil, surfactant, and co-surfactant that forms a system that is thermodynamically stable and has droplets larger than 0.15 microns, resulting in a transparent solution. [2]

Microemulgel is regarded as a prospective advancement in innovative delivery systems because of its bimodal action, integrating both gel and emulsion properties. Furthermore, studies have demonstrated that the incorporation of an emulsion into a gel matrix enhances its stability. The selection of a microemulsion system was primarily based on its superior solubilization potential and its improved capacity to efficiently skin penetration. [3]

Emulgel intended for dermal applications possesses various advantageous characteristics, including thixotropic behavior, non-greasy texture, ease of spreadability and removal, emollient effects, non-staining nature, water solubility, extended shelf life, transparency, and an aesthetically pleasing appearance. Hydrophobic drugs

***Corresponding Author:** Ms. Bansi Zalavadia

Address: Faculty of Pharmacy, Nootan Pharmacy College, Sankalchand Patel University, Visnagar, India.

Email ✉**:** zalavadiabansi1012@gmail.com

Tel.: +91-7041193122

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cannot be directly incorporated into gel bases due to their low solubility. Emulgels address this limitation by facilitating the addition of lipophilic drugs in the oil phase, which is subsequently dispersed in the water phase, forming an oil-in-water emulsion. A prepared emulsion can subsequently be integrated into a gel base. As a result, emulgel formulations exhibit greater stability compared to other topical preparations. For instance, powders may be hygroscopic and absorb environmental moisture upon exposure, creams may undergo phase inversion, and ointments may become rancid due to their oil content. Additionally, emulgel offers a higher drug-loading capacity than niosomes and liposomes, which are prone to leakage, leading to reduced entrapment efficiency.[4]

Halobetasol propionate is a potent topical corticosteroid used in the treatment of psoriasis. It functions by reducing leukocyte migration to inflammatory sites and attaching to glucocorticoid receptors, triggering gene expression changes that result in multiple downstream effects over a period of hours to days. Glucocorticoids reduce phospholipase activity, suppress neutrophil apoptosis, and prevent demargination, thereby reducing the production of arachidonic acid derivatives, which helps in managing psoriasis. However, due to its hydrophobic nature, the therapeutic efficacy of halobetasol propionate is limited when formulated in an aqueous cream base.[5]

Furthermore, because halobetasol is a xenobiotic, it cannot be effectively absorbed through the stratum corneum, which is made up of dead cells rich in keratin that are embedded in a lipid matrix. Since the stratum corneum contains large quantities of epidermal lipids, lipid carriers that enable lipid exchange with the stratum corneum have shown promise for enhancing penetration rates as well as boosting solubilization and bioavailability of hydrophobic drugs. Microemulsions are thought to be the best delivery systems for these drugs, which are often less soluble in water. It is hypothesized that steroids like HBT when incorporated in microemulgel will exhibit enhanced penetration and present a possibility of dose reduction. In this context, the goal of the current study was to develop a topical delivery system based on microemulsions for halobetasol propionate (HBT) to increase loading capacity, improve penetration through biological membranes, and increased bioavailability.

MATERIALS AND METHODS

Materials

Halobetasol propionate purchased from the Clickchem Research Laboratory, Ankleswar. Sunflower oil, peceol, corn oil, oleic acid, olive oil, PEG 400, and PG were procured from Chemdye Corporation, Rajkot. Span-20, Span-80, Polysorbate-80, and Polysorbate-20 were procured from SD Fine Chemical, Vadodara. Captex 355, Capryol PGMC, Capmul MCM C8, Capmul-MCM®, Capmul-PG8® procured from Abitec Corporation, Janesville. Transcutol ® HP, Labrafil M 2125CS, Labrasol, Labrafac PG were procured from Gateffose Corporation. Acrysol EL 135 procured from Corel Pharma Chemical, Ahmedabad. Additional compounds of analytical grade were used to prepare the formulations.

Preformulation Study

Identification drug and compatibility studies of drug and excipient[6]

To check the authenticity of API, the drug was characterized by FTIR in which the drug was blended with the KBR in proportion of 1:1 and by using a hydraulic press KBR disc was prepared and analyzed for FTIR spectra. The reference spectra were then compared with sample spectra of Halobetasol.

Compatibility of halobetasol propionate, Capmul MCM C8, Acrysol EL 135, and Transcutol ® HP was recorded using FTIR (Nicolet 6700 model, Thermo Scientific).

