Advances in Bioresearch
Adv. Biores., Vol 14 (5) September 2023: 327-337

Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.14.5.327337

Advances in Bioresearch

ORIGINAL ARTICLE

Formulation and Evaluation of Ethosomal Patch of Tretinoin for the Treatment of Psoriasis

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ABSTRACT
The objective of the present study was to formulate and evaluate an ethosomal transdermal patch containing tretinoin for the treatment of psoriasis. Ethosomes were prepared by using different concentration of soya lecithin and ethanol by using cold method and optimized by using 3 x 3 Box-Behnken design (BBD) and then the prepared ethosomes were characterized for particle size, zeta potential, SEM, % Entrapment efficiency and stability studies. Drug loaded ethosomes were then incorporated into an HPMC based transdermal patch. Further, patches were examined for variation in weight, its thickness, folding endurance, in-vitro drug release and stability studies. The vesicle size of ethosomes was found in range of 219.1 to 273.27 nm and entrapment efficiency was found in range of 69.62 to 77.14 %. Zeta potential came in range of -20.96 mV to -31.1 mV. Stability studies showed that ethosomal patch stored at 4 °C / 60 ± 5RH were most stable. The optimized ethosomal formulation F5 with soya lecithin concentration of 2.5% and ethanol concentration 30% had size of 219.1 nm, zeta potential (-31.1) and entrapment efficiency of 77.14%. The in-vitro drug release of optimized ethosomal patch B5 was found to be 91.856% at 12 h. These findings suggest that transdermal tretinoin delivery in the form of an ethosomal patch can give a prolonged effect in the management of psoriasis.
Keywords: *Tretinoin, Ethosomes, Ethanol, Psoriasis, Ethosomal patch.*

Received 15.06.2023 Revised 23.07.2023 Accepted 15.09.2023

How to cite this article:
Yash J, Nadeem F, Pritesh P, Darshan J, Nimita M. Formulation and Evaluation of Ethosomal Patch of Tretinoin for the Treatment of Psoriasis. Adv. Biores. Vol 14 [5] September. 2023. 327-337.

INTRODUCTION

Psoriasis, a persistent inflammatory skin condition caused by abnormal immune system reaction, have an uncertain aetiology which may be attributed to an imbalance in Keratinocyte proliferation and differentiation, which is accompanied by inflammatory cell infiltration, mainly composed of T-lymphocytes, macrophages, and neutrophils. Distinguished by appearance of scaly plaques on the skin's surface which are well-circumscribed, round, red with a grey or silvery-white scales which appear on the knees, elbows, scalp, lumbosacral region, soles, palms and body folds [1]. The global prevalence is around 2% (roughly 125 million individuals) [2].There are various treatment options available for psoriasis such as topical therapy like immunosuppressants, corticosteroids, Vitamin D analouges; Systemic therapy like cyclosporine, tofacitinib, Methotrexate etc. but all these drugs suffer from major limitations like various side effects like redness, irritation and erythema of skin, Hepatotoxicity, renal toxicity, requires frequent dosing and also limited drug absorption into skin layers [3].

Tretinoin, a retinoid derivative of vitamin A, has shown promising therapeutic effects in psoriasis treatment by its antiproliferative, differentiation normalizing, and anti-inflammatory effects [4]. However, its clinical efficacy is hindered by limited skin permeation due to skin's barrier properties, various side effects like redness, irritation and erythema and also has biological half-life of 0.5 – 2 hrs requires frequent dosing [5, 6]. To overcome these limitations, novel drug delivery approaches have been investigated to enhance tretinoin's therapeutic efficacy while minimizing adverse effects.

The discovery of vesicle derivatives termed as ethosomes was a big breakthrough in vesicle research. Ethosomes are soft, flexible nanocarriers and are a type of non-invasive drug delivery system which helps the drug to reach into the deeper layers of skin and then to the systemic circulation. They are mainly

composed of various phospholipids, high ethanol concentration and water [7]. Ethanol is known as an efficient penetration enhancer and facilitate permeation across stratum corneum. Ethosomes have numerous benefits over traditional formulations, particularly enhanced drug bioavailability, reduced systemic absorption, enhanced patient compliance due to reduced frequency of application, and minimized local side effects [8].

Hence the objective of the present study was to formulate a ethosomal patch for improved drug delivery system of anti-psoriatic drug i.e. Tretinoin and also optimize using BBD and toevaluate its performance against various evaluation parameters. By employing the unique properties of ethosomes as a carrier system and the advantages of a transdermal patch, this research holds promise for improving therapeutic outcomes while lowering the negative effects caused by conventional formulations. Ultimately, this approach may pave the way for more effective management strategies that alleviate symptoms and improve quality of life for individuals living with psoriasis.

MATERIAL AND METHODS

Tretinoin was obtained as a gift sample from Leeford Healthcare Ltd, Mumbai. Soya lecithin was obtained from Central Drug House Ltd, Delhi. Ethanol was obtained from Changshu Hongs heng Fine Chemicals Co. Ltd., China. Propylene glycol, HPMC, Acetone and Glycerin were obtained from Loba Chemie Pvt. Ltd, Ghaziabad. All other reagents and solvents used were of Analytical grade. Distilled water was used throughout the study.

