RESEARCH PAPER

Formulation, Optimization, and Characterization of Crisaborole-Loaded Proniosomes Using a Factorial Design Approach

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ABSTRACT

Crisaborole is a topical anti-inflammatory agent used to treat atopic dermatitis; however, its clinical efficacy is limited by inadequate skin permeation and short retention time. This study aimed to formulate and optimize crisaborole-loaded proniosomes using a design of experiments (DoE) approach to enhance drug encapsulation and achieve controlled drug release. Proniosomes were prepared using non-ionic surfactants and cholesterol, and a 3^2 factorial design was employed to optimize the formulation variables. Encapsulation efficiency and in vitro drug release were selected as critical quality attributes. The optimized formulation demonstrated high encapsulation efficiency (≈90.63%) and sustained drug release (≈85.51% over 7 h). Statistical analysis confirmed the significant influence of the formulation variables, and response surface methodology validated the robustness of the optimized system. These findings suggest that DoE-optimized crisaborole-loaded proniosomes are promising vesicular carriers for enhanced topical drug delivery.

Keywords: Crisaborole, Proniosomes, Design of Experiment, Topical delivery, Vesicular drug delivery

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INTRODUCTION

Atopic dermatitis is a chronic inflammatory skin disorder characterized by itching, erythema, and recurrent skin lesions that require prolonged topical therapy for effective disease management [1,2]. Topical drug delivery is generally preferred for dermatological conditions because it enables localized drug action while minimizing systemic side effects. However, conventional topical formulations often exhibit limitations, such as poor skin permeation, rapid drug loss from the application site, and inadequate drug retention within the deeper layers of the skin, ultimately leading to suboptimal therapeutic outcomes [1,3].

Crisaborole, a non-steroidal phosphodiesterase-4 (PDE-4) inhibitor, is approved for the treatment of mild-to-moderate atopic dermatitis. By inhibiting PDE-4 activity, crisaborole reduces the production of proinflammatory cytokines and helps control inflammatory responses associated with dermatological disorders [3–5]. Despite its therapeutic benefits, the topical efficacy of crisaborole is limited by inadequate permeation through the stratum corneum and reduced residence time at the target site. To overcome these limitations, several advanced drug delivery approaches, including nanoemulgels, microsponge systems, vesicular carriers, and in-situ gels, have been explored to enhance drug delivery and improve therapeutic performance [5,18–20].

Recent studies have demonstrated that nano-based and vesicular drug delivery systems can significantly enhance drug stability, skin permeation, and controlled release characteristics. For instance, nanoemulgel-based delivery platforms have been successfully investigated to improve topical drug delivery and therapeutic compliance in various dermatological conditions [20]. Similarly, microsponge and gastro-retentive systems have shown promising results in controlling drug release and improving formulation stability [18,19]. These advancements highlight the importance of innovative drug delivery systems in improving therapeutic outcomes.

Among vesicular drug delivery systems, proniosomes have gained significant attention owing to their improved stability, enhanced drug encapsulation efficiency, and controlled drug release characteristics. Proniosomes are dry, free-flowing, provesicular formulations composed of non-ionic surfactants that form niosomal vesicles upon hydration. Compared with conventional vesicular systems, proniosomes offer advantages, such as better

storage stability, ease of transportation, and improved drug loading capacity, making them suitable carriers for topical and transdermal drug delivery [6–8,14–21].

The performance of proniosomal systems is significantly influenced by formulation variables, such as surfactant type, surfactant concentration, and membrane stabilizers, such as cholesterol. Therefore, the systematic optimization of these parameters is essential to obtain a robust formulation with desirable physicochemical characteristics. Traditional trial-and-error approaches are often time-consuming and inefficient. In contrast, the quality by design (QbD) approach using design of experiment (DoE) enables the systematic investigation of formulation variables and their interactions while reducing the number of experimental trials [12,13,24–26]. Additionally, recent QbD-based analytical and formulation studies have demonstrated the effectiveness of systematic experimental design approaches in optimizing pharmaceutical formulations and analytical methods [17].

Therefore, the present study aimed to formulate, optimize, and characterize crisaborole-loaded proniosomes using a 3^2 factorial design of experiments. Span 60 and cholesterol concentrations were selected as independent formulation variables, whereas encapsulation efficiency and in vitro drug release were considered critical quality attributes. The developed system was expected to enhance drug encapsulation, improve stability, and provide controlled drug release for effective topical delivery.