Solubility studies of halobetasol propionate

Solubility examination was carried out using the shake flask technique. The solubility of the drug was assessed in different surfactants, co-surfactants and oils. For screening suitable components, an excess amount of HBT was added to each medium and subjected to solubilization in an ultrasonic bath for 30 minutes. This was followed by continuous shaking in an orbital shaker (Remi Instrument Pvt. Ltd.) for 72 hours to achieve a homogeneous mixture. Followed by centrifugation, the collected supernatant was dissolved in methanol and examined spectrophotometrically using a Shimadzu instrument at 238 nm. [7-9]

Construction of pseudo-ternary phase diagram

Capmul MCM C8, Acrysol EL 135, and Transcutol ® HP were selected for formulation based on the HBT maximum solubility. Using the phase titration approach, the pseudo-ternary phase diagram was created.[10,11] The surfactant-to-co-surfactant (S:Co-S) or Smix proportion was varied at 1:1, 2:1, 3:1, and 4:1. Oil and Smix were combined in a ratio ranging from 1:9 to 9:1 in order to get a wide range of microemulsions. Employing an aqueous phase titration approach, with the endpoint being determined by looking for cloudiness or turbidity, gives distinct areas for microemulsion formulation.

Preparation of drug-loaded microemulsions

Once, the microemulsion zone depicted on the phase diagram was identified, the chosen microemulsion was prepared by simply mixing the weighted components to create a transparent microemulsion as per the aqueous phase titration method. Vortex mixing/stirring of oil + Surfactant+ Co-surfactant. Addition of drug in the above mixture followed by vortex mixing. The addition of water drop-wise gives clear dispersion.[12]

Optimization of HBT Microemulsion by Mixture Design

The largest area of microemulsion was found in 3:1 from the pseudo ternary-phase diagram.

After the determination of the concentration range, independent factors like the quantity of oil (X1), Smix (X2) and water (X3) were selected. The dependent factors, such as globule size (Y1) and percentage transmittance (Y2), were selected. Simplex lattice design is used to optimize the microemulsion and to study the interaction between factors.[1,13] The composition design can forecast the properties of all possible formulations using Design Expert 10.0.1. A total 12 batches were prepared and their composition with coded value and layout of design were displayed in Tables 1 and 2, respectively.

Evaluation Parameters of Microemulsion

Dilution and dye tests

Upon the addition of water to the microemulsion, the oil-in-water system remained stable, whereas the water-in-oil system exhibited microemulsion breakdown. As per the dye test, sudan red was introduced into the microemulsion and examined under a microscope. The observed red-colored globules with a colorless background confirmed the successful formulation of an oil-in-water system.[14,15]

Table 1: Composition with coded and actual value

Independent factor	*Coded level*		*Uncoded level*	
(Amount in % v/v)	Low	High	Low	High
X1 = Amount of oil	-1	1	5	15
X2 = Amount of smix	-1	1	40	50
X3 = Amount of water	-1	1	45	55
Dependent factors				
Y1= Globule size in nm				
Y2= %Transmittance				

Table 2: Simplex lattice design layout

Run	*Composition (%)*			*Composition (mL)*		
	X1	*X2*	*X3*	*X1*	*X2*	*X3*
HBT 1	5	50	45	0.5	5	4.5
HBT 2	5	46.667	48.333	0.5	4.7	4.8
HBT 3	5	43.333	51.667	0.5	4.3	5.2
HBT 4	5	40	55	0.5	4	5.5
HBT 5	8.333	46.667	45	0.8	4.7	4.5
HBT 6	8.333	40	51.667	0.8	4	5.2
HBT 7	8.333	43.333	48.333	0.8	4.3	4.8
HBT 8	8.333	43.333	48.333	0.8	4.3	4.8
HBT 9	11.666	43.333	45	1.2	4.3	4.5
HBT 10	11.667	40	48.333	1.2	4	4.8
HBT 11	15	40	45	1.5	4	4.5
HBT 12	15	40	45	1.5	4	4.5

Estimation of globule size, zeta potential, PDI

The average globule size and PDI of HBT-ME were ascertained using photon correlation spectroscopy. After diluting the sample with distilled water, it was examined to determine the zeta potential and evaluate the stability of the microemulsion. All measurements were conducted at 25°C.[14,15]

%Transmittance

This investigation demonstrates product clarity by using a Shimadzu UV spectrophotometer to scan a microemulsion at 650 nm using deionized water as a reference. Microemulsion should preferably be visually transparent compared to traditional emulsions, with a higher percentage transmittance indicating superior transparency and quality of the microemulsion.[16]

Dispersion stability study of optimized HBT-ME

For 30 minutes, selected compositions were centrifuged at 3000 rpm. No phase separation formulations were anticipated for the freeze-thaw cycle, in a hot air oven, six cycles were run between 4 to 45°C, while being stored at each temperature for a minimum of 48 hours.[17]

Formulation of microemulsion-based gel

For the development of the gel base, HPMC K100M at concentrations of 1, 1.5, and 2% w/w was dissolved in an adequate quantity of water, followed by being allowed to hydrate throughout the night. Microemulsion-based gel was prepared by incorporation of optimized formation of HBT-ME into HPMC K100M gel base by constant stirring at room temperature to prevent lump formation and achieve the desired consistency for the formulation.[18] The composition of emulgel is shown in Table 3.

Evaluation Parameters of Microemulgel [18-20]

Viscosity and pH

The viscosity was determined using a digital viscometer. Spindle number 4 was dipped in a 250 mL beaker containing 100 g of microemulsion-based hydrogel preparation and revolved at room temperature at 5, 10, 20, and 50 rpm in order to measure the viscosity of emulgel. Spindle number SPL4 was utilized to measure the viscosity.