Preparation of Tretinoin Loaded Ethosomes

Ethosomes of Tretinoin were prepared by cold method as described by (Touitou et. al., 2000). Phospholipid (1 - 4 % w/v), drug and ethanol (20-40 %) were collected in a round bottom flask. After that, it was vigorously mixed with help of magnetic stirrer at 700 rpm and temperature of 30 °C. To prevent ethanol evaporation, it was covered. Propylene glycol was added dropwise during mixing. In separate vessel distilled water was warmed to 30 degrees Celsius. The ethosomal colloidal suspensions were then obtained by gently adding it under continuous stirring. The resulting ethosome suspension was left at room temperature for 30 minutes. Further, prepared ethosomes were sonicated for (5-6) mins. Formulation was stored in refrigerator. The composition of various ethosomal formulations were represented in table 1.

Table 1: Composition of Tretinoin loaded ethosomes

Formulation code	Drug (mg)	Soya lecithin (mg)	Ethanol (ml)	Propylene glycol (ml)	Water (ml)
F1	25	100	2	2	6
F2	25	100	3	2	5
F3	25	100	4	2	4
F4	25	250	2	2	6
F5	25	250	3	2	5
F6	25	250	4	2	4
F7	25	400	2	2	6
F8	25	400	3	2	4
F9	25	400	4	2	5

Optimization of Tretinoin Loaded Ethosomes

Design-Expert software (Trial Version 8.0.7.1, Stat-Ease Inc., MN) was used to generate a Box-Behnken design with 3 variables 3 levels were used to optimize formulations. Given the variation in dependent variables throughout 13 batches, Box-Behnken design was used in formulation development to analyze effect of independent variables on dependent variables. Phospholipid concentration (%) (A), Ethanol (%) (B), and Sonication time (min) (C) were independent variables. The dependent variables were vesicle size (nm) (Y1), entrapment efficiency (%) (Y2), and zeta potential (Y3) (Table 4.3). The experimental arrangement of several ethosome batches is shown in Table 2 [21].

Statistical model, including the polynomial terms was used to estimate the response shown by general binomial equation.

$$Y = b0 + b1X1 + b2X2 + b3X3 + b4X12 + b5X1X2 + b6X1X3 + b7X22 + b8X2X3 + b9X32 + E$$

Where, Y is the selected response, b0– intercept, b1–b9 are the regression coefficients, X1, X2 and X3 are the factors studied and E is an error term [11].

Table 2. Variables in Box-Behnken design for the preparation of Tretinoin loaded ethosomes

Variables	Levels		
Independent variables	-1 (low)	0 (medium)	+1 (high)
Phospholipid concentration (%)	1	2.5	4
Ethanol (%)	20	30	40
Sonication time (min)	5	5.5	6
Dependent variables			
Vesicle size (nm)	Minimize		
Entrapment efficiency (%)	Maximize		
Zeta potential (mV)	Maximize		

Table 3. Observed responses in "Box–Behnken design" for Tretinoin loaded ethosomes formulations

	Independent variables			Dependent variables		
Run	X_1 (%)	X_2 (%)	X_3 (min)	Y_1 (nm)	Y_2 (%)	Y_3 (mV)
1	1	20	5.50	240.91	69.62	- 20.96
2	1	30	5	249.3	71.32	- 26.4
3	1	30	6	246.1	72.11	- 28.76
4	1	40	5.50	266.2	71.32	- 22.8
5	2.50	20	5	233.3	75.56	- 26.2
6	2.50	20	6	235.7	75.99	- 29.6
7	2.50	30	5.50	219.1	77.14	- 31.1
8	2.50	40	5	243.70	73.98	- 27.8
9	2.50	40	6	245.64	74.01	- 24.45
10	4	20	5.50	271.39	74.25	- 28.1
11	4	30	5	268.28	74.43	- 28.9
12	4	30	6	269.17	75.45	- 27.33
13	4	40	5.50	273.27	70.79	- 25.14

X_1: Phospholipid concentration (%), X_2:Ethanol (%), X_3: Sonication time (min), Y_1: Vesicle size (nm), Y_2: Entrapment efficiency (%), Y_3: Zeta potential (mV)

Table 4. Overview of regression analysis results for responses Y1, Y2, and Y3 for quadratic model fitting

Quadratic model	R_2	Adjusted R_2	Predicted R_2	SD	% CV
Response Y1- Vesicle size	0.99	0.99	0.96	1.41	0.58
Response Y2- Entrapment efficiency	0.98	0.98	0.97	0.43	0.58
Response Y3- Zeta potential	0.97	0.94	0.63	0.59	2.10
Regression equation of fitted quadratic model					

CV= coefficient of variation, SD= standard deviation

Preparation of Ethosomal Patch

The solvent casting technique was used to formulate the tretinoin ethosomal patch. Ethosomal suspension containing tretinoin ethosomes were used. First the polymer HPMC was taken in a container. It was dispersed in casting solvent (acetone: distilled water in ratio 9: 1). The drug suspension was then added and the solution was mixed and sonicated for 2 mins to remove air bubbles. Then, as a plasticizer, glycerine was added. The dispersion was then poured in a 5cm × 5cm petri dishes. To regulate the speed of solvent evaporation, the petri dishes were covered with funnels and the molding solvent was left to evaporate overnight to get the dried patches. The patches were cut into small patches containing the equivalent of 25 mg of the medication per patch and kept in desiccators within layers of wax paper for subsequent tests [10].