MATERIALS AND METHODS

Crisaborole was obtained as a gift sample from a reputed pharmaceutical source. Span 20, Span 40, Span 60, Span 80, cholesterol, and lecithin were used as excipients. Analytical-grade ethanol and methanol were used as solvents. All other chemicals and reagents used were of analytical grade and were used without further purification.

Preformulation Studies of Crisaborole

Organoleptic Properties

The drug samples were evaluated for color, odor, appearance, and physical state through visual inspection.

Melting Point Determination

The melting point of crisaborole was determined using the capillary method. A small quantity of the drug was filled in a capillary tube and heated gradually; the temperature at which melting occurred was recorded.

Solubility Study

The solubility of crisaborole was determined in distilled water, phosphate buffer (pH 7.4), 0.1 N HCl, acetone, and methanol. Excess drug was added to each solvent, shaken for 24 h, filtered, and analyzed.

Determination of Partition Coefficient

The partition coefficient (log P) of crisaboroles was determined using an n-octanol/phosphate buffer (pH 7.4) system to assess lipophilicity.

Identification and Determination of λmax

A stock solution of crisaboroles was prepared in methanol and diluted. The solution was scanned between 200 and 400 nm using a UV–visible spectrophotometer to determine the wavelength of maximum absorbance (λmax).

Preparation of Calibration Curve

Standard solutions of crisaborole (5–25 µg/mL) were prepared in methanol. Absorbance was measured at the predetermined λmax, and a calibration curve was plotted for the relationship between concentration and absorbance.

FT-IR Spectroscopic Analysis

FT-IR analysis of crisaborole was performed using the potassium bromide pellet method. The spectra were recorded in the range of 4000–400 cm − 1 and compared with reference spectra to confirm the drug identity.

Preparation of Crisaborole-Loaded Proniosomes

Proniosomes were prepared using the coacervation phase separation method. Accurately weighed quantities of surfactant (Span), cholesterol, and crisaborole were dissolved in ethanol by gentle heating. The solution was added to mannitol powder and subjected to rotary evaporation to remove the solvent, resulting in a dry proniosomal powder. The prepared proniosomes were stored in airtight containers for further evaluation.

Preliminary Trial Batches

Multiple preliminary batches were prepared using different grades of Span to identify a suitable surfactant composition based on vesicle size, encapsulation efficiency, and drug release.

Design of Experiment (DoE) for Optimization

A 3^2 factorial design was employed for optimization using Design-Expert® software. The concentrations of Span 60 (X_1) and cholesterol (X_2) were selected as independent variables at three levels (low, medium, and high). Encapsulation efficiency (Y_1) and percentage drug release (Y_2) were selected as the dependent variables.

Characterization of Proniosomes

Vesicle Size Analysis

The proniosomal dispersion was then hydrated and diluted appropriately. The vesicle size was measured using a particle size analyzer.

Encapsulation Efficiency

The entrapment efficiency was determined using dialysis, followed by centrifugation. The amount of entrapped drug was quantified using UV spectrophotometry and calculated using the following formula:

$$\%EE = \frac{\text{Amount of drug entrapped}}{\text{Total amount of drug}} \times 100$$

In-Vitro Drug Release Study

In vitro drug release was carried out using a Franz diffusion cell with phosphate buffer (pH 7.4) as the receptor medium. Samples were withdrawn at predetermined time intervals for up to 7 h and analyzed spectrophotometrically.

Surface Morphology

The surface morphology of the optimized proniosomes was examined by scanning electron microscopy (SEM).

Statistical Analysis

The experimental data were analyzed using analysis of variance (ANOVA) to evaluate the significance of the formulation variables. Response surface and contour plots were generated to study the interaction effects and identify the optimized formulation.

RESULTS

Preformulation Studies of Crisaborole

Crisaborole was obtained as a white, crystalline powder with a characteristic odor. The observed melting point (130–132 °C) was consistent with the reported values, indicating drug purity and stability. Solubility studies showed that crisaborole was slightly soluble in water but freely soluble in organic solvents, such as methanol and acetone, confirming its lipophilic nature. The partition coefficient (log P ≈ 3.34) suggests adequate lipophilicity for vesicular and topical drug delivery.