The digital pH analyzer was used to assess pH. A 2.5 g hydrogel based on microemulsion was carefully measured

Table 3: Composition of emulgel (% w/w)

Components	*HBT 16*	*HBT 17*	*HBT 18*
HBT (%)	0.05	0.05	0.05
Capmul MCM C8	5	5	5
Acrysol EL 135+ Transcutol HP (3:1)	40	40	40
Water	55	55	55
HPMC K100M	1	1.5	2

and diluted in 25 mL of distilled water. Buffer solutions with pH 4.0, 7.0, and 9.0 were used to calibrate pH meter before each measurement. Three separate measurements of the formulation's pH were made, and mean values were calculated.

Spreadability test

The two 10 X 10 cm glass slides were taken in a device. Glass slides held a 0.5 g gel. A 100 g load was applied to the upper slide, and the diameter or length of the circle that had been marked was measured. The time required for the sample to spread was recorded. The formula is given as:

$$S = M \times L/T$$

Where,

T is time, L is length or diameter, and M is weight.

Drug content of optimized emulgel

An adequately weighted amount of HBT-loaded emulgel was placed in a volumetric flask containing 5 mL methanol and agitated for 30 minutes, adjusting the volume to 10 mL with methanol. To obtain a 10 µg/mL solution, the resultant mixture was again diluted, and the prepared solution was then filtered using Whatman filter paper and analyzed for absorbance at 238 nm using a UV spectrophotometer.

Comparison of *in-vitro* drug permeation of HBT-Emulgel and HBT-marketed gel, HBT-ME, HBT dispersion

Franz diffusion cell was utilized to study *in-vitro* drug permeation tests by employing cellophane paper as a membrane. A thermometer and a sample arm were both included in the water-Jacketed recipient compartment, with 25 mL capacity. The donor chamber with an internal diameter of 2 cm, was positioned to ensure contact only with the diffusion medium in the receptor chamber. The receptor compartment was filled with phosphate-buffered saline and kept at 37 ± 1°C and continuously stirred at 100 RPM.

The donor compartment was then treated with 1 g of emulgel containing HBT. At regular intervals, after removing 1-mL of the receptor medium, an equal volume of fresh medium was promptly incorporated into the receptor chamber. The treatment was repetitive for a total of 12 hours. All samples were passed through Whatman filter paper and analyzed using a UV spectrophotometer at 238 nm. The same procedure was performed for the marketed HBT gel (Psoricort H) 0.05% w/w.

Ex-vivo Drug Permeation Study of HBT-Optimized Gel and HBT-Marketed Gel

Goat skin was used for an ex-vivo permeation of drugs from HBT-gel and HBT emulgel formulations. Skin thickness ranged from 0.28 to 0.06 mm on average. The open-ended diffusion was positioned with the stratum corneum facing the donor compartment and the dermal side facing the receiver compartment after the skins had hydrated for an hour. The receptor compartment was kept at 37 ± 0.5°C and swirled at 100 rpm throughout the experiment filled with phosphate buffer (pH 6.8). A goat skin containing 1 g of HBT-emulgel was fastened to one end of an open-ended glass cylinder and dipped into a newly made phosphate buffer on a magnetic stirrer. At regular intervals, 1-mL of receptor medium was removed and the sink condition was maintained. The treatment was repeated for a total of 12 hours. The samples were filtered using Whatman filter paper and examined using a UV spectrophotometer set to 238 nm. The same procedure was performed for HBT-marketed gel 0.05% w/w.

Stability Study

The collapsible tube containing the optimized HBT-Emulgel was kept at 40 ± 1°C and 75% relative humidity for 3 months. Samples were assessed for physicochemical characteristics such as viscosity, spreadability and drug content at intervals of 1 month.

Results And Discussion

FTIR study

Fig. 1 presents the FTIR spectrum of HBT and excipients, while the interpreted data is summarized in Table 4. The presence of major peaks in the spectrum confirms the existence of distinctive functional groups in the molecule. Thus, the API sample was identified as halobetasol propionate and the selected excipients were compatible with the drug sample.

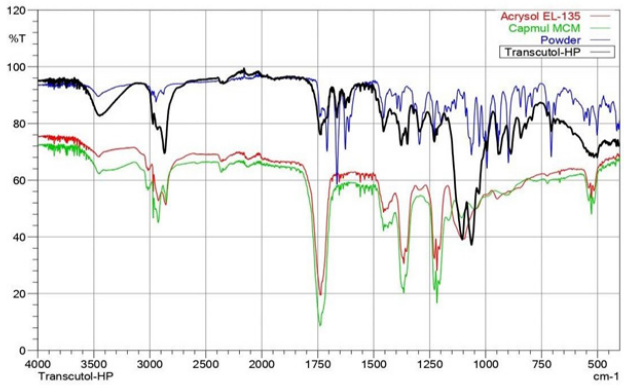

Fig. 1: FTIR spectra of pure drug and drug with excipient

Table 4: FTIR interpretation data of drug and drug with excipients

Functional group	*Observed spectra (cm^{-1})*			
	Pure drug	*Drug+ Acrysol EL 135*	*Drug+ Capmul MCM*	*Drug+ Transcutol HP*
C=O strecthing	1739	1738.21	1739.65	1738.21
C=C strecthing	1610	1609.25	1615.85	1610.89
O-H strecthing	3650	3650.97	3630.94	3649.54
C-F strecthing	1394	1366.25	1367.68	1377.70