Table 5: Composition of Ethosomal patch

Formulation code	Drug in suspension equivalent to 25mg (ml)	HPMC E15 (mg)	Glycerin (ml)	Acetone: Distilled water (9:1) ml
B1	5	200	1	10
B2	5	300	1	10
B3	5	400	1	10
B4	5	450	1	10
B5	5	500	1	10
B6	5	600	1	10

Characterization of Tretinoin loaded Ethosomes

1. **Particle size, Polydispersity index (PDI) and zeta potential**
   Particle size and polydispersity index were assessed using the Malvern zeta sizer nano ZS the material was diluted 1 in 10 ml with Phosphate buffer saline (PBS) 6.8 and measurements were done at 25 °C. Malvern zeta nano ZS zetasizer was used to find zeta potential. A current is delivered across a pair of electrodes at each end of a cell housing the particle dispersion. Charged particles get drawn to oppositely charged electrode and their velocity recorded. Zeta potential values less than -30mV or more than +30mV are considered stable formulations [12].
2. **Scanning Electron Microscopy (SEM)**
   Scanning electron microscopy was used to examine the morphology of ethosomes (Quanta FEG 450, FEI, Netherlands). A drop of ethosomal suspension was applied to the stub's surfaces. The sample was dried and coated with platinum for 50 seconds using an auto fine coater (JFC1600, Jeol, Japan) at current intensity 20 mA. SEM was used to evaluate the sputter-coated sample at a 20 kV accelerating voltage [13].
3. **Differential Scanning Calorimetry**
   A DSC investigation was done using Mettler Toledo DSC equipment, with Pyris software to record the spectra. Tretinoin and optimized ethosomal formulation were weighed in an aluminium pan (weight should be between 5-25 mg), and it was sealed with aluminium lid using hydraulic press. The pan was put in DSC with a heating range of 20-350°C and a heating rate of 50°C/min in a nitrogen environment. The graph was recorded, with temperature on X-axis and heat flow on Y-axis [14].
4. **Entrapment Efficiency**
   Unentrapped drug concentration in aqueous medium was used to calculate entrapment efficiency. In Eppendorf tubes, 1 ml of drug-loaded ethosomes dispersion was put in Eppendorf tubes and centrifuged to about10,000 rpm for 30 mins. Near the bottom of tubes, the ethosomes and encapsulated medication were separated. As a control, plain ethosomes lacking Tretinoin were centrifuged in the same way. UV absorbance of the supernatant at 322 nm The UV absorbance of supernatant at 322 nm was determined to find free drug concentration [15]. Entrapment efficiency was obtained by equation :

$$\%\ EE = \frac{(total\ amt\ of\ drug\ added - total\ amount\ of\ drug\ in\ supenatant)}{total\ amt\ of\ drug} \text{x } 100$$

Characterization of Ethosomal Patch

Thickness and Weight Variation

By using a digital vernier calliper, thickness of ethosomal patches were measured at several locations, and mean values were determined. To evaluate weight variation, 3 patches from the same batch were weighed and the SD was calculated [15].

Folding Endurance and Tensile Strength

Folding endurance was evaluated by folding the patch multiple times at the same location until the patch broke. The number of times a patch can fold without breaking gives the folding endurance value [21].

By using a tensiometer, tensile strength was tested. The patch assembly was fastened, and the weight at which the patch was broken was recorded [16]. Tensile strength was estimated using the following formula:

$$\text{Tensile strength (Kg / cm sq.)} = \frac{\textbf{Force at break (Kg)}}{\textbf{Cross-sectional area of the sample (cm sq)}}$$

% Moisture Content

Moisture content was determined by putting patches in desiccator with calcium chloride at room temperature for 24 hours. A 2 × 2 cm patch strip was cut from the ethosomal patch and weighed until a consistent weight is reached [17].The average, denoted as ±SD, was found using equation:

$$\%\ Moisture\ content\ = \frac{(Initial\ weight - Final\ weight)}{Final\ weight} \times 100$$

In-vitro Drug release from Ethosomal Patch

In-vitro release of ethosomal patch was measured utilizing a diffusion cell via a cellulose acetate membrane. The ethosomal patch was kept in donor compartment. 100 ml phosphate buffer pH 7.4 was poured in receptor compartment. The media was stirred continuously over a magnetic stirrer and the temperature was maintained at 37 ± 0.5 °C. Samples (1 ml) were withdrawn at regular time periods up to 72 h. The same volume of fresh buffer was placed in receptor compartment. Tretinoin concentration in samples was estimated utilizing UV spectroscopy at 322 nm. The % cumulative drug rlease was calculated using drug concentration [18, 19].

Stability study

The drug retention ability were utilized for finding stability of ethosomal patch. The patch was covered in aluminium foil and kept at 4°C and 25°C with a relative humidity of 60 gm/m^3. After 7, 15, 30, 60, and 90 days, the ethosomal patch was characterized, which included weight variation, % moisture content, and an in-vitro study [20].

RESULTS AND DISCUSSION

Characterization of Ethosomes

Particle Size, Polydispersity Index (PDI) and Zeta Potential

The vesicle size of ethosomes were found in range of 219.1 to 273.27 nm. The particle size is shown in Table 3.The PDI was found in range of 0.146 to 0.267. Particle size analysis revealed that the increase in size of particles is directly proportional to the increase in amount lipid. But by using different concentration of ethanol, the particle size is minimized. Further, it was observed when soya lecithin concentration was 1% to 2.5% particle size decreased but on using 4% soya lecithin the particle size increased. Also, the lower values of polydispersity index correspond to the wide distribution of particles. Among all ethosomes formulation, formulation F5 with soya lecithin concentration 2.5 % and ethanol concentration 30 % was considered as an optimized formulation.

