RESEARCH PAPER

Development, Optimization, and Evaluation of Luliconazole-Loaded Proniosomal Gel for Enhanced Topical Delivery

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ABSTRACT

Luliconazole is an effective antifungal drug with limited aqueous solubility and skin permeation, which may affect its topical therapeutic efficacy. The present study aimed to develop and optimize a Luliconazole-loaded proniosomal gel to enhance topical drug delivery. Preformulation studies, including organoleptic evaluation, melting point determination, solubility analysis, UV spectroscopy, Fourier-transform infrared spectroscopy, and differential scanning calorimetry, confirmed the drug purity and suitability for formulation. Proniosomes were prepared using the coacervation phase separation method and evaluated for vesicle size, drug content, encapsulation efficiency, and in vitro drug release. A 3^2 factorial design was employed to optimize the formulation variables. The optimized proniosomal dispersion was incorporated into a carbopol-based gel, and its physicochemical properties and in vitro drug diffusion were evaluated. The optimized formulation demonstrated good encapsulation efficiency, controlled drug release, satisfactory gel characteristics, and improved diffusion. These findings suggest that proniosomal gels are a promising approach for enhancing the topical delivery of Luliconazole.

Keywords: Luliconazole, Proniosomes, Topical gel, Design of Experiments, Controlled release, Dermal drug delivery, Antifungal formulation.

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INTRODUCTION

Superficial fungal infections are among the most common dermatological disorders worldwide and remain a significant therapeutic concern because of their recurrent nature, prolonged treatment duration, and reduced patient adherence to therapy. Topical antifungal treatment is generally preferred for localized fungal infections because it delivers the drug directly to the affected site while minimizing systemic exposure and related adverse effects.[1,2] Luliconazole is a broad-spectrum imidazole antifungal agent with potent activity against dermatophytes, yeasts, and other pathogenic fungi, and it has shown considerable effectiveness in the treatment of superficial mycoses.[1,2] However, its poor aqueous solubility and limited permeation through the stratum corneum may reduce the therapeutic efficacy of conventional topical dosage forms.[1,3]

Vesicular drug delivery systems have received substantial attention in topical and transdermal drug delivery to overcome these limitations. Among these, niosomes and proniosomes are considered promising carriers because they can improve drug solubilization, enhance skin permeation, protect the entrapped drug from degradation, and provide controlled drug release.[3-7] Proniosomes are dry or semisolid formulations that are converted into niosomal vesicles upon hydration and offer several advantages over conventional niosomal dispersions, including better physical stability, ease of storage, convenient handling, and improved formulation flexibility.[6,7] The behavior of such vesicular systems is strongly influenced by the type and concentration of non-ionic surfactants, membrane stabilizers, and lipid components, which collectively determine vesicle formation, entrapment efficiency, membrane fluidity, and drug release characteristics.[8]

In recent years, the development of topical vesicular systems has increasingly adopted systematic optimization tools such as Quality by Design (QbD) and

Design of Experiments (DoE). These approaches provide scientific understanding of the relationship between formulation variables and critical quality attributes, thereby supporting the development of robust, reproducible, and high-performance dosage forms.[8,9] QbD-driven formulation development has proven useful not only in analytical method development but also in the rational optimization of advanced drug delivery systems.[10] In addition, recent formulation studies involving microsponges, floating in-situ gels, nanoemulgels, and proniosomal systems have demonstrated the importance of optimization-based design in improving entrapment, release behavior, stability, and therapeutic performance.[11-14]

Particularly, proniosomal systems optimized through factorial design have shown considerable promise for improving the topical delivery of poorly water-soluble drugs by enhancing drug loading and modulating release kinetics.[[14] Considering the physicochemical limitations of luliconazole and the advantages associated with proniosomal carriers, the present study was undertaken to develop, optimize, and evaluate a luliconazole-loaded proniosomal gel for enhanced topical delivery. A 3^2 factorial design was employed to optimize the formulation variables, and the optimized proniosomal system was subsequently incorporated into a gel base and evaluated for its physicochemical characteristics and in vitro performance.