Solubility Studies of Halobetasol Propionate

With all different oils, HBT has exhibited the maximum solubility in Capmul MCM C8 (18 ± 0.05 mg/mL), highest solubility of HBT has been shown in different surfactants and co-surfactants, respectively in acrysol EL 135 (21.5 ± 0.04 mg/mL), transcutol ® HP (25 ± 0.09 mg/mL). Non-ionic surfactants were selected for this investigation due to being typically considered safe, biocompatible, and less impacted by pH changes. According to the results, acrysol EL 135 showed the maximum emulsification efficiency in the oily phase. Co-surfactants increase the area of the microemulsion region by decreasing surface tension as it accumulates with surfactants at the interfacial layer. Solubility data is shown in Table 5.

Development of pseudo-ternary phase diagram

A pseudo-ternary phase diagram created by ternaryplot.com using the Water titration approach to obtain a stable microemulsion with a precise concentration range. The acrysol EL 135, a surfactant: Transcutol HP, a co-surfactant, was used in 1:1, 2:1, 3:1, and 4:1 ratios to create the diagram displayed in Fig. 2-(A), (B), (C), and (D), respectively, reveal the composition of oil, water and Smix. The zone of micro-emulsion that was created is seen. A larger 3:1 area was chosen, and from that area concentration of oil, and water, S_{mix} was optimized by using a design expert.

Experimental Design

A simplex lattice design was utilized for the optimization of HBT microemulsion by using the spontaneous emulsification method. Three independent variables were chosen: The quantity of oil (X1), Smix (X2), and water (X3), while, globule size (Y1) and %T (Y2) were selected as dependent variables or response factors for evaluating

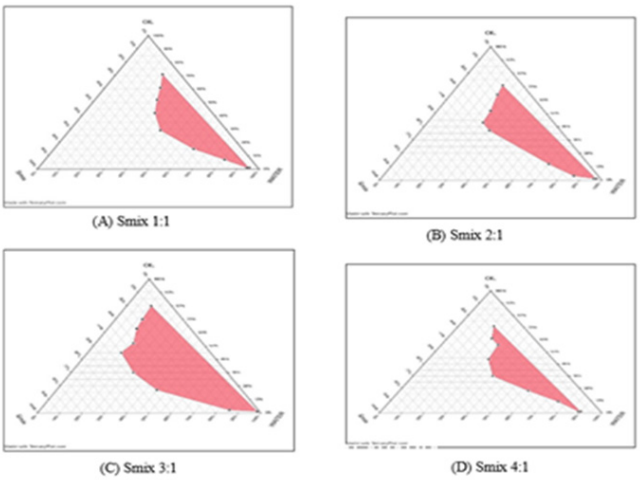

Fig. 2: Pseudo-ternary phase diagrams with different ratios of Smix (A)1:1, (B) 2:1, (C) 3:1, (D) 4:1 for HBT loaded MEs

the preparation of HBT microemulsion. The size of the globule of all batches of microemulsion was observed as in the range of 88.25 ± 2.2 to 330.6 ± 1.37 nm. Indicating all droplets were in the nanometer range and %T was found to be in the range of 96.8 ± 0.03 to 99.7 ± 0.02% indicating clarity of microemulsion. The smaller the globule size, the greater %T may increase the transparency of the microemulsion. Table 6 displays the result of measured responses and experimental runs according to the simplex lattice design.

Globule size and %T were analyzed using Design Expert for the prepared microemulsion displayed in the figure. A positive coefficient signifies a synergistic effect, whereas a negative coefficient implies an antagonistic effect. A polynomial equation of Y1 and Y2 is shown in equation.

The polynomial equation for $Y1 = +341.01 * X1 + 92.70 * X2$

Table 5: Solubility of HBT in different oil, surfactant and co-surfactant

Oils	*Solubility (mg/mL)*	*Surfactants*	*Solubility (mg/mL)*	*Co-surfactants*	*Solubility (mg/mL)*
Sunflower oil	02 ± 0.02	Polysorbate-80	15 ± 0.03	Labrasol	19.8 ± 0.03
Corn oil	2.8 ± 0.06	Polysorbate-20	12 ± 0.05	Labrafil M 1944CS	8.5 ± 0.05
Captex 200P	1.4 ± 0.08	Span-80	8.7 ± 0.09	Labrafil M 2125CS	7.8 ± 0.07
Oleic acid	05 ± 0.01	Span-20	9.8 ± 0.07	Transcutol ® HP	25 ± 0.09
Captex 355	2.3 ± 0.05	Acrysol EL 135	21.5 ± 0.04	Acconon MC 8®	12.5 ± 0.05
Labrafac PG	5.2 ± 0.04			PEG 400	10.9 ± 0.07
Olive oil	3.5 ± 0.09			PG	11.8 ± 0.08
Peceol	10 ± 0.02				
Capryol PGMC	09 ± 0.09				
Miglyol ® 812	4.8 ± 0.08				
Capmul MCM C8	18 ± 0.05				
Capmul-MCM®	15 ± 0.04				
Capmul-PG8®	11 ± 0.07				