The zeta potential values were found in the range of -20.96 mV to -31.1 mV. The zeta potential values are shown in Table 3. Stability of ethosomes depends on high zeta potential value which points toward better stability of ethosomes since it prevents aggregation between vesicles. In present investigation, there is not much difference in zeta potential of different formulations and ethosomes shows quite average values of zeta potential and shows moderate stability of ethosomes.

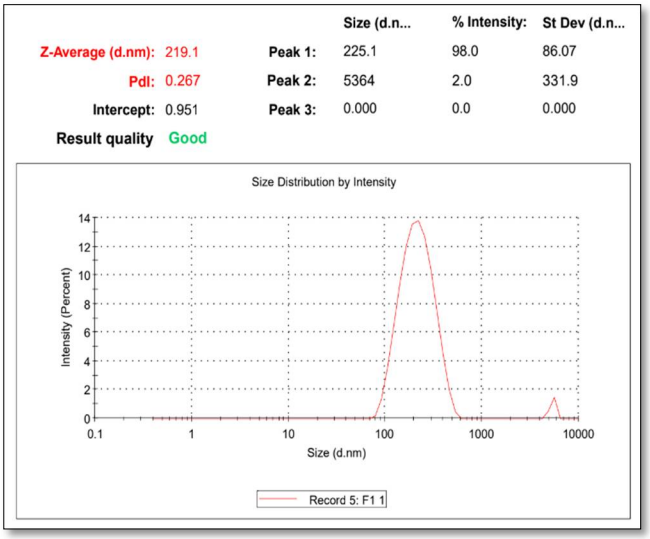


Figure 1. Particle size of optimized ethosomal formulation F5

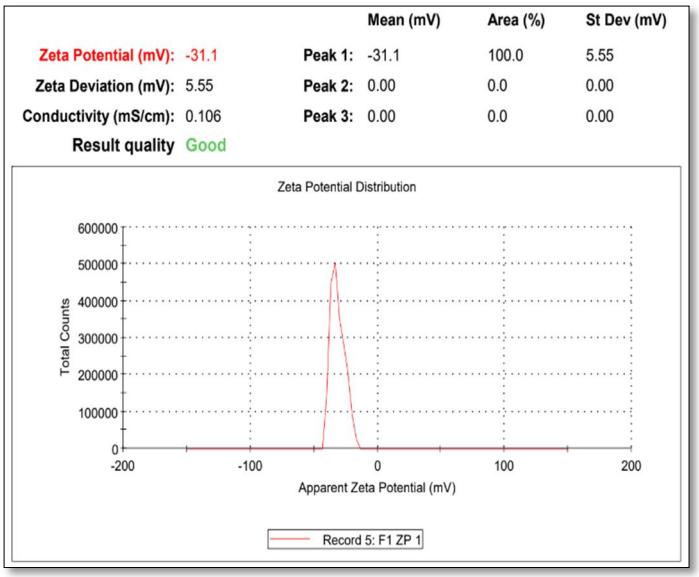


Figure 2. Zeta potential of optimized ethosomal formulation F5 Scanning Electron Microscopy (SEM)

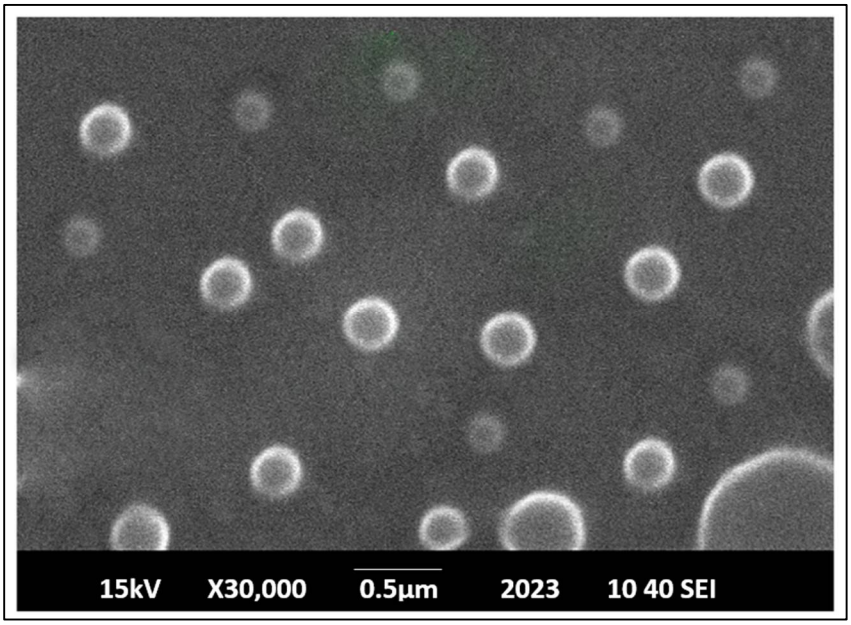
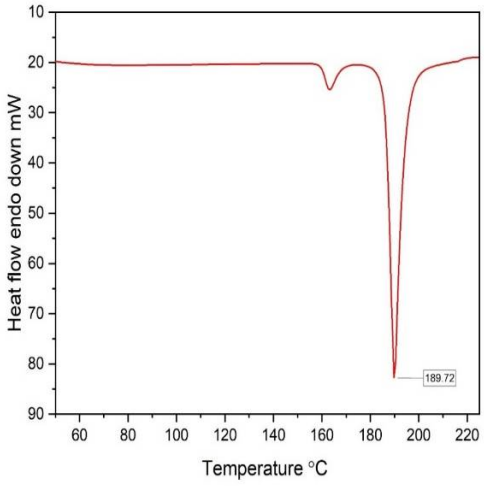


