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Original Article

A 3^2 FULL FACTORIAL DESIGN FOR TOPICAL CONTROLLED RELEASETAZAROTENE MICROSPONGE USING HPMC GEL

NISHANT OZA*, SATYAJIT SAHOO, SWATI SAGAR

C. U. Shah College of Pharmacy and Research, Wadhwan City 363030, Gujarat, India
Email: ozanishant@gmail.com

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ABSTRACT

Objective: The aim of present work was to the development of control release 0.1% tazarotene microsponge and incorporated into a HPMC K-100M gel.

Methods: Drug compatibility with polymer was evaluated by FT-IR spectrum. Tazarotene microsponge was prepared by quasi-emulsion solvent diffusion method. On the basis of preliminary results, 3^2 full factorial design was employed to study the effect of Eudragit RS-100 conc. (X_1) and PVA conc. (X_2) on as particle size (Y_1), % drug entrapment (Y_2) and time required to 80% drug release (Y_3). Multiple linear regression analysis, ANOVA and graphical representation of the influence factor by 3D plots were performed by using Sigma plot 11.0. In this study, the following constraints were arbitrarily used for the selection of an optimized batch: particle size<200 µm, drug entrapment>70 %, and time required to 80% drug release>360 min. The optimized formulation was subjected to SEM study. Tazarotene microsponge incorporates in 3% HPMC K-100M gel evaluated for viscosity, pH, drug content, spreadability, *In vitro* diffusion study, release kinetic study and photostability study.

Results: The FT-IR result showed that there was no chemical interaction and SEM photograph indicates that microsponges are spherical and pores. From the results of multiple regression analysis, it was found that all factors had a statistically significant influence on all dependent variables.

Conclusion: The optimized formulation of gel release kinetics having good linearity (R^2= 0.987) of zero-order kinetic and it was found to be stable in the stability evaluation.

Keywords: Tazarotene, Microsponge, Controlled release, Topical gel, 3^2full factorial designs

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INTRODUCTION

Conventional topical drug delivery systems require high concentrations of drug for effective therapy because of their low efficiency as delivery systems. Thus, the need exists for topical delivery systems to maximize the period of time active ingredient is present, either on skin surface or in epidermis. Microsponges are porous and polymeric microspheres that are mostly used for prolonged topical administration. Microsponges are designed to minimum dose, enhance stability, reduce side effects and modify drug release profiles [1, 2].

Tazarotene is a retinoid prodrug which is converted to its active form, the cognate carboxylic acid of tazarotene by rapid de-esterification in animals and man. Tazarotene, 0.1% was US Food and Drug Administration (USFDA) approved in 2012 for the treatment of acne vulgaris. Tazarotene systematic bioavailability is very low (approximately 1%) because of minimum systemic absorption and rapid metabolism. It causes severe side effect like skin irritation, sensitization, and phototoxicity. Tazarotene microsponge will minimize the side effect and allow control release delivery. The limited penetration of tazarotene from microsponge retards the rapid metabolism and its helps to prevent the drug build up in the body's lipophilic tissues [3-5].

So, the present work was carried out to develop tazarotene microsponge for topical drug delivery in the form of hydrophilic gel formulation which will prevent side effect of the drug and reduce its metabolites in skin.

MATERIALS AND METHODS

Materials and reagents

Tazarotene was received as a generous gift from Sun Pharma, Baroda, India. Eudragit RS-100 was obtained from Evonic Degusa, Mumbai, India. Eudragit RL-100, HPMC K-100M, Ethyl Cellulose and Polyvinyl alcohol were purchased from Loba Chemicals, Mumbai. Dichloromethane and methanol were obtained from Ren Chem labs, New Delhi, India. All other materials and chemicals used were of either pharmaceutical or analytical grade.

Drug excipients compatibility study

Drug-Excipients interaction plays a vital role in achieving the stability of the drug in dosage form. Fourier transform infrared spectroscopy (FT-IR) was used to study the physical and chemical interactions between drug and excipients. FT-IR spectra of Tazarotene, Eudragit RS-100 and Mixture (Tazarotene and Eudragit RS-100) were recorded using KBr mixing method on FT-IR instrument. (FTIR-1700, Shimadzu, Kyoto, Japan) [6, 7].