$+ 108.62 * X3 - 219.59 * X1X2 - 198.75X1X3 - 55.38X2X3$
The polynomial equation for $Y2 = +96.87 * X1 + 99.76 * X2 + 99.41 * X3 - 1.42 * X1X2 - 2.00 * X1X3 - 2.19 * X2X3$

Effect of oil, Smix and water on globule size and %T

Fig. 3 shows the contour plot and 3-D surface plot for globule size. From the polynomial equation for Y1, it was concluded that oil, Smix and water have a positive effect on globule size. While the combination effect shows the negative impact.

Fig. 4 displays the contour plot and 3-D surface plot for %T. From the polynomial equation for Y2, it was concluded that all the components have a positive effect individually while in combination showing a negative effect. The combined effect of independent factors was observed which shows a positive effect. Here X1, X2, X3, X1X2, X2X3 and X1X3 show significant effects because the *p-value* is less than 0.05.

Checkpoint batch analysis and optimization based on desirability

The checkpoint batches were prepared from the different areas of design to confirm the productivity of the model. Two batches were compared with the predicted value provided by the software and findings showed no discernible variation between predicted and experimental data, indicating that the implemented design was appropriate. Based on the criteria like minimum globule size, and maximum %T, the desirability of 0.914 was found shown in Fig. 5. The composition of checkpoint batches and optimized batches with results are shown in Table 7.

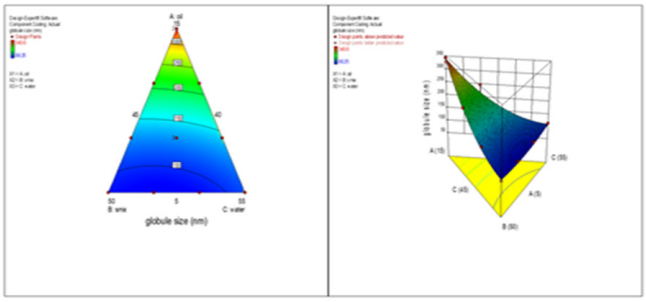

Fig. 3: Contour plot and 3-D surface plot for globule size

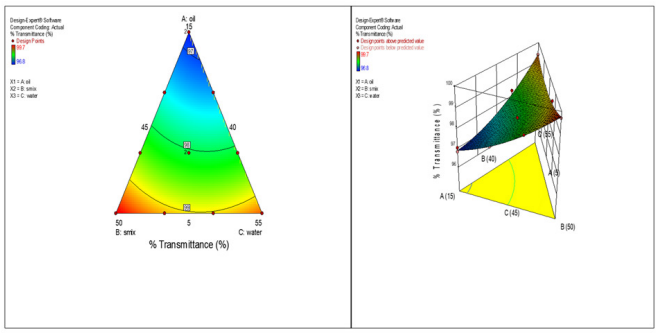

Fig. 4: Contour plot and 3-D surface plot for %Transmittance

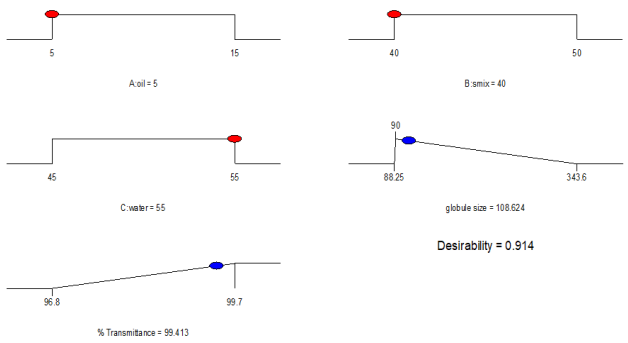

Fig. 5: Graphical presentation of optimization based on desirability

Evaluation of optimized batch of microemulsion

O/W type of emulsion was confirmed based on dilution and dye test. The zeta potential of the optimized batch was noted, -11.2 ± 0.05 mV indicating good stability of the formulation and PDI was found to be 0.203 which confirms the narrow size distribution of systems shown in Fig. 6. The size of the globule of the optimized batch was noted as 119.3 nm, confirming the nanometer size of the developed formulation. %T with 98.8 ± 0.02% indicating clear emulsion. Dispersion stability study was determined in an optimized batch of microemulsion shows no prominent variations in average globule size or phase separation have been observed. No significant alterations were noticed, and the microemulsion was reported to have remained transparent and clear. The stability study of the optimized microemulsion is shown in Table 8.