Figure 3. SEM of tretinoin loaded ethosomes

Scanning electron microscopy (SEM) was utilized for evaluating the surface morphology and 3D behaviour of ethosomes. Figure 3 shows SEM image of optimized ethosomal formulation F5, which showed that ethosomes were sphere-shaped with well-defined borders, indicating that the manufactured dosage forms have acceptable morphology. Notably, the dense particle in the picture suggests the existence of higher density lipids over particles, implying that controlled release of ethsomes is a possibility.

Differential Scanning Calorimetry (DSC)

DSC was used to study the thermal properties of drug Tretinoin and optimized ethosomal formulation and monitored the thermal event against increasing temperature. Along with increased temperature, drug substance was reached to the melting point, exhibited a folding transition. DSC spectra of Tretinoin showed a sharp endothermic peak at 189.72 °Cas compared to its melting point, thus indicating the purity of drug sample. This was compared with literature values [8]. The melting peaks obtained for Tretinoin loaded ethosomal formulation were seen at 196.5 °C, with broad and low intensity endothermic peaks as compared to the pure drug. This specifies that drug structure in the lipid bilayer has been forming a new phase which is shifted towards left and also indicates drug exist in an crystalline form [3]. The DSC spectra of Tretinoin and optimized ethosomal formulation are shown in Figure 4 and 5.



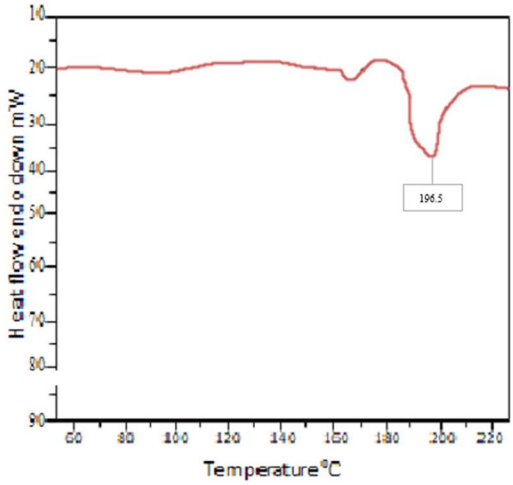


Figure 4. DSC Spectra of Tretinoin Figure 5. DSC Spectra of optimized ethosomal formulation

% Entrapment Efficiency

Entrapment efficiency of all ethosomes formulation were found in range of 69.2 – 77.14 %. The results are shown in Table 3. Entrapment Efficiencyof drug in the ethosomes depends on the soya lecithin concentration and also on the ethanol concentration. The results show that when soya lecithin concentration was increased from 1% to 2.5% the EE also increased but when it is 4% EE decreased slightly. So, formulation F2 with soya lecithin concentration of 1% and ethanol concentration 30% showed EE of 72.11 %. When soya lecithin concentration was 4% and ethanol concentration of 30% showed EE of 75.45%. When ethanol concentration was increased from 20% to 30%, EE was increased but when increased to 40% EE was found to decrease as the vesicle's membrane gets more permeable and the drug leached out from the membrane. It can be seen all formulations with ethanol concentration of 40% i.e., formulation F3, F6 and F9 showed a decreased EE. Formulation F8 with soya lecithin concentration of 2.5 % and ethanol concentration of 30% showed a maximum EE of 77.14 % and from the results F5 was considered as an optimized formulation.

Response surface analysis

The design expert software created 3D graphs showing impact of various variables on particular responses. All of the observed response surfaces formed hillsides with large curvatures confirms that they were typically influenced by the interaction effect of concentrations of dependent factors. Interactive effect of different variables (A & B) on various responses Y1, Y2 and Y3 was indicated in 3D plots, depicted in figures 6-8.

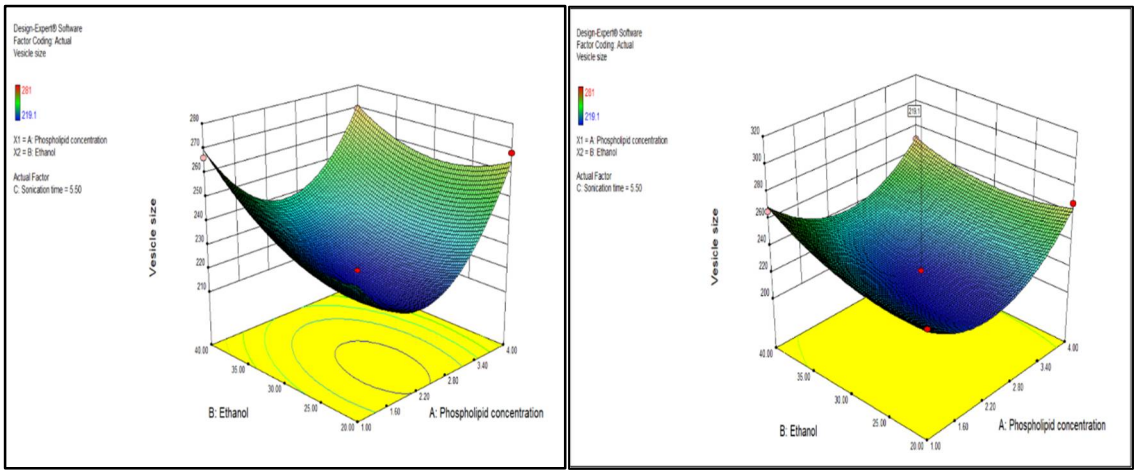


Figure 6. 3D Plot Represented the Impact of Phospholipid Concentration (A) and Ethanol (B) Concentration on Y1 and Y1 showing Centre Point