MATERIALS AND METHODS

3.1 Materials

Luliconazole was used as the active ingredient. Cholesterol, soya lecithin, glyceryl monolinoleate, propylene glycol monocaprylate, Tween 20, Span 20, carbopol 934, methyl paraben, propyl paraben, triethanolamine, methanol, potassium bromide, phosphate buffer (pH 7.4), and other analytical-grade reagents were employed for formulation and evaluation studies. All chemicals and solvents used were of analytical grade.

3.2 Equipment

The study utilized a UV–visible double-beam spectrophotometer, digital pH meter, Brookfield digital viscometer, sonicator, centrifuge, differential scanning calorimeter (DSC), Fourier-transform infrared (FT-IR) spectrophotometer, Franz diffusion cell, mechanical shaker, magnetic stirrer, and standard laboratory glassware.

3.3 Preformulation Studies of Luliconazole

3.3.1 Organoleptic Evaluation

Physical appearance, color, odor, and state of the drug were evaluated visually by direct observation.

3.3.2 Determination of Melting Point

The melting point was determined using the capillary method. The drug sample was filled into a capillary tube and heated in a paraffin bath, and the temperature at which melting occurred was recorded.

3.3.3 UV Spectroscopic Analysis and Determination of λmax

A stock solution (1000 µg/mL) of luliconazole was prepared using a methanol–water (1:1) solution. Dilutions were prepared and scanned between 200 and 400 nm using a UV–visible spectrophotometer to determine the maximum absorption wavelength (λmax).

3.3.4 Preparation of Calibration Curve

Stock and working solutions were prepared using methanol and phosphate buffer (pH 7.4). Serial dilutions (2–10 µg/mL) were analyzed spectrophotometrically at 295–296 nm, and a calibration curve of concentration versus absorbance was generated.

3.3.5 Solubility Study

Equilibrium solubility was determined by adding excess drug to various solvents, followed by stirring at 37 °C for 24 h. The samples were centrifuged at 5000 rpm for 10 min, filtered, and analyzed using UV spectroscopy.

3.3.6 Determination of Partition Coefficient

The partition coefficient was determined using n-octanol and water (1:1 ratio). After equilibration for 24 h, the drug concentrations in both phases were quantified using UV spectroscopy, and log P was calculated.

3.3.7 FT-IR Spectroscopic Analysis

Drug samples were mixed with potassium bromide (1:100), compressed into pellets, and scanned over 4000–400 cm^{-1} to assess their structural integrity and compatibility.

3.3.8 Differential Scanning Calorimetry (DSC)

Thermal analysis was performed under a nitrogen atmosphere using DSC. The samples were scanned from 25 to 300 °C at a controlled heating rate using an empty aluminum pan as a reference.

3.4 Preparation of Proniosomes

Proniosomes were prepared using the coacervation–phase separation method. Required quantities of surfactants, lipids, and drugs were added to a wide-mouthed glass vial containing a small amount of alcohol. The mixture was heated in a water bath at 60–70 °C for approximately 5 min until it completely dissolved. The aqueous phase was added, and the mixture was warmed until a clear solution was formed. Upon cooling, a proniosomal gel was obtained, which formed niosomal vesicles upon hydration.

3.5 Characterization of Proniosomal Formulations

3.5.1 Entrapment Efficiency

Proniosomal dispersion was reconstituted with a phosphate buffer (pH 7.4), sonicated, and centrifuged at

25,000 rpm for 30 min at 20 °C. The supernatant containing the unentrapped drug was analyzed spectrophotometrically. The entrapment efficiency (%EE) was calculated using the following equation:

$$\%\mathbf{EE} = \frac{(\mathbf{C_t} - \mathbf{C_r})}{\mathbf{C_t}} \times \mathbf{100}$$

where Ct and Cr are the total and free drug concentrations, respectively.

3.5.2 Drug Content Determination

A known quantity of proniosomal dispersion was dissolved in a phosphate buffer (pH 7.4), shaken for 2 h, filtered, and analyzed using spectrophotometry.

3.5.3 In-Vitro Drug Release Study

Drug release was studied using a dialysis membrane containing a phosphate buffer (pH 7.4) maintained at 37 ± 2 °C and stirred at 50 rpm. Samples were withdrawn at predetermined intervals and analyzed using UV spectroscopy.