Preliminary screening of formulation parameters and development of tazarotene microsponge

Preliminary trial of tazarotene microsponge was done by selecting parameters such as polymer conc., Speed and PVA concentration on % drug entrapment, % yield, drug content and mean particle size. Tazarotene microsponge was prepared by a quasi-emulsion solvent diffusion method. In this, method internal phase was prepared by dissolving required amount of tazarotene and polymer (Eudragit RS-100, Eudragit RL-100, Ethyl cellulose) in 100 ml dichloromethane and 8 ml methanol at 60 °C. External phase was prepared by dissolving 0.5% and 1% polyvinyl alcohol (PVA) in distilled water as shown in table 1. Internal phase was gradually added into external phase at 500 rpm, 1000 rpm and 1500 rpm with help of Magnetic Stirrer (REMI Equipment, India). After emulsification, the mixture was continuously stirred for 3 h. Then, the mixture was filtered and separates the microsponges. This prepared microsponge was washed with distilled water and dried by hot air oven at 40 °C for 24 h. All the batches were stored properly and evaluation was carried out [8, 9].

Evaluation parameters of tazarotene microsponge

Particle size analysis: Particle size analysis of tazarotene microsponge was analyzed by optical microscopy method, using calibrated eye piece and stage micrometer slide.

% Yield: The % yield of the tazarotene loaded microsponge can be determined by the following equation:

$$\text{Production yield} = \frac{\text{Practical Mass of Microsponges}}{\text{Theoretical Mass (Polymer + Drug)}} \times 100$$

% Drug entrapment: The % Drug entrapment of the microsponges can be calculated according to the following equation:

$$\%\ Drug\ entrapment = \frac{\text{Actual Drug Content in microsponges}}{\text{Theoretical Drug Content}} \times 100$$

Morphology and Surface topography: Developed tazarotene microsponge coated with gold-palladium under an argon atmosphere at room temperature and surface morphology studied by scanning electron microscopy (SEM). Fractured microsponge SEM was also taken to illustrate its ultra-structure [10, 11].

Drug content: 100 mg of tazarotene microsponge dissolved in methanol and phosphate buffer solution pH 7.4 and allowed to stand for 24 h. The solution was filtered through whatman filter paper (No.41) and drug content was analyzed spectrophotometrically (Shimadzu 1700) at 350 nm, against standard methanolic and phosphate buffer solution pH 7.4.

In vitro dissolution study for the time required to 80% drug release: The dissolution profile of tazarotene microsponges studied by use of USP Type-I dissolution apparatus with a modified basket consisted of 5µm stainless steel mesh. A sample equivalent to 100 mg of tazarotene nitrate was taken in the basket. The 100 rpm and temperature of 37±0.5 w ere maintained throughout the experiment. The dissolution medium (900 ml) is phosphate buffer pH 7.4 while considering solubility of actives to ensure sink conditions. At fixed intervals, aliquots were withdrawn and replaced with fresh dissolution medium. Samples from the dissolution medium can be analysed by UV spectrophotometer (Shimadzu 1700) at 350 nm at specific time intervals (1, 2, 3, 4, 5, 6, 7, and 8 hour). The concentration of drug released at different time intervals was determined by measuring absorbance [12, 13].

Optimization of tazarotene microsponge by 3^2 full factorial design

A 3^2 full factorial design was employed in the present study. In this design 2 factors were evaluated, each at 3 levels and experimental trials was performed for all 9 possible combinations. Preliminary Screening Two variables, the concentration of Polymer and concentration of PVA were found critical. So, they were optimized using different trials, while other parameters were kept constant. On the basis of preliminary results, concentration of Polymer (X_1) and concentration of PVA (X_2) were chosen as independent variables in 3^2 full factorial design, while Particle Size (Y_1), % Drug entrapment (Y_2), Time required to 80% drug release (Y_3) was selected as dependent variables. Multiple linear regression analysis, ANOVA and graphical representation of the influence of factor by 3D plots were performed using of sigma plot software 11.0. The experimental runs and measured responses of 3^2 full factorial design batches of tazarotene microsponge depleted in table 2 [14, 15].