Determination of λmax and Calibration Curve

UV–visible spectroscopic analysis of crisaborole showed a maximum absorbance (λmax) at 252 nm (Figure 1), which is in agreement with the official and reported data. A calibration curve was constructed for the analytes over the concentration range of 5–25 µg/mL. The calibration plot exhibited good linearity with a correlation coefficient ($R^2 > 0.99$), indicating the suitability and reliability of the analytical method for quantitative estimation of Crisaborole during formulation development and evaluation.figure 2

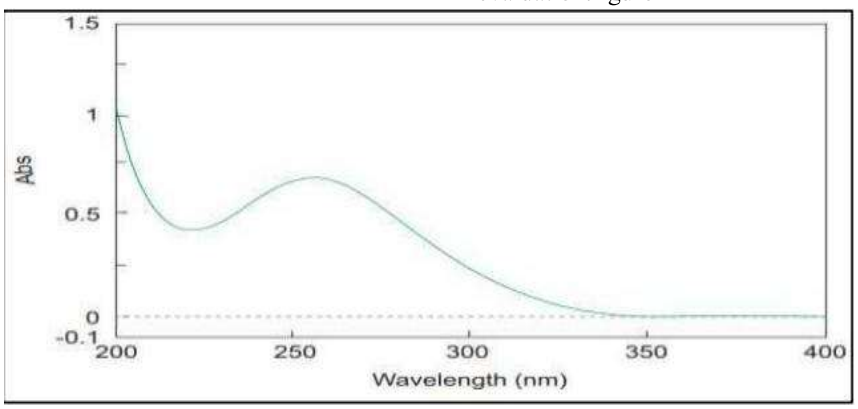

Figure 1 Wavelength max (λmax) of Crisaborole

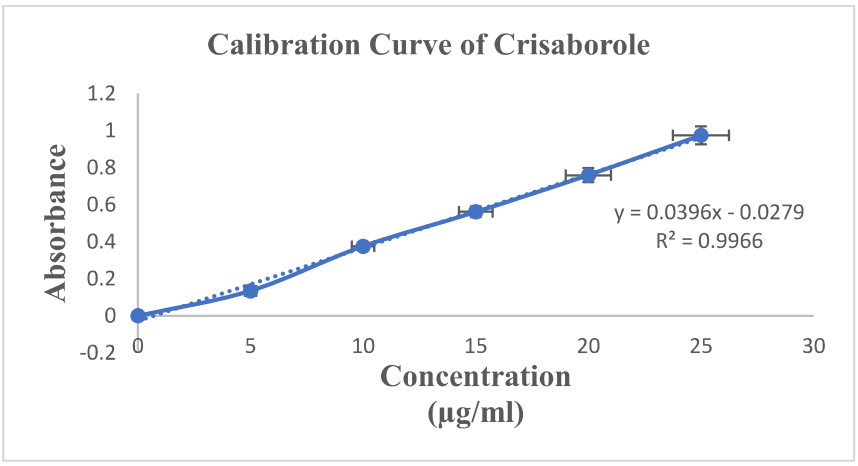

Figure 2 Calibration Curve of Crisaborole

FT-IR Spectroscopic Analysis

FT-IR spectroscopy was conducted to assess the compatibility of crisaborole with formulation excipients. The spectrum of crisaborole displayed characteristic absorption peaks corresponding to the O–H stretching, C–H stretching, and C=O functional groups. These peaks were preserved in the optimized proniosomal formulation without notable shifts or losses, indicating no chemical interaction between the drug and excipients. This confirms the compatibility of crisaborole with proniosomal components and supports its suitability for vesicular formulations.

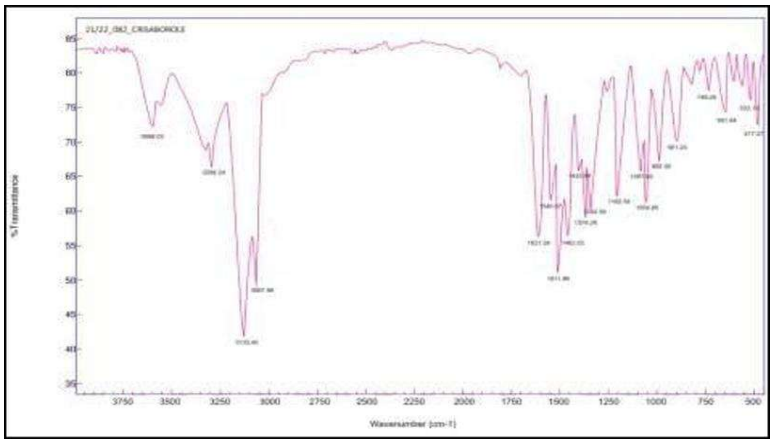

Figure 3 FTIR of Crisaborole

Particle Size Analysis

Particle size analysis of the optimized crisaborole-loaded proniosomes (Figure 4) demonstrated a uniform vesicle size distribution within the micrometer range. The consistently small vesicle size is advantageous for topical delivery, enhancing skin contact, and potentially improving drug permeation. Additionally, uniformity in particle size reflects good formulation stability and effective vesicle formation during proniosomal preparation.