3.6 Preparation of Proniosomal Gel

Methyl and propyl parabens were dissolved in water, followed by the addition of carbopol 934 with continuous stirring until swelling occurred. Proniosomal dispersion was incorporated, and triethanolamine was gradually added to neutralize the gel and obtain a uniform consistency.

3.7 Evaluation of Proniosomal Gel

3.7.1 Physical Appearance and Homogeneity

The prepared gels were visually inspected for color, consistency, and the presence of aggregates.

3.7.2 Clarity

Clarity was visually evaluated against black and white backgrounds and graded as turbid (+), clear (++), or very clear (+++).

3.7.3 pH Measurement

One gram of the gel was dispersed in purified water, and the pH was measured using a calibrated digital pH meter.

3.7.4 Viscosity Measurement

Viscosity was measured using a Brookfield digital viscometer at 37 °C with suitable spindle speed variations.

3.7.5 Spreadability

A known quantity of gel was placed between the two glass plates under a specified weight and the increase in diameter after 5 min was recorded.

3.7.6 Extrudability

Extrudability was determined by measuring the force required to extrude a 0.5 cm ribbon of gel from a collapsible tube in 10 s.

3.7.7 In-Vitro Drug Diffusion Study

Drug diffusion was evaluated using a modified Franz diffusion cell fitted with a cellulose dialysis membrane. Phosphate buffer (pH 7.4) maintained at 37 °C served as the receptor medium. Samples were withdrawn at predetermined intervals and analyzed spectrophotometrically.

3.8 Experimental Design and Optimization

A 3^2 factorial design was employed to optimize the formulation variables. Soya lecithin (X1) and glyceryl monolinoleate (X2) were selected as independent variables, while percentage drug content and drug release were considered dependent responses. Formulation batches were prepared according to coded and decoded factorial design combinations and optimized based on critical quality attributes.

3.9 Statistical Analysis

All experiments were performed in triplicate, and the results are expressed as the mean ± standard deviation. Statistical evaluation was conducted to assess the influence of the independent formulation variables on the response parameters.

RESULTS

4.1 Preformulation Studies of Luliconazole

Preformulation studies were conducted to assess the physicochemical properties of luliconazole and ensure its suitability for the development of a proniosomal gel formulation. The studies included organoleptic evaluation, melting point determination, solubility analysis, wavelength determination, calibration curve preparation, and characterization using FT-IR and DSC.

4.1.1 Organoleptic Characteristics of Luliconazole

Organoleptic evaluation revealed that luliconazole was a white crystalline solid powder with a characteristic odor. The observed physical appearance was consistent with the reported properties of the pure drug, indicating the absence of visible impurities or degradation. These findings confirmed the identity and acceptable physical characteristics of the drug prior to formulation development.

4.1.2 Melting Point Determination

The melting point of luliconazole was determined to assess its purity and thermal stability. The observed melting point range was 150–153 °C, which is close to the reported standard range of 149–154 °C. The narrow melting range indicates the crystalline nature and high purity of the drug sample, confirming its suitability for further formulation studies.

4.1.3 Solubility Study of Luliconazole

The solubility of luliconazole in different solvents was investigated to understand its dissolution behavior and to select appropriate formulation components. The drug exhibited very slight solubility in water (0.061 ± 0.05 mg/mL), whereas significantly higher solubility was

observed in a phosphate buffer at pH 7.4 (3.31 ± 0.01 mg/mL) and 0.1 N HCl (1.05 ± 0.07 mg/mL). Luliconazole exhibited maximum solubility in organic solvents, such as acetone (9.04 ± 0.014 mg/mL) and methanol (10.12 ± 0.06 mg/mL), indicating its lipophilic nature.

These results suggest that the drug has poor aqueous solubility, which justifies the need for a vesicular carrier system, such as proniosomes, to improve solubility and enhance topical delivery. The higher solubility of these compounds in organic solvents supports their use during formulation preparation.