Development of 0.1% tazarotene microsponge topical gel

The topical gel was developed by dissolving 3% w/w HPMC K100 M in a sufficient amount of pH 7.4 citrate phosphate buffer. Gel was kept overnight to remove air bubble and add benzyl alcohol (1% v/v) as a preservative. Then, add a tazarotene microsponge (0.1 %w/w) to gel with geometric dilution [16, 17].

Evaluation of 0.1 % tazarotene microsponge topical gel

Viscosity: The viscosity of the gel was determined by Brookfield Viscometer (Model-LVDV-E). It was determined using with spindle no. 64 at 100 rpm at temperature 25°C. Rotate the spindle in the microsponge gel till get a constant dial reading.

pH: The pH of gel was determined by a digital pH meter. One gram of gel was dissolved in 100 ml distilled water and stored for 2 hr. Then, electrode was the dipped into gel for 30 min until constant reading obtained.

Drug content: 1 gm of microsponge gel was accurately weighed and dissolved in pH 7.4 citrate phosphate buffer using sonicator. A sample from this aliquot was analyzed by UV spectrophotometer (Shimadzu 1700) at 350 nm [18, 19].

Spreadability: Spreadability apparatus consists of a wooden block with a ground glass plate (20X20) fixed on to it. A pre-determined amount of gel was placed on ground glass plate and it was sandwich with another glass plate. Accurately 500 gm weight was placed on the top of the two glass plate to expel the air and provide a uniform film of the gel between the plates. Excess of gel was wiped off. The top plate was subjected to a put 10 gm weight and allows slipping the plate. The spreadability was calculated by using the following equation.

$$S = ML/T.$$

Where, S= spreadability M = weight on top plate (10 gms) L= length of the glass plate, T=time taken to separate the plat completely from each other.

In-vitro diffusion study: The release from the gels was examined through a cellophane membrane using a modified Franz diffusion cell. Prior to study, the cellophane membrane was soaked in diffusion medium for 4 hr and then placed on diffusion cell assembly. An aqueous solution of citrate phosphate buffer pH 7.4 was used as the receptor medium and 1 gm of the test gel was placed on the donor side. The receptor medium was kept at 37±0.5 °C. At predetermined time intervals, sample was taken from the receptor compartment and replaced with the fresh citrate phosphate buffer pH 7.4. Absorbance of the solutions was measured spectrophotometrically (Shimadzu 1700) at 350 nm [20, 21].

Kinetic Modelling of Dissolution Data: In order to understand the kinetics and release mechanisms of drug, the result of *in vitro* diffusion study of gel was fitted in with various kinetics models like zero order, first order, Higuchi model and Korsmeyer Peppas model. The linearity of the plots was obtained from the value of regression co-efficient (R). The model with the highest linearity (R^2 value) was chosen as the Best-fit kinetic model [22, 23].

Photostability study: Prepared 0.1% tazarotene microsponge containing gel was filled in clear polypropylene syringes, one for test and other for control. It was assayed by UV spectrophotometry immediately after preparation and analyzed the drug content. This study was carrying out for measurement of initial concentration. Then same tazarotene microsponge containing gel (0.1%) were exposed to UV light with an integrated intensity from 352 nm of 22 watt/m for 8 h. This spectral region was selected to provide a more energetic exposure than visible light and is consistent with the International Conference on Harmonization (ICH) guidelines for photostability testing [24].

RESULTS AND DISCUSSION

Drug excipients compatibility study

Fourier transform infrared spectroscopy (FT-IR) was used to study the physical and chemical interactions between drug and excipients. FT-IR spectra of tazarotene and mixture of tazarotene with eudragit RS-100 were recorded using KBr mixing method on FT-IR instrument. The drug exhibited peaks due to amide group, alcohol group and C-H, C=O, C-O, C-N and C=C stretching. It was observed that there were no or very minor changes in drug main peaks in the IR spectra of the mixture and pure drug. The FTIR study revealed no physical or chemical interaction of tazarotene with eudragit RS-100 [25].