TEM analysis

A transmission electron microscopy investigation was carried out to assess smooth surface and spherical size globule. Fig. 7 displays a TEM picture of the HBT formulation in an optimized batch. The TEM image verified that the molecules of the drug were successfully integrated inside the formulation and droplet size in microemulsion was uniform.

Evaluation of optimized gel

For the preparation of microemulgel, an optimized batch of HBT -ME (HBT-15) loaded into gel base containing HPMC K100M with 1, 1.5, and 2% w/w various concentrations formulated three batches of HBT loaded microemulgel. Found that as the concentration of HPMC K100M enhances the spreadability diminishes and the viscosity enhances. Viscosity is a crucial physicochemical characteristic for topical drug delivery systems since it affects jellification, spreadability, and drug release. Spreadability reflects how easily a formulation can be applied, and is crucial in ensuring an accurate delivery of a drug dosage. The spreadability and viscosity of optimized batch HBT-18 were observed to be 3.58 ± 0.08 g.cm/sec and 9862 ± 15.28 cps, respectively. The pH was found to be favorable

Table 6: Result of globule size and %T

Batches	*X1 (mL)*	*X2 (mL)*	*X3 (mL)*	*Y1 (nm)*	*Y2 (%)*
HBT 1	0.5	5	4.5	88.25 ± 2.25	99.7 ± 0.02
HBT 2	0.5	4.7	4.8	90.5 ± 3.36	99.3 ± 0.07
HBT 3	0.5	4.3	5.2	98.9 ± 1.98	98.9 ± 0.06
HBT 4	0.5	4	5.5	115.3 ± 3.87	99.4 ± 0.01
HBT 5	0.8	4.7	4.5	135.2 ± 1.98	98.5 ± 0.02
HBT 6	0.8	4	5.2	126 ± 1.25	98.3 ± 0.03
HBT 7	0.8	4.3	4.8	117.5 ± 1.20	98.1 ± 0.07
HBT 8	0.8	4.3	4.8	115.4 ± 1.18	98.0 ± 0.08
HBT 9	1.2	4.3	4.5	213.6 ± 2.69	97.5 ± 0.04
HBT 10	1.2	4	4.8	248 ± 1.83	97.1 ± 0.05
HBT 11	1.5	4	4.5	330.6 ± 1.37	97.0 ± 0.04
HBT 12	1.5	4	4.5	330.6 ± 1.37	96.8 ± 0.03

(mean ± SD, n=3)

to skin conditions and wouldn't cause any skin irritation. The drug content was observed to be 96.35 ± 0.21%. Drug content data demonstrated that the oil and emulsifier were chosen appropriately.

Comparison study of in-vitro drug permeation of HBT emulgel, HBT marketed gel, HBT-ME, HBT dispersion

Fig. 8 shows the *in-vitro* permeation of the produced optimized batch of HBT emulgel with marketed gel (Psoricort H) 0.05% w/w and prepared optimized HBT-ME with a simple drug dispersion comparison study. After 12 hours the optimized HBT-emulgel, HBT-marketed gel, HBT-ME and HBT-dispersion shows drug release 93.56 ± 0.47, 46.82 ± 0.07, 98.5 ± 0.34, 41.5 ± 0.82%, respectively. Thus, prepared optimized formulations were found with better *in-vitro* diffusion than the others, this is due to co-surfactant and surfactant being incorporated into formulations.

Ex-vivo permeation of HBT-emulgel and commercially available HBT gel

Fig. 9 shows the comparison of the *ex-vivo* assessment of permeation in the optimized batch of HBT emulgel with