4.1.4 Determination of Partition Coefficient of Luliconazole

The partition coefficient (log P) of luliconazole was determined to evaluate its lipophilicity and skin permeation potential. The observed log P value was 4.28, which is in close agreement with the reported standard value (log P = 4.27). *This result confirms the lipophilic nature of the drug.*

Lipophilicity plays a significant role in membrane permeation, therapeutic activity, and pharmacokinetic behavior, particularly in topical and transdermal delivery systems. As the stratum corneum acts as a lipophilic barrier, drugs with moderate to high lipophilicity generally exhibit improved dermal permeation. *The obtained log P value indicated that luliconazole possesses suitable lipophilic characteristics for effective skin penetration, supporting its selection for incorporation into a proniosomal carrier system to enhance topical delivery.*

4.1.5 Identification and Determination of Wavelength Maximum (λmax) of Luliconazole

The UV–visible spectrum of luliconazole was recorded to determine its wavelength of maximum absorbance (λmax). A stock solution of the drug was prepared in methanol and appropriately diluted prior to scanning in the range of 200–400 nm. *The maximum absorbance was observed at 296.52 nm, which is close to the reported pharmacopoeial value of 296 nm.*

The close agreement between the observed and reported λmax values confirmed the identity and purity of the drug and established the suitability of UV spectroscopy for further quantitative estimation during formulation and evaluation studies.

4.1.6 Calibration Curve of Luliconazole

A calibration curve for luliconazole was developed to define the correlation between its concentration and absorbance for quantitative analysis. Standard solutions across the chosen concentration range exhibited a steady increase in absorbance at 295–296 nm, confirming a direct proportionality between drug concentration and absorbance.

The linearity of this calibration curve confirmed that luliconazole adheres to Beer–Lambert's law within the studied concentration range, validating the analytical method for assessing drug content, entrapment efficiency, and in vitro drug release in the subsequent experiments. Consequently, this calibration curve served as a reliable analytical reference throughout the formulation study.

Figure 1 illustrates the calibration curve constructed using standard solutions ranging from 0 to 6 µg/mL, with an absorbance measured at 295 nm. *A strong linear relationship was observed, which is consistent with Beer–Lambert law. The regression equation obtained was $y = 0.1272x + 0.0141$, with a correlation coefficient (R^2) of 0.9939, indicating excellent linearity and reliability of the method.* This established calibration curve was employed for the quantitative determination of drug content, entrapment efficiency, and in vitro release throughout the formulation development process.

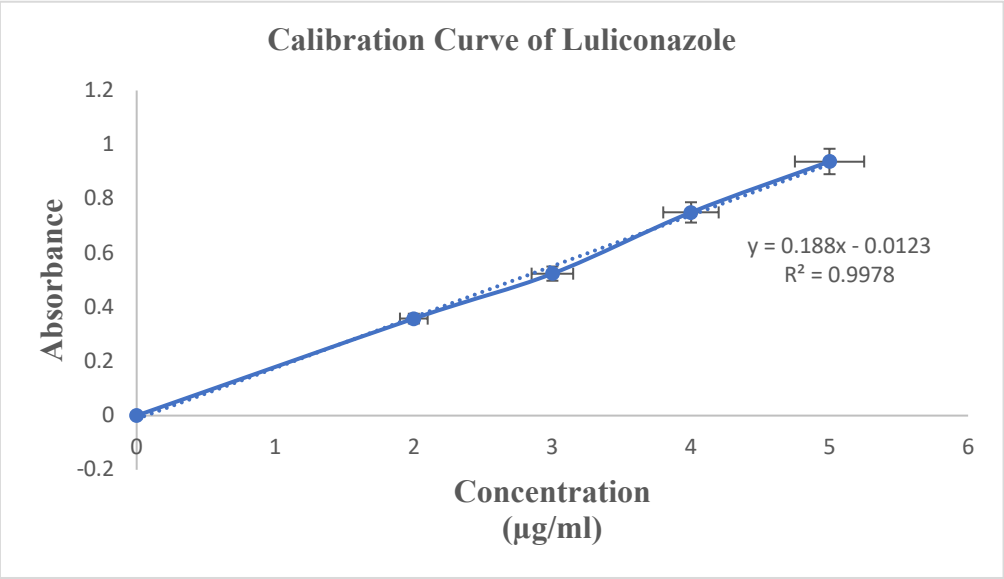

Figure 1. Calibration Curve of Luliconazole

4.1.7 Identification of Luliconazole by FT-IR Spectroscopy

Fourier Transform Infrared (FT-IR) spectroscopy was utilized to verify the identity and structural integrity of luliconazole. The characteristic absorption peaks corresponding to C–H stretching, C≡N stretching, C=N stretching, and C–Cl stretching vibrations appeared at wavelengths consistent with the standard reference values, as detailed in Table 1. The lack of notable peak shifts or loss of characteristic bands confirmed that the drug retained its chemical integrity and did not degrade during the analysis. These results validated the purity and compatibility of luliconazole for subsequent formulation studies. Figure 2.