Preliminary screening of formulation parameters

Preliminary trial of tazarotene microsponge result was shown in table 1. Good % of yield and mean particle size observed in batch T-1 which containing eudragit RS-100. Stickiness was detecting in batch T-2 which containing eudragit RL-100. Particle size found uneven when we use ethyl cellulose in batch T-3. HPMC K4M was separate out form the solvent in batch T-4. So, further investigation was using with eudragit RS-100. Uneven particle size was observed in batch T-5 and T-7. So, 1000 rpm was selected for further Preliminary trial batch. Batch T-8 was given a higher % of yield compare to batch T-9. The results of preliminary study revealed that eudragit RS100 and PVA both required achieving the desired release profile. Hence, further trials were carried out using various combinations eudragit RS100 and PVA in order to understand their effect and to optimize concentration of both for desired release profile.

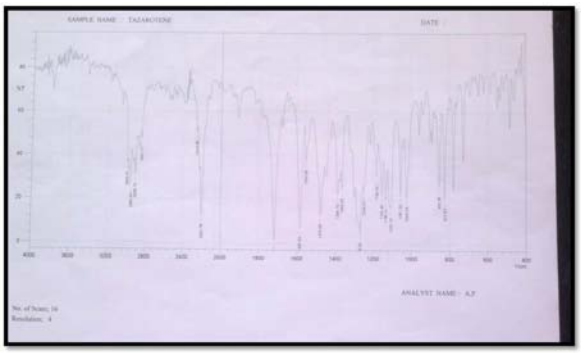

Fig. 1: IR spectrum of tazarotene

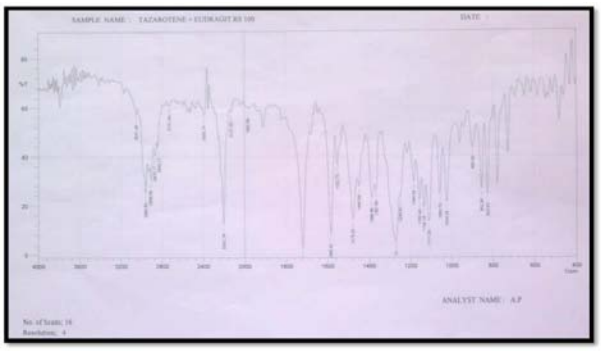

Fig. 2: IR spectrum of tazarotene and eudragit RS-100

3^2 Full factorial design model evaluation

A statistical model incorporating interactive and polynomial terms was used to evaluate the responses:

$$Y=b_0+b_1X_1+b_2X_2+b_{11}X_1^2+b_{22}X_2^2+b_{12}X_1X_2$$

where, Y is the dependent variable, b_o is the arithmetic mean response of the 9 runs and any bi is the estimated coefficients for the related factor X_i. The main effects (X_1 and X_2) represent the average result of changing one factor at a time from its low to high value. The polynomial terms (X_1^2 and X_2^2) are included to investigate nonlinearity. The interaction term "X_1X_2" shows how the response changes when the two factors change simultaneously. Evaluation data for tazarotene microsponge were presented in table 2. The fitted equations relating the responses that is, particle size (Y_1), % drug entrapment (Y_2), the time required to 80% drug release (T_{80}) (Y3) was to the transformed factor are shown in table 3. The polynomial equations can be used to draw conclusions after considering the magnitude of coefficient and the mathematical sign it carries (i.e. positive or negative). The results of ANOVA suggested that calculated F values for particle size, % drug entrapment, time required to 80% drug release (T_{80}) are 99.077, 9.666 and 14.673 respectively (table 4). Tabulated F value was found to be 9.013 at α = 0.05. Calculated F values are greater than tabulated for all dependent variables, therefore, factors selected have shown significant effects. From the results of multiple regression analysis, it was found that all factors had statistically significant influence on all dependent variables as $p<0.05$ [26, 27].