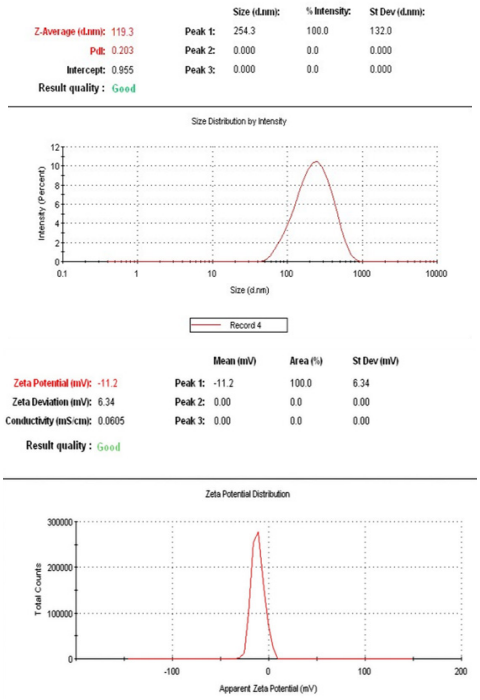

Fig. 6: Globule size, PDI and zeta potential of optimized batch

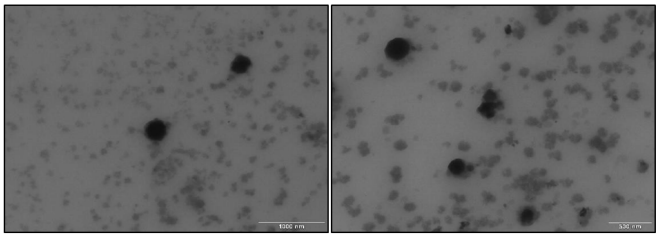

Fig. 7: TEM image of an optimized batch of HBT-loaded microemulsion

marketed gel. Drug permeation data of both formulations are 91.92 ± 0.48 and 44.59 ± 0.32%, respectively, which is a twofold enhanced permeability comparison with HBT-marketed gel. Improvements in drug permeation could lead to a greater therapeutic impact, reduced dose frequency, and better patient compliance with topical delivery.

Table 7: Composition and result checkpoint batches and optimized batch

Batches	*Amount of oil*	*Amount of Smix*	*Amount of water*	*Globule size (nm) Y1*		*%Transmittance Y2*	
	(%) X1	*(%) X2*	*(%) X3*	*Predicted*	*Actual*	*Predicted*	*Actual*
Composition and results of checkpoint batches							
HBT-13	6.08	47.43	46.49	94.95	105.5 ± 0.25	99.00	98.5 ± 0.45
HBT-14	12.43	42.57	45.00	235.34	251.9 ± 0.35	97.37	96.8 ± 0.44
Composition and results of an optimized batch							
(HBT-15)	5	40	55	108.6	119.3 ± 0.58	99.41	98.8 ± 0.02
Desirability					0.914		

(mean ± SD, n=3)

Table 8: Stability study of optimized microemulsion

Batch code	*Temperature (°C)*	*Inference*
HBT-15	4 (°C) Refrigerator	No separation of phases
	Room Temperature (30°C)	No separation of phases
	(45°C) in Hot air oven	No separation of phases

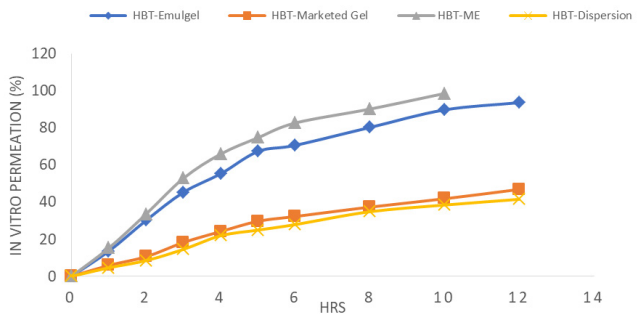

Fig. 8: Comparison of *in-vitro* drug permeation of HBT emulgel, HBT marketed gel, HBT-ME, HBT dispersion

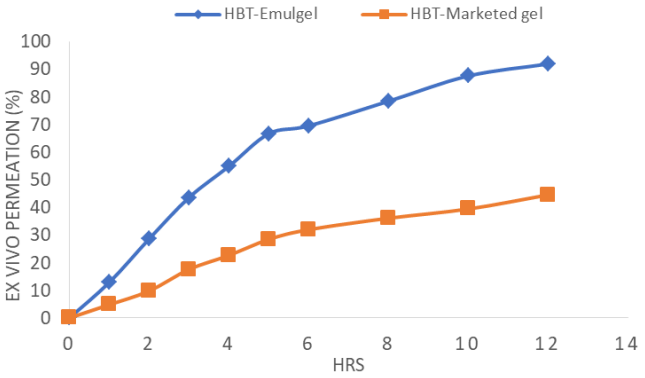

Fig. 9: Comparison of *ex-vivo* permeation of optimized batch of HBT emulgel with marketed gel

Stability study of emulgel

The optimized formulation of HBT-emulgel was examined for accelerated stability. Eventually, after three months of accelerated stability testing, an optimized emulgel formulation was found to have good stability and to have undergone no significant changes in spreadability, drug content and viscosity.