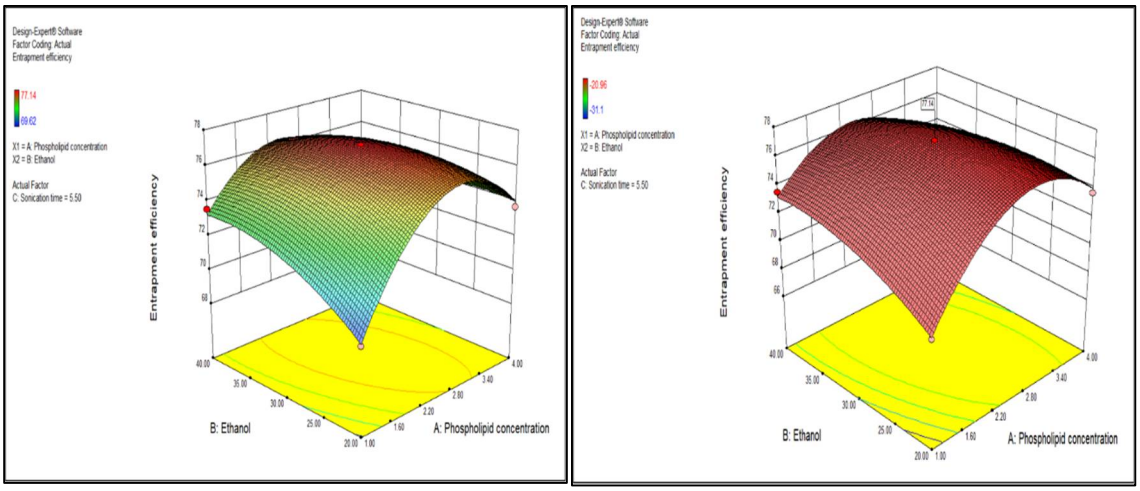


Figure 7. 3D Plot Represented the Impact of Phospholipid Concentration (A) and Ethanol (B) Concentration on Y2 and Y2 Showing centre Point

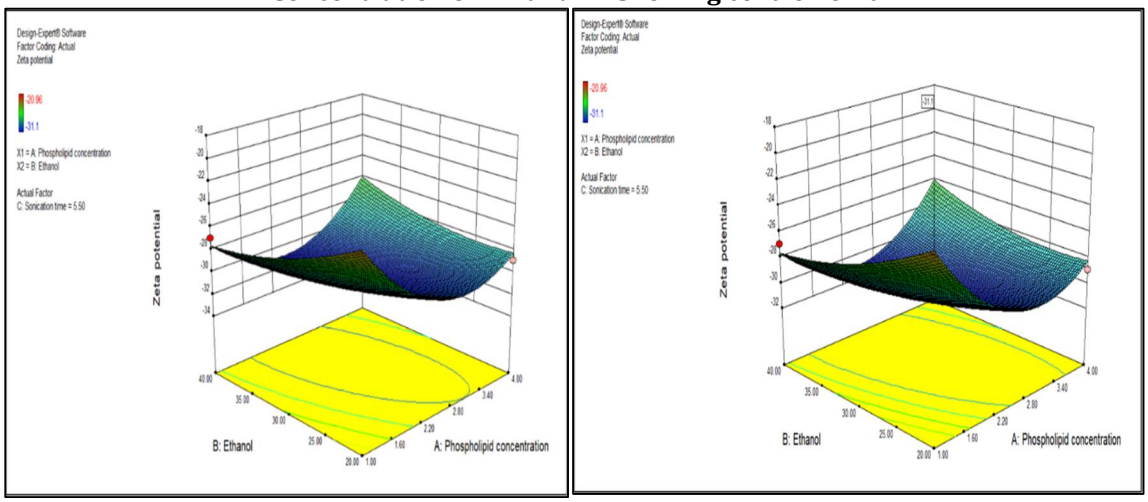


Figure 8. 3D Plot Represented the Impact of Phospholipid Concentration (A) and Ethanol (B) Concentration on Y3 and Y3 Showing Centre Point

Characterization of Ethosomal Patch

Thickness and Weight Variation

Thickness of the patches taken from the three point of the same patch was found to be in range of 0.14 ± 0.049 mm to 0.39 ± 0.032 mm for ethosomal patches. The results are shown in Table 7. The weight of prepared patches was found to be in range of 348.15 ± 0.52 mg to 713.29 ± 0.38 mg.

Folding Endurance and Tensile strength

Folding endurance of the Tretinoin ethosomal patches was foundin range of 13 ± 4 to 30 ± 5. Folding endurance of the ethosomal patches were moderate which showed patches formulated with HPMC shows a good strength.

Tensile strength helps to examine mechanical strength of patches. Tensile strength forethosomal patch was found to be in range of15.8 ± 0.98 to 22.21 ± 0.13. Results show that the patches prepared with HPMC are stable and will maintain their integrity during the application on the skin.