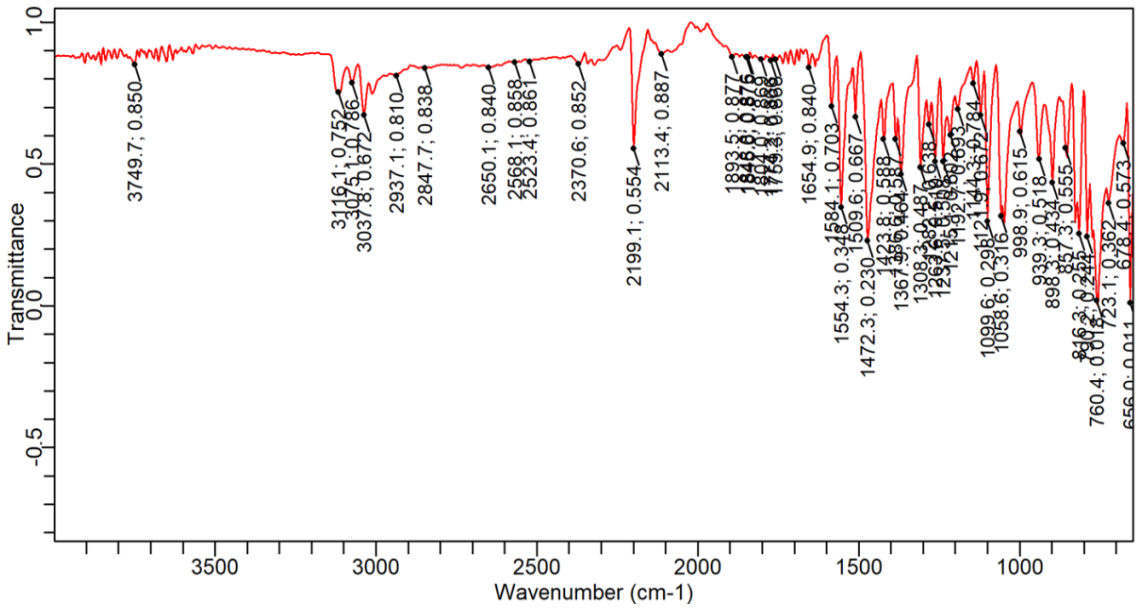

Figure 2 -FTIR of Luliconazole

Table 1. Characteristic FTIR Peaks of Luliconazole

Type of Vibration	Standard Wave Number (Cm^{-1})	Observed Wave Number (Cm^{-1})
C-H stretching	3000-2500	2847.68
C≡N stretching	2400-2000	2199.12
C=N stretching	1320-1000	1192.74
C-Cl stretching	800-600	678.37

4.1.8 Differential Scanning Calorimetry (DSC) Analysis

Differential scanning calorimetry (DSC) was used to assess the thermal properties and crystallinity of luliconazole. The DSC thermogram displays a distinct endothermic peak corresponding to the drug melting point, which is in accordance with the standard reference data. This sharp endothermic peak confirms the crystalline structure and high purity of luliconazole. The absence of additional thermal events indicates no degradation or significant impurities, confirming the suitability of the drug for incorporation into proniosomal formulations. Refer to Figure 3.