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REFERENCES

1. Patel N, Chaudhary S, Chaudhary A. Formulation development and evaluation of apremilast nanoemulsion. Research Journal of Pharmacy and Technology. 2023;16(6):2859-2866. DOI: 10.52711/0974-360X.2023.00471
2. Thombre NA, Niphade PS, Ahire ED, Kshirsagar SJ. Formulation development and evaluation of microemulsion based lornoxicam gel. Biosciences Biotechnology Research Asia. 2022;19(1):69-80. DOI: http://dx.doi.org/10.13005/bbra/2968
3. Dandagi PM, Pandey P, Gadad AP, Mastiholimath VS. Formulation and evaluation of microemulsion based luliconazole gel for topical delivery. Indian J. Pharm. Educ. Res. 2020;54(2):293-301. DOI: 10.5530/ijper.54.2.34
4. Kapadiya B, Gohil D, Patel D, Patel S, Aundhia C, Shah N, Pandya K. Formulation and evaluation of spironolactone loaded emulgel for topical application. J Pharm Sci Bioscientific Res. 2016;6(5):740-752. DOI: https://www.researchgate.net/publication/324794617
5. Chung M, Yeroushalmi S, Hakimi M, Bartholomew E, Liao W, Bhutani T. A critical review of halobetasol propionate foam (0.05%) as a treatment option for adolescent plaque psoriasis. Expert Review of Clinical Immunology. 2022;18(10):997-1003. DOI: http://dx.doi.org/10.1080/1744666X.2022.2110071
6. Shah N, Patel K, Singhvi I. Topical Delivery of Eberconazole Nitrate Loaded Microemulsion: Formulation, Design and Evaluation. International Journal of Pharmaceutical Sciences and Drug Research. 2023;15(4):478-487. DOI: https://doi.org/10.25004/IJPSDR.2023.150412
7. Mahajan N, Mujtaba MA, Fule R, Thakre S, Akhtar MS, Alavudeen SS, Anwer MK, Aldawsari MF, Mahmood D, Alam MS. Self-emulsifying drug delivery system for enhanced oral delivery of tenofovir: formulation, physicochemical characterization, and bioavailability assessment. ACS omega. 2024;9(7):8139-8150. DOI:10.1021/acsomega.3c08565
8. Varshney HM, Chatterjee A. Solubility enhancement of poorly hydrophilic drugs by using different newer techniques: A Review. International journal of Therapeutic applications. 2012; 6:8-13. DOI: https://www.researchgate.net/publication/232747066
9. Bhagwat DA, Swami PA, Nadaf SJ, Choudhari PB, Kumbar VM, More HN, Killedar SG, Kawtikwar PS. Capsaicin loaded solid SNEDDS for enhanced bioavailability and anticancer activity: in-vitro, in-silico, and in-vivo characterization. Journal of pharmaceutical sciences. 2021;110(1):280-291. DOI:10.1016/j.xphs.2020.10.020
10. Syed HK, Peh KK. Identification of phases of various oil, surfactant/co-surfactants and water system by ternary phase diagram. Acta Pol Pharm. 2014;71(2):301-309. DOI: https://www.researchgate.net/publication/261133602
11. Moghimipour E, Salimi A, Karami M, Isazadeh S. Preparation and characterization of dexamethasone microemulsion based on pseudoternary phase diagram. Jundishapur journal of natural pharmaceutical products. 2013;8(3):105-112. DOI: 10.17795/jjnpp-9373
12. Gibaud S, Attivi D. Microemulsions for oral administration and their therapeutic applications. Expert opinion on drug delivery. 2012;9(8):937-951. DOI: 10.1517/17425247.2012.694865
13. Ali FR, Shoaib MH, Yousuf RI, Ali SA, Imtiaz MS, Bashir L, Naz S. Design, development, and optimization of dexibuprofen microemulsion based transdermal reservoir patches for controlled drug delivery. BioMed research international. 2017;2017(1):1-15. DOI:10.1155/2017/4654958
14. Behera J, Keservani RK, Yadav A, Tripathi M, Chadoker A. Methoxsalen loaded chitosan coated microemulsion for effective treatment of psoriasis. International Journal of Drug Delivery. 2010;2(2):159-167. DOI:10.5138/ijdd.2010.0975.0215.02025
15. Saudagar RB, Vaishnav S. Pharmaceutical Nano emulsion as a Rational Carrier for Drug Delivery. Research Journal of Pharmacy and Technology. 2016;9(3):298-304. DOI: 10.5958/0974-360X.2016.00055.X
16. Furlanetto S, Cirri M, Piepel G, Mennini N, Mura P. Mixture experiment methods in the development and optimization of microemulsion formulations. Journal of pharmaceutical and biomedical analysis. 2011;55(4):610-617. DOI: https://doi.org/10.1016/j.jpba.2011.01.008

17. Zhu S, Zeng J, Pan C, Chai Y, Bai M, Li J, Chen A. Reverse microemulsions as nano-carriers of tea polyphenols retard oxidation of Eucommia ulmoides oliver seed oil. Colloids and Surfaces A: Physicochemical and Engineering Aspects. 2023;671:687-698. DOI: https://doi.org/10.1016/j.colsurfa.2023.131687
18. Rasool BK, Abu-Gharbieh E, Fahmy S, Saad H, Khan S. Development and evaluation of ibuprofen transdermal gel formulations. Tropical Journal of Pharmaceutical Research. 2010;9(4):355-363. DOI: 10.4314/tjpr.v9i4.58928
19. Beg S, Sandhu PS, Batra RS, Khurana RK, Singh B. QbD-based systematic development of novel optimized solid self-nanoemulsifying drug delivery systems (SNEDDS) of lovastatin with enhanced biopharmaceutical performance. Drug delivery. 2015;22(6):765-784. DOI: 10.3109/10717544.2014.900154
20. Sabale V, Vora S. Formulation and evaluation of microemulsion-based hydrogel for topical delivery. International journal of pharmaceutical investigation. 2012;2(3):140-149. DOI: 10.4103/2230-973X.104397

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