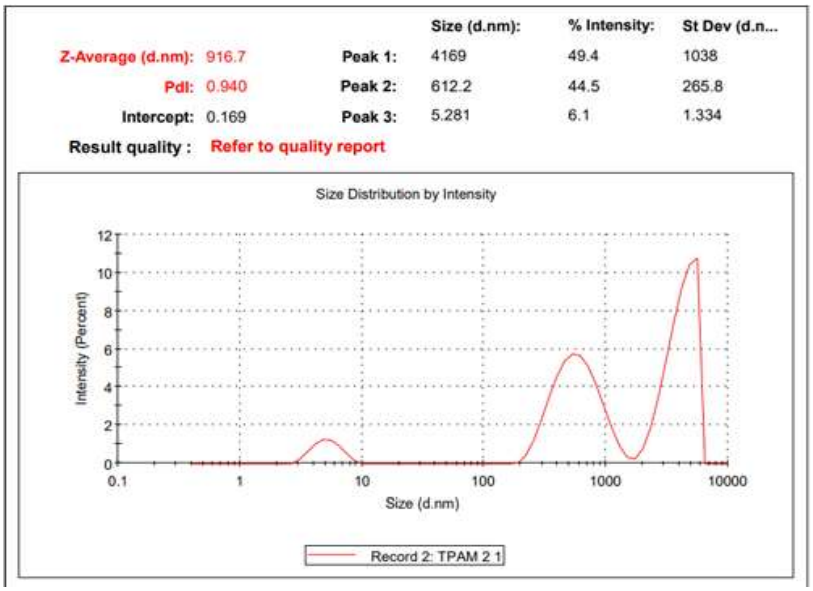

Figure 4 Particle Size Study

Preliminary Trial Batches of Proniosomes

Preliminary trial batches prepared using different grades of Span demonstrated that the surfactant type significantly influenced vesicle characteristics. Formulations containing Span 60 exhibited smaller vesicle size, higher encapsulation efficiency, and more controlled drug release than those containing other Spans. This behavior can be attributed to the higher phase transition temperature and longer alkyl chain length of Span 60, resulting in improved bilayer rigidity and drug retention in the vesicles. Based on these findings, Span 60 was selected for further optimization. Table 1

Table 1. Preliminary Trial Batch of Crisaborole loaded Proniosome

	CBP 1	CBP 2	CBP 3	CBP 4	CBP 5	CBP 6	CBP 7	CBP 8	CBP 9	CBP 10
Crisaborole(mg)	40	40	40	40	40	40	40	40	40	40
Span20(mg)	1800				900	900	900			
Span40(mg)		1800			900			900	900	
Span60(mg)			1800			900		900		900
Span80(mg)				1800			900		900	900
Cholestrol(mg)	200	200	200	200	200	200	200	200	200	200
Lecithin(mg)	1800	1800	1800	1800	1800	1800	1800	1800	1800	1800
Ethanol(ml)	1	1	1	1	1	1	1	1	1	1
Phosphate buffer pH 7.4 (ml)	1	1	1	1	1	1	1	1	1	1

Characterization of Preliminary Trial Batches

Preliminary trial batches of crisaborole-loaded proniosomes were characterized to evaluate the influence of different non-ionic surfactants on vesicle size, encapsulation efficiency, and in vitro drug release (Table 2). The results indicated that the formulations prepared using Span 60 exhibited smaller vesicle size, higher encapsulation efficiency, and controlled drug release compared to those prepared using other Span grades. The enhanced performance of Span 60 may be attributed to its higher phase transition temperature and longer alkyl chain, which impart improved bilayer rigidity and drug retention properties. Therefore, Span 60 was selected as the surfactant for further optimization using a design of experiments approach. Figure 5.