Table 1: Evaluation of preliminary screening batch of tazarotene microsponge

Batch	Polymer	Speed (RPM)	PVA Conc. (%)	% Yield	% Drug entrapment	Particle size (µm)	Time required to 80% drug release
T-1	0.1 % Eudragit RS100	1000	0.5	68.50±1.75	67.64±1.12	178±4	360±4
T-2	0.1 % Eudragit RL100	1000	0.5	71.75±2.45	63.45±2.78	456±5	350±3
T-3	0.1 % Ethyl cellulose	1000	0.5	62.50±0.89	55.90±0.36	576±1	310±5
T-4	0.1 % HPMC K4M	1000	0.5	-	-	-	-
T-5	0.1 % Eudragit RS100	500	0.5	71.25±2.56	66.95±0.78	778±6	340±5
T-6	0.1 % Eudragit RS100	1000	0.5	76.00±1.13	72.29±0.34	207±3	390±5
T-7	0.1 % Eudragit RS100	1500	0.5	80.90±1.67	72.04±1.78	158±6	440±3
T-8	0.1 % Eudragit RS100	1000	0.5	74.00±0.56	67.25±0.67	156±4	400±2
T-9	0.1 % Eudragit RS100	1000	1.0	43.15±2.23	42.05±1.25	716±6	320±4

n=6

Table 2: Runs and measured responses of 3^2factorial design for tazarotene microsponge

Batch code	% of Eudragit RS-100(X_1)	Concentration of PVA (X_2)	Particle size (µm) (Y_1)	% Drug entrapment (Y_2)	Time required to 80% drug release (Y3)
F1	-1	-1	158±2	73.20±2.34	390±4
F2	-1	0	180±5	74.95±0.82	415±1
F3	-1	1	196±2	66.70±1.11	430±5
F4	0	-1	193±5	77.80±2.31	380±1
F5	0	0	204±4	89.19±1.09	415±3
F6	0	1	227±2	75.46±0.86	420±6
F7	1	-1	213±4	72.09±1.34	435±2
F8	1	0	226±3	84.67±2.51	440±5
F9	1	1	238±2	78.93±0.88	445±3
Factors and the levels in the design					
Independent variables			Low (-1)	Medium (0)	High (1)
% of Eudragit RS100(X_1)			0.05	0.1	0.15
% of PVA (X_2)			0.25	0.50	0.75

Full and reduced model for particle size

*Particle size = 207.444+(23.833 * X_1)+(16.167 * X_2)-(6.167 * X_1^2)+(0.833 * X_1^2)-(3.250 * X_1X_2)*

From the 3D plot (fig. 3) and the regression coefficient values of factors, it was concluded that when % of eudragit RS-100and % of PVA was increased that time particle size also increase and it's lead to more drug entrapment. The results also indicated that the eudragit RS-100was given a more significant on particle size. Both the eudragit RS-100and % of PVA showed significant effect in the model. Interaction and nonlinearity were not observed. For particle size, the significance levels of the coefficients b_1^2, b_2^2 and b_{12} were

found to be P= 0.073, 0.738 and 0.136respectively, so they were omitted from the full model to generate a reduced model. The coefficients b_1 and b_2 were found to be significant at P<0.05; hence, it was retained in the reduced model. SEM of tazarotene microsponge was shown in fig. 6. The reduced model for Particle Size,

$$=207.444+(23.833 * X_1)+(16.167 * X_2)$$

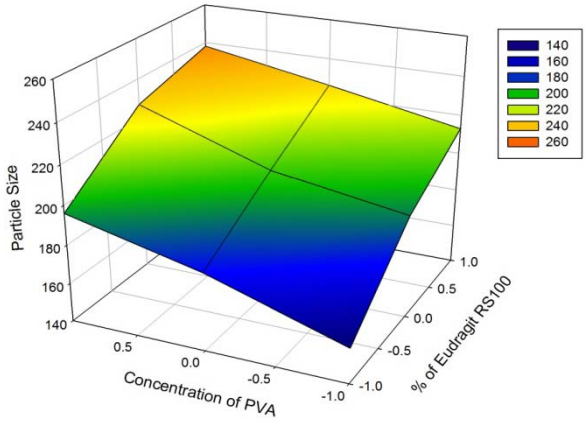

Fig. 3: 3D plot showing the effect of % of eudragit RS-100(X_1) and PVA (X_2) on particle size (Y_1)