Table 6. Evaluation of Tretinoin Ethosomal Patches

Formulation code	Weight variation (mg)	Thickness (mm)	Folding endurance	Tensile strength	% Moisture content	In -vitro drug release in 12 h (%)
B1	348.15 ± 0.52	0.14 ± 0.049	13 ± 4	17.45 ± 0.32	2.94 ± 0.025	88.97
B2	470 ± 0.86	0.17 ± 0.009	15 ± 9	16.44 ± 0.66	3.41 ± 0.01	87.65
B3	519.11 ± 0.45	0.25 ± 0.022	25 ± 8	18.75 ± 0.11	3.02 ± 0.77	90.01
B4	559.23 ± 0.73	0.30 ± 0.057	22 ± 4	15.8 ± 0.98	2.33 ± 0.45	90.11
B5	630.44 ± 0.98	0.35 ± 0.058	30 ± 5	19.86 ± 0.66	2.82 ± 0.34	91.856
B6	713.29 ± 0.38	0.39 ± 0.032	28 ± 5	22.21 ± 0.13	4.17 ± 0.32	89.25

% Moisture Content

The results of % moisture content is shown in Table 7. % Moisture content for the Tretinoin ethosomal patches was found to be in range of 2.94 ± 0.025 % to 4.17 ± 0.32 %. Low moisture content indicates that the formulation will remain stable on longer duration of storage and also reduce the brittleness of the patches.

In-vitro Drug Release from Ethosomal Patch

In-vitro release of Tretinoin ethosomal patches were studied using Franz diffusion cell and the results were shown in figure 10. Ethosomal patch containing HPMC shows % drug release in the range of 87.65 % to 91.856 % drug release in 12 h. They show a high drug release due to the presence of ethanol in the ethosomes which act as an efficient permeation enhancer.

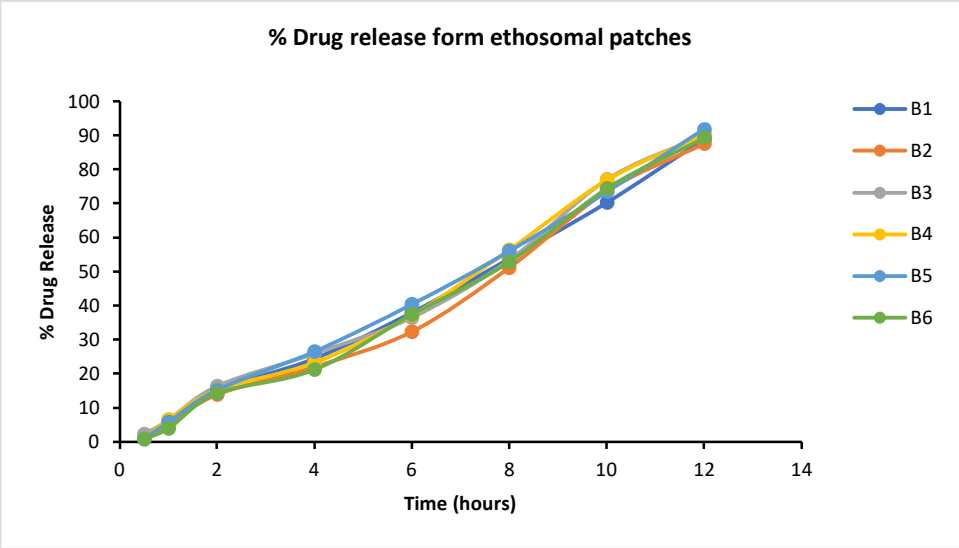


Figure 6. In-vitro Drug Release studies of Ethosomal Patch Formulation

Release Kinetics of Ethosomal Patches

Table 7. Kinetic data of Tretinoin Ethosomal patches

Formulation	Zero order (r^2)	First order (r^2)	Higuchi (r^2)	Kros-peppas (r^2)
B5	0.9965	0.9829	0.916	0.9062
B4	0.9939	0.9784	0.9121	0.8993