Table 2. Characterization of Preliminary Trial Batch of Crisaborole-loaded Proniosome

Batch	Mean Vesicle size (µm)	Encapsulation efficiency	% Drug release (7 Hrs)
CBP 1	6.56 ±0.20	82.26 ±2.67	67.38 ±1.45
CBP 2	5.91 ±0.42	86±1.26	72.35±2.67
CBP 3	3.31 ±0.15	87.36±1.34	75.68±2.34
CBP 4	4.76 ±0.24	81.39±1.26	77.68±1.26
CBP 5	4.21 ±0.15	86.21±1.58	75.68±1.26
CBP 6	3.61 ±0.67	89.26±1.26	81.68±2.34
CBP 7	3.81 ±0.24	82.34±1.78	70.57±1.36
CBP 8	4.36 ±0.57	91.31±1.57	82.35±1.16
CBP 9	5.21 ±0.49	84.61±1.45	74.67±1.67
CBP 10	6.53 ±0.67	85.28±1.67	72.35±1.26

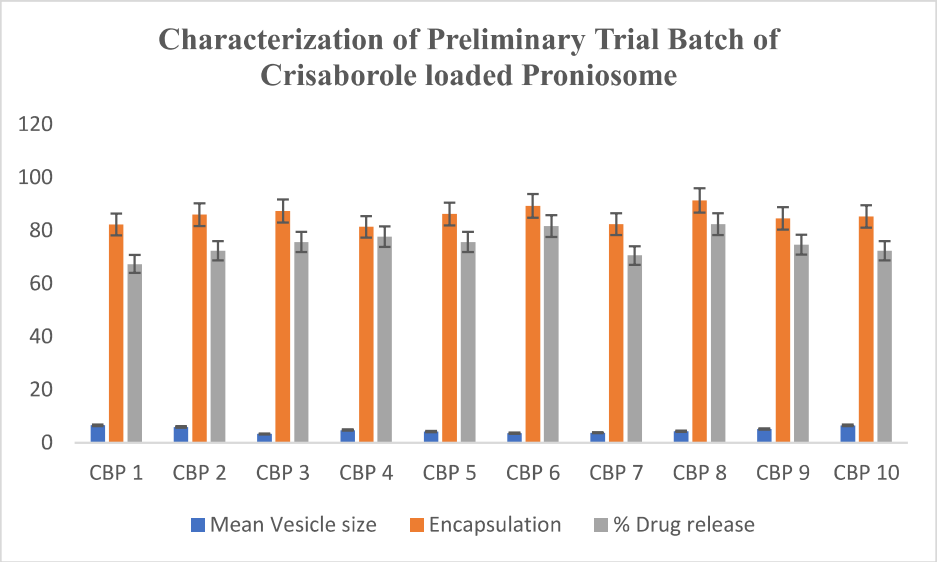

Figure 5 Preliminary Trial Batch of Crisaborole-loaded Proniosome

Formulation and Development of Crisaborole loaded Proniosome by Design of Experiment (DoE) Approach

3^2 Factorial Design Approach

A 3^2 factorial design was employed to optimize the CRZ-loaded proniosomal formulation. Two formulation variables were selected as independent variables: Span 60 concentration (X_1) and cholesterol concentration (X_2), each studied at three levels (low, medium, and high). Encapsulation efficiency (Y_1) and percentage of in vitro drug release (Y_2) were selected as the dependent response variables. This design enabled the evaluation of the individual and interactive effects of the independent variables on the critical quality attributes of the formulation. Table 3

Independent Variables

- **X_1:** Span 60 concentration
- **X_2:** Cholesterol concentration

Dependent Variables

- **Y_1:** Encapsulation efficiency (%)
- **Y_2:** Percentage drug release (%)

Table 3. 3^2 Factorial Design Approach

Independent variables of formulations			
Independent variables (X1)	**Low (-1)**	**Medium (0)**	**High (+1)**
SPAN 60 (mg)	700	1400	2100
Cholesterol (mg)	185	195	205
Dependent variables			
Y1= Encapsulation Efficiency			
Y2= % Drug release			

Compositions of Factorial Batches in Coded and Decoded Form

Based on a 3^2 factorial design, nine experimental batches were prepared to study the effects of formulation variables on proniosomal characteristics. The coded levels (−1, 0, +1) corresponded to low, medium, and high concentrations of Span 60 (X_3) and cholesterol (X_2), respectively. The actual and coded compositions of the factorial batches are listed in Table 4.