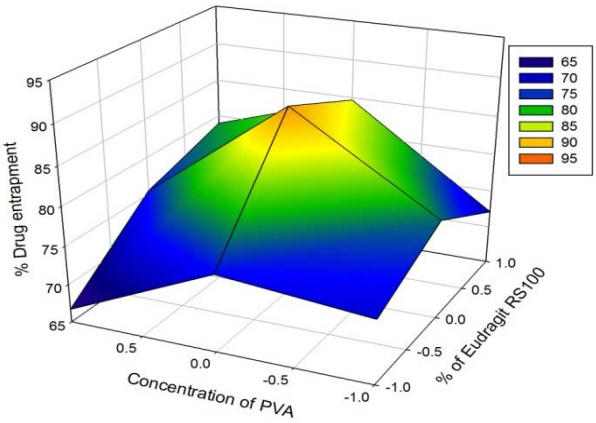

Fig. 4: 3D plot showing the effect of eudragit RS-100(X_1) and PVA (X_2) on % of drug entrapment (Y_2)

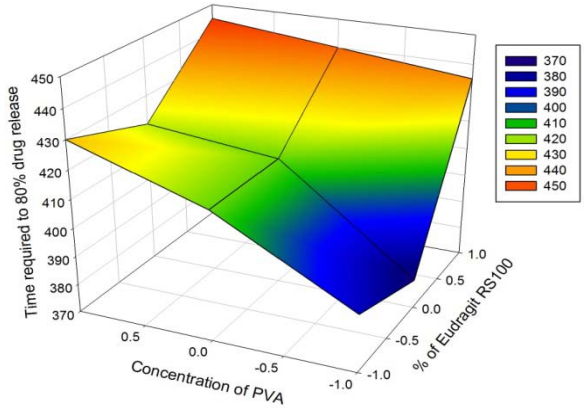

Fig. 5: 3D plot showing the effect of eudragit RS-100(X_1) and PVA (X_2) on time required to 80% drug release

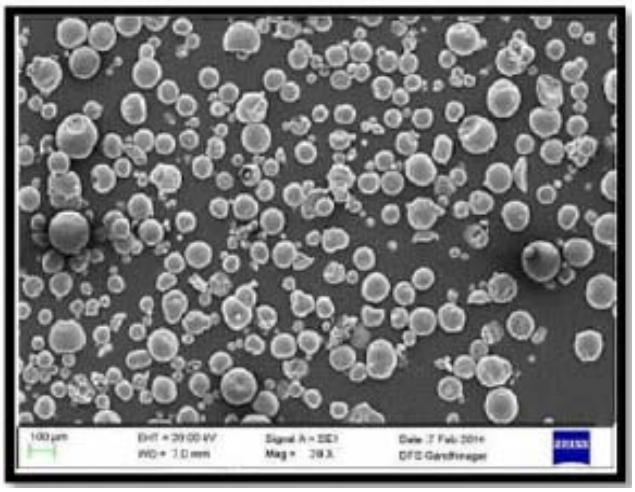

Fig. 6: SEM of tazarotene microsponge

Full and reduced model for % of drug entrapment

% of drug entrapment = 86.754+(3.473 X_1)-(0.333 X_2)-(5.727 X_1^2)-(8.907 X_2^2)+(3.335 X_1 X_2)

From the 3D plot (fig. 4) and the regression coefficient values of factors, it was concluded that corresponding increase in the % drug entrapment of microsponge was observed with increase in con. of eudragit RS-100. From regression, it is observed that X_1 was significant model terms which affect the % of drug entrapment. Interaction and non-linearity was not observed. For % of drug entrapment, the significance levels of the co-efficients b_2, b_{11} and b_{12} were found to be P= 0.779, 0.056 and 0.087, respectively. So, they were omitted from the full model to generate a reduced model. The co-efficients b_1 and b_{22} were found to be significant at P<0.05; hence they were retained in the reduced model. The reduced model for % drug entrapment,