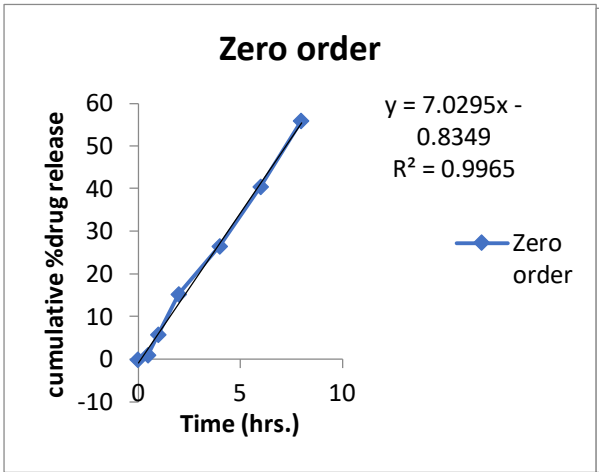


Figure 7. Zero Order Release Kinetics

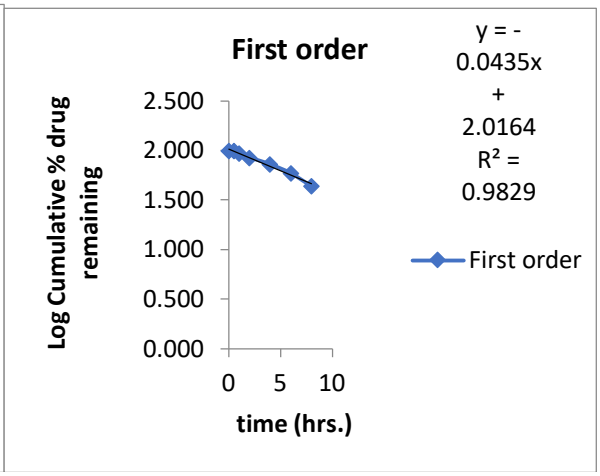


Figure 8. First Order Release Kinetics

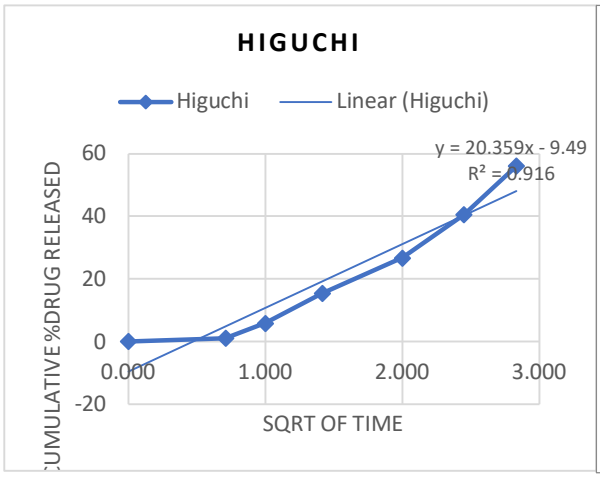


Figure 9.Higuchi Model Release

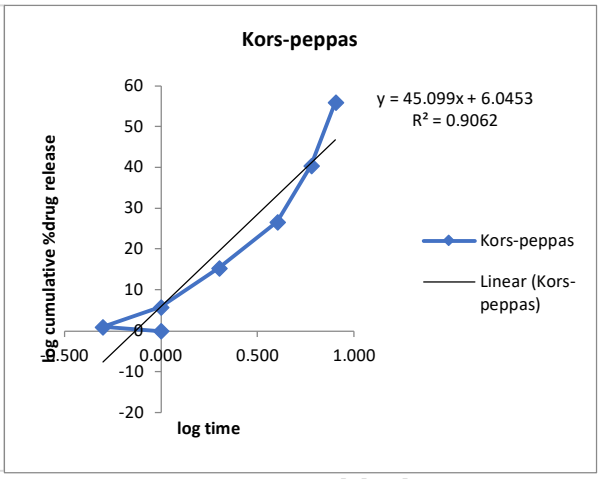


Figure 10. Kros-Peppas Model Release Kinetics

Stability Study

Stability was done for 3 months at a different temperature to determine the capability of the patch to retain drug and would remain stable for a longer duration of time based on weight variation, % moisture content and in-vitro release study were done. Patch B5 was selected for stability studies. The results are shown in table 8. It was found that the patch shows a more decrease in the in-vitro release of drug when stored at 25 °C/ 60 ± 5RH as compared to storage at 4 °C / 60 ± 5RH. Therefore 4 °C/60 ± 5 RH was considered as an optimal condition for storage of ethosomal patch.

Table 8. Stability study ofEthosomal Patch

Time (days)	Weight variation (mg)		% Moisture content		% In-vitro release	
	4 °C	25 °C	4 °C	25 °C	4 °C	25 °C
Initial	630.44 ± 0.98	630.44 ± 0.98	2.82 ± 0.34	2.82 ± 0.34	91.85	91.85
7	630.91 ± 0.18	631.78 ± 0.01	2.86 ± 0.71	2.65 ± 0.46	89.87	85.9
15	631.01 ± 0.20	632.64 ± 0.36	2.98 ± 0.36	3.01 ± 0.49	88.46	80.85
30	632.65 ± 0.10	634.74 ± 0.99	3.04 ± 0.54	5.22 ± 0.87	86.5	77.11
60	633.77 ±0.26	636.48 ±0.11	3.26 ± 0.66	6.33 ± 0.68	81.06	71.44
90	634.74 ±0.20	640.33 ± 0.34	4.41 ± 0.11	8.25 ± 0.71	76.59	65.18

CONCLUSION

In this study, the ethosome formulations containing Tretinoin have been been prepared by varying the concentration of lipid and ethanol, optimized by Box Behnken design and then prepared ethosomes were incorporated into the HPMC based ethosomal patch. The most satisfactory formulation F8 with soya lecithin concentration of 2.5% and ethanol concentration of 30% showed better EE of 77.14% and had smaller vesicle size of 219.1, so it was selected as the optimized formulation. When incorporated into the transdermal patch it showed maximum release of drug in 12 h. Therefore, the inclusion of ethanol in ethosomes might play a vital role in enhancement of tretinoin permeation across skin. Thus, it can be concluded that ethosomes and ethosomal patch-based systems are a very promising solutions for treating skin disorders like psoriasis. Based on this work, further studies involving safety on skin, mechanism for inhibition action of tretinoin ethosomes on psoriatic skin and pharmacological effects etc. needed to be done to bring ethosomal transdermal patch into its clinical realization.

ACKNOWLEDGEMENTS

The authors are thankful to the leeford health care ltd, Mumbai India for provided APIand Department of pharmacy, Indore Institute of Pharmacy for providing necessary facilities for successful accomplishment of this research work.

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