Table 4. Compositions of Factorial Batches in Coded & Decoded Form

CBPN 3^2 = batches				
Batches	**Variable level in coded form**		**Variable level in coded form**	
	SPAN 60 (mg) (X1)	**Cholesterol (mg) (X2)**	**SPAN 60 (mg) (X1)**	**Cholesterol (mg) (X2)**
CBPN 1	0	0	1400	195
CBPN 2	-1	+1	700	205
CBPN 3	+1	-1	2100	185
CBPN 4	+1	0	2100	195
CBPN 5	-1	0	700	195
CBPN 6	0	+1	1400	205
CBPN 7	-1	-1	700	185
CBPN 8	+1	+1	2100	205
CBPN 9	0	-1	1400	185

Characterization of Batches CBPN 1–CBPN 9

The factorial batches (CBPN 1–CBPN 9) were evaluated for encapsulation efficiency and percentage in vitro drug release to study the effect of Span 60 and cholesterol concentrations (Table 5). The results demonstrated noticeable variations among the batches, indicating the significant influence of formulation variables on proniosomal performance. Batches containing intermediate levels of Span 60 and cholesterol exhibited higher encapsulation efficiency and controlled drug release, whereas extreme concentrations resulted in reduced efficacy of the liposomes. These findings support the suitability of the factorial design for the systematic optimization of crisaborole-loaded proniosomes. Figure 6.

Table 5. Characterization of Batches CBPN 1-CBPN 9

Batch	**Encapsulation Efficiency**	**% Drug release**
CBPN 1	94.26	88.26
CBPN 2	82.26	79.24
CBPN 3	81.67	80.26
CBPN 4	83.24	80.26
CBPN 5	80.59	78.26
CBPN 6	90.35	85.64
CBPN 7	78.54	76.59
CBPN 8	77.98	75.68
CBPN 9	88.26	84.35

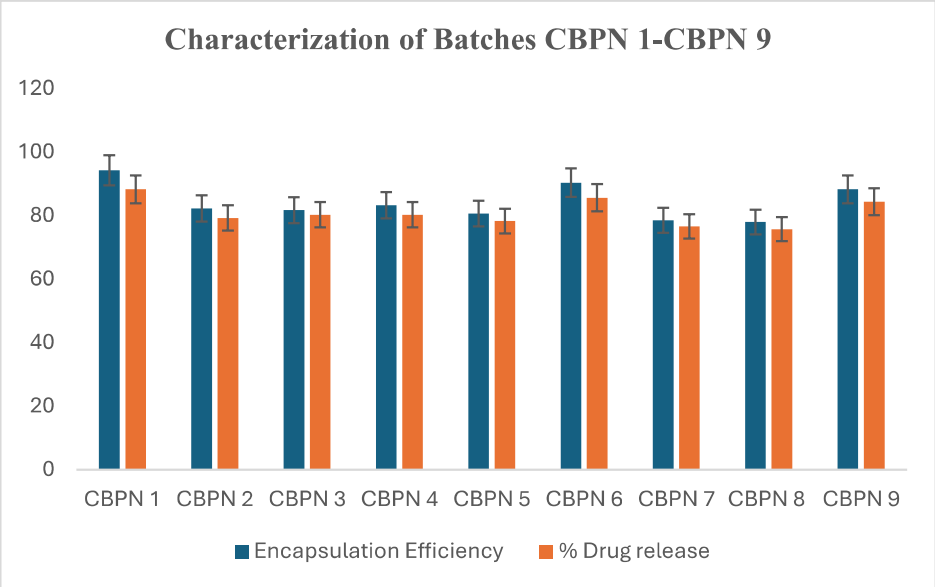

Figure 6 Characterization of Batches CBPN 1-CBPN 9

ANOVA for Percentage Encapsulation Efficiency (%EE)

The effects of formulation variables on the percentage encapsulation efficiency (%EE) were analyzed using analysis of variance (ANOVA) based on a quadratic response surface model. The ANOVA results indicated that the model was statistically significant ($p < 0.05$), confirming the suitability of the selected design for optimization. Among the model terms, the quadratic term of Span 60 (A^2) showed a significant effect, whereas the linear terms of Span 60 (A) and cholesterol (B) exhibited a comparatively lower influence. The interaction term (AB) showed a moderate effect on the encapsulation efficiency, as shown in Table 6.

The regression analysis demonstrated good agreement between the experimental and predicted values, indicating the reliability of the model. The response surface and contour plots revealed that the optimal concentrations of Span 60 and cholesterol resulted in maximum encapsulation efficiency, whereas excessive levels led to reduced drug entrapment due to bilayer saturation and rigidity. Overall, the ANOVA findings confirmed that formulation variables significantly influenced and validated the use of the 3^2 factorial design for optimizing CRL-loaded proniosomes.