$$= 86.754+(3.473 X_1)-(8.907 X_2^2)$$

Table 3: Summary of regression output of factors for measured responses

Responses	Model	Coefficient of regression parameters						
		b_0	b_1	b_2	b_{11}	b_{22}	b_{12}	R^2
Particle Size	Full	207.444	23.833	16.167	6.167*	0.833*	3.250*	0.994
	Reduced	207.444	23.833	16.167	-	-	-	
% Drug entrapment	Full	86.754	3.473	0.333*	5.727*	8.907	3.335*	0.942
	Reduced	86.754	3.473	-	-	8.907	-	
Time required to 80% drug release	Full	409.444	14.167	15.000	20.833	6.667*	7.500*	0.961
	Reduced	409.444	14.167	15.000	20.833	-	-	

*indicated the coefficient with p>0.05

Table 4: Results of the ANOVA for dependent variables

Particle size					
Source of variation	DF	SS	MS	F	P
Regression	5	5096.028	1019.206	99.077	0.002
Residual	3	30.861	10.287		
Total	8	5126.889	640.861		
% Drug entrapment					
Source of variation	DF	SS	MS	F	P
Regression	5	341.787	68.357	9.666	0.045
Residual	3	21.215	7.072		
Total	8	363.002	45.375		
Time required to 80% drug release					
Source of variation	DF	SS	MS	F	P
Regression	5	3736.111	747.222	14.673	0.026
Residual	3	152.778	50.926		
Total	8	3888.889	486.111		

Full and reduced model for time required to 80% drug release

*Time required to 80% drug release = 409.444+(14.167 X_1)+(15.000 X_2)+(20.833 X_1^2)-(6.667 X_2^2)-(7.500 * X_1 X_2)*

From the 3D plot (fig. 5) and the regression coefficient values of factors, it was concluded that corresponding increase in the time required to 80% drug release of microsponge was observed with increase in concentration of polymer and PVA concentration. From regression it is observed that X1 and X2 were equivalent significant model terms which affect the on drug release. Interaction and nonlinearity were not observed. For time required to 80% drug release, the significance levels of the coefficients b_{22} and b_{12} were found to be P= 0.278 and 0.126 respectively. So, it was omitted from the full model to generate a reduced model. The coefficients b_1, b_2 and b_{11} were found to be significant at P<0.05; hence they were retained in the reduced model. The reduced model for time required to 80% drug release [28, 29]

= 409.444+(14.167 X_1)+(15.000 X_2)+(20.833 X_1^2)

Formulation of checkpoint batch

To validate the evolved mathematical models, a checkpoint batches CP1 was prepared and evaluated. The observed and predicted values for batch CP1 were shown in table 5. Good correlation was found between observed and predicted values shown in table 6. Hence, it was concluded that the evolved models may be used for theoretical prediction of responses within the factor space.

Table 5: Formulation of checkpoint batches

Batch code	**Variable level**			
	Coded value		**Actual value**	
	X_1	**X_2**	**X_1(mg)**	**X_2(ml)**
CP1	-0.5	-0.5	0.075	0.375

Table 6: Evaluation of checkpoint batches and comparison with the predicted value

Parameter	**Actual value**	**Predicted value**
Particle Size (µm) (Y_1)	78±2	80.812
% Drug entrapment (Y_2)	84.24±1.22	87.244
Time required to 80% drug release (Y_3)	403±4	409.943

(n=6)

Selection of optimized batch in the factorial design study

In the present study, the following constraints were arbitrarily used for the selection of an optimized batch: particle size<200 µm, drug entrapment>70 %, and time required to 80% drug release>360 min. Batches F_1, F_2, F_3, and F_4 met the selection criteria. Batch F_1 showed lowest particle size (158 µm) and 80 % drug release in 390 min. Hence, Batch F_1 was selected as an optimized batch. The optimized formulation was added into the 3% HPMC K-100M gel. [29, 30]