Table 6. ANOVA for Percentage Encapsulation Efficiency (%EE)

ANOVA for Response Surface Quadratic model						
Analysis of variance table [Partial sum of squares - Type III]						
	Sum of		**Mean**	**F**	**p-value**	
Source	**Squares**	**df**	**Square**	**Value**	**Prob > F**	
Model	240.99	5	48.20	15.52	0.0236	significant
A-Span 60	0.37	1	0.37	0.12	0.7512	
B-Cholesterol	0.75	1	0.75	0.24	0.6571	
AB	13.73	1	13.73	4.42	0.1263	
A^2	209.85	1	209.85	67.56	0.0038	
B^2	16.28	1	16.28	5.24	0.1060	
Residual	9.32	3	3.11			
Cor Total	250.30	8				

Final Equation in Terms of Coded Factors

%EE = +92.86 + 0.25 * A + 0.35 * B - 1.85* AB - 10.24 * A2 - 2.85* B2

ANOVA for Percentage Drug Release

Analysis of variance (ANOVA) was performed to evaluate the effect of the formulation variables on the percentage drug release using a quadratic response surface model, as shown in Table 7. The ANOVA results demonstrated that the model was statistically significant ($p < 0.05$), indicating the adequacy of the selected design for optimization. Among the model terms, the quadratic effect of Span 60 (A^2) showed a significant influence on drug release, whereas the linear effects of Span 60 (A) and cholesterol (B) were comparatively less significant. The interaction term (AB) had a moderate effect on drug release behavior.

The response surface and contour plots revealed that drug release increased with an increase in Span 60 concentration up to an optimum level, beyond which further increases reduced the release owing to enhanced bilayer rigidity. Cholesterol concentration plays a crucial role in modulating membrane permeability and controlling drug diffusion. Overall, the ANOVA findings confirmed the significant influence of formulation variables on drug release and validated the robustness of our factorial design.

Table 7. ANOVA for Drug Release

ANOVA for Response Surface Quadratic model						
Analysis of variance table [Partial sum of squares - Type III]						
	Sum of		**Mean**	**F**	**p-value**	
Source	**Squares**	**df**	**Square**	**Value**	**Prob > F**	
Model	140.25	5	28.05	18.13	0.0189	significant
A-Span 60	0.74	1	0.74	0.48	0.5384	
B-Cholesterol	0.068	1	0.068	0.044	0.8471	
AB	13.07	1	13.07	8.45	0.0622	
A^2	118.63	1	118.63	76.67	0.0031	
B^2	7.74	1	7.74	5.00	0.1114	
Residual	4.64	3	1.55			
Cor Total	144.89	8				

Final Equation in Terms of Coded Factors

%DR = +87.39 + 0.35* A - 0.11 * B - 1.81* AB - 7.70 * A2 - 1.97* B2

Design of Experiment (DoE) Optimization

A 3^2 factorial design was employed to study the effects of Span 60 (X_1) and cholesterol (X_2) on the encapsulation efficiency (Y_1) and percentage drug release (Y_2). The encapsulation efficiency ranged from approximately 78% to 94%. Analysis of variance (ANOVA) results confirmed the statistical significance of the quadratic model ($p < 0.05$). The response surface and contour plots revealed that intermediate concentrations of Span 60 and cholesterol resulted in maximum encapsulation efficiency, whereas excessive levels led to reduced drug entrapment due to bilayer saturation.

The percentage of drug release after 7 h ranged from approximately 75% to 88%. An optimized cholesterol concentration plays a crucial role in controlling membrane permeability and sustaining drug release. Overlay plot analysis identified an optimized formulation that satisfied both response parameters.

Validation and Surface Morphology

The checkpoint analysis showed a close agreement between the predicted and experimental values, confirming the robustness of the DoE model. The optimized formulation exhibited high encapsulation efficiency (~90.63%) and sustained drug release (~85.51% over 7 h). Scanning electron microscopy of optimized proniosomes revealed discrete spherical vesicles with smooth surfaces, confirming successful proniosome formation.

DISCUSSION

The present study focused on the development and optimization of crisaborole-loaded proniosomes using a factorial design of experiment (DOE) approach to overcome the limitations associated with conventional topical formulations. Effective management of inflammatory skin disorders, such as atopic dermatitis, requires drug delivery systems capable of enhancing drug retention at the target site while providing sustained therapeutic action [1–3]. Although crisaborole is clinically effective in reducing inflammatory responses, its limited permeation across the stratum corneum necessitates the development of advanced carrier-based drug delivery systems [3–5].

Preformulation studies confirmed that crisaborole exhibits lipophilic characteristics and limited aqueous solubility, making it suitable for incorporation into vesicular drug delivery systems, such as proniosomes. The analytical method developed for drug estimation demonstrated excellent linearity and reliability, ensuring accurate quantification throughout formulation development. Fourier-transform infrared (FT-IR) analysis confirmed the

compatibility between crisaborole and formulation excipients, indicating that no significant chemical interactions occurred during formulation preparation.

The preliminary trial batches revealed that the type of surfactant plays a significant role in determining vesicle characteristics, such as particle size, encapsulation efficiency, and drug release behavior. Among the evaluated surfactants, Span 60 produced proniosomes with superior encapsulation efficiency and sustained drug release. This observation can be attributed to the higher phase transition temperature and longer saturated alkyl chain of Span 60, which enhances bilayer rigidity and promotes efficient drug entrapment within the vesicular structure [6–8,9–11]. Similar findings have been reported in previous proniosomal formulations, wherein Span 60 demonstrated improved vesicle stability and controlled drug release properties [14–21].

Risk assessment of the formulation variables identified encapsulation efficiency and in vitro drug release as critical quality attributes, whereas Span 60 and cholesterol concentrations were considered critical formulation variables. Cholesterol plays an important role in stabilizing the vesicular bilayer structure by modulating membrane fluidity and permeability. However, excessive cholesterol concentrations may increase bilayer rigidity and reduce drug release, emphasizing the importance of systematic optimization [6–8,15].

The application of a 3^2 factorial design within a QbD framework enabled the systematic investigation of the effects of formulation variables and their interactions on the response parameters [12,13,24–26]. ANOVA results confirmed the statistical significance of the quadratic models for both encapsulation efficiency and drug release responses. The significant quadratic effect of Span 60 suggests that an optimum surfactant concentration is necessary to achieve maximum drug encapsulation, whereas excessive concentrations may lead to bilayer saturation and reduced drug entrapment efficiency.

The optimized formulation exhibited high encapsulation efficiency (~90.63%) and sustained drug release (~85.51% over 7 h). The sustained-release profile may be attributed to the formation of a stable vesicular bilayer that acts as a diffusion barrier for drug release. These findings are consistent with those of previously reported vesicular and nanobased delivery systems developed for improved drug delivery performance [18–20].

Recent formulation strategies, such as microsponge-based delivery systems, floating in situ gels, and nanoemulgel platforms, have also demonstrated improved drug release and therapeutic performance for various pharmaceutical agents [18–20]. Additionally, QbD-based analytical and formulation development approaches have been successfully applied to improve method robustness and formulation reliability in pharmaceutical research [17]. These studies further support the importance of a systematic experimental design in pharmaceutical formulation development.

Checkpoint analysis demonstrated good agreement between the predicted and experimental responses, confirming the robustness and predictive capability of the developed DoE model. SEM analysis further confirmed the formation of discrete spherical vesicles with smooth surfaces, indicating the successful formation of proniosomal vesicles.

In summary, the present study demonstrates that the QbD-based factorial design of experiment approach provides a reliable and efficient strategy for optimizing crisaborole-loaded proniosomes. The optimized proniosomal formulation exhibited favorable physicochemical properties, high encapsulation efficiency, and sustained drug release, suggesting its potential as an effective carrier system for topical drug delivery.

CONCLUSION

In the present study, we successfully developed and optimized crisaborole-loaded proniosomes using a 3^2 factorial design of experiments. The optimized formulation demonstrated high encapsulation efficiency (~90.63%) and sustained drug release (~85.51% over 7 h), indicating effective drug entrapment and controlled release behavior. Statistical analysis confirmed the significant influence of formulation variables and validated the robustness of the developed model. Overall, the optimized proniosomal system shows promising potential as a stable vesicular carrier for enhanced topical delivery of crisaborole. Further in vivo and skin permeation studies are recommended to confirm its therapeutic effectiveness.

Conflict of Interest

The authors declare no conflicts of interest regarding the publication of this research. All authors have approved the final manuscript and have agreed to its submission.

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