Evaluation of 0.1% tazarotene microsponge topical gels

The optimized tazarotene microsponge formulation batch F-1 was subjected to further characterization studies and incorporated into gel to get homogenous based delivery systems. The gel was prepared by using 3% HPMC K-100M. The prepared gel was evaluated for physicochemical characteristics and it showed desired drug content, *in vitro* diffusion, spreadability, pH and viscosity as per standard criteria as shown in table 7. The gel color was white and that color was stable along the period of evaluation. The drug content was found 87.27±2.32%. It showed a good content uniformity for the prepared microsponge. The viscosity of the gel was found 2933.33±12 cp. The pH of tazarotene microsponge gel was found 7.06±0.21 and it was indicated topical gel was safe, stable and non-irritate. The values of spreadability indicated that the gel was easily spreadable by a small amount of shear. Spreadability of tazarotenemicrosponge gel was found to be 16.98±0.51 gm. cm/sec indicating that spreadability of drug-loaded microsponge gel was good. The *in-vitro* diffusion studies were carried out for tazarotenemicrosponge gel using citrate phosphate buffer pH 7.4.

In vitro diffusion of formulation is shown in fig. 7. It was observed that the gel formulation showed a drug diffused upto 10 hr. The results indicated that the cumulative amount of drug permeated per unit skin surface area from the microsponge loaded gel formulation was 93.40% for 10 hr. To determine the kinetics of release, drug diffusion data were treated with different kinetic equations. Obtained drug diffusion data was fitted to Zero order, First order, Higuchi model and Korsmeyer-peppas model. The correlation coefficient (R) was used to study the release mechanism of tazarotenemicrosponge gel is reported in table 7. The model that gave the high 'R' value was considered as the best fit of release data. From the result, the best fit model for tazarotenemicrosponge gel formulation is Zero order (R^2= 0.987). 0.1% Tazarotene Microsponge Topical Gel was kept for photostability study to UV light with an integrated intensity from 352 nm of 22 watt/m for 8 h. Initial drug content was found 87.27±2.32 % and after 8 hdrug content was 80.63±1.42 %. There is no significant difference in drug content after photo stability study result shown in table 8.

Table 7: Evaluation of 0.1% tazarotene microsponge topical gel

Parameter	Topical gel
Viscosity	2933.33±12.56 cp
pH	7.06±0.21
Spreadability	16.98±0.51 gm. cm/sec
Drug content	87.27±2.32 %
Zero order R^2	0.987
First order R^2	0.939
Higuchi model R^2	0.985
Korsmeyer-peppas model R^2	0.965

(n=6)

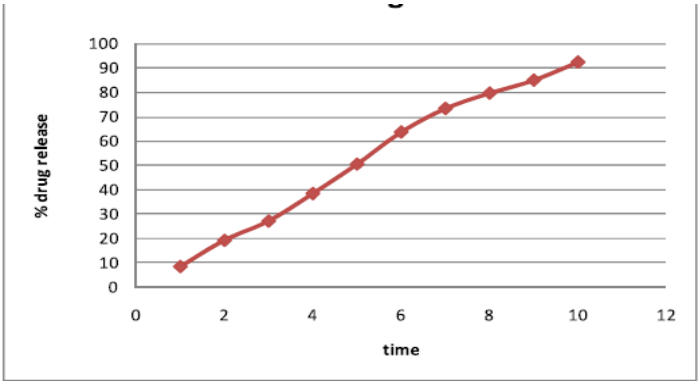

Fig. 7: *In vitro* diffusion study tazarotene microsponge topical gel

Table 8: Photostability study of 0.1% tazarotene microsponge topical gel

Description	Initial drug content	Drug content after 8 h
Test sample	87.27±2.32 %	80.63±1.42 %
Control sample	87.27±2.32 %	87.26±0.89 %

CONCLUSION

The present study concluded successful preparation and optimization of 0.1 % tazarotene loaded microsponge gel with the enhanced the availability of drug at the site of action. *In vitro* andKinetic Modelling of Dissolution Data evaluation of microsponge gel revealed remarkable and enhanced topical retention of drug for prolonged period of time. A controlled release of tazarotene onto the skin over a prolonged period of time was beneficial for psoriasis treatment. This study provides future insights for developing controlled release microsponge gels for topical applications containing retinoid.

AUTHORS CONTRIBUTIONS

All the author have contributed equally

CONFLICT OF INTERESTS

Declared none

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