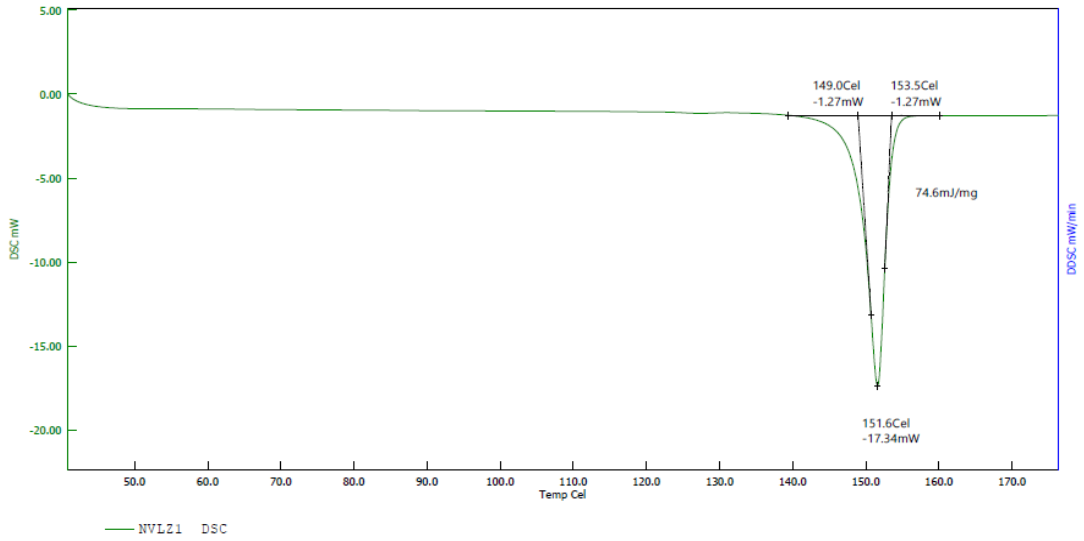

Figure: 3 Differential Scanning Calorimetry of Luliconazole

4.2 Composition of Preliminary Proniosomal Formulations

A series of preliminary proniosomal formulations (LPN1–LPN6) were prepared, as detailed in Table 2, by varying the types and concentrations of surfactants and lipids while maintaining constant levels of the drug and cholesterol. Adjustments were made to the soya lecithin and surfactant compositions to evaluate their effects on vesicle properties, drug encapsulation efficiency, and release profiles. This systematic variation in excipients facilitated the identification of optimal formulation components for subsequent refinement.

Table 2. Composition of different formulations of Proniosomes

Batch	LPN1	LPN2	LPN3	LPN4	LPN5	LPN6
Luliconazole (mg)	100	100	100	100	100	100
Cholesterol (mg)	200	200	200	200	200	200
Soya lecithin (mg)	700	700	1000	1000	1600	1600
Propylene glycol mono caprylate (mg)	1600	-	1600	-	-	-
Glyceryl Monolinoleate (mg)	-	1600	-	1600	-	-
Tween 20 (mg)	-	-	-	-	1600	-
Span 20 (mg)	-	-	-	-	-	1600
Alcohol (ml)	2.4	2.4	2.4	2.4	2.4	2.4
Phosphate buffer pH 7.4 (ml)	1.4	1.4	1.4	1.4	1.4	1.4

4.3 Characterization of Proniosomal Formulations

The prepared proniosomal formulations demonstrated satisfactory drug content, vesicle size, encapsulation efficiency, and drug release profile. The drug content ranged from approximately 75% to 97%, as detailed in Table 3 and illustrated in Figure 4, indicating the efficient incorporation of luliconazole into the vesicular system. Vesicle sizes were measured in the micrometer range, with smaller vesicles generally correlating with enhanced drug release behavior.

The encapsulation efficiency values varied between 83% and 91%, reflecting the capacity of the proniosomal system to effectively entrap lipophilic drugs. Formulations with higher lipid concentrations exhibited improved drug entrapment and controlled release characteristics. In vitro drug release studies revealed sustained release profiles, with cumulative drug release reaching 88.88%, underscoring the potential of proniosomes for prolonged topical delivery of luliconazole.

Table 3. Characterization of different formulations of Proniosomes

Batch	% Drug content	Mean Vesicle size (µm)	Encapsulation efficiency	% Drug Release
LPN 1	75.34±1.45	4.46 ±0.20	84.15 ±2.67	77.23 ±1.26
LPN 2	80.12±1.34	4.81 ±0.42	88.13±1.26	78.38 ±1.45
LPN 3	90.43±1.67	2.21 ±0.15	89.25±1.34	80.74 ±1.24
LPN 4	86.23±1.26	3.66 ±0.24	83.28±1.26	82.15 ±1.15
LPN 5	93.23±1.48	3.11 ±0.15	88.32±1.58	84.76 ±1.18
LPN 6	97.33±1.67	2.51 ±0.67	91.37±1.26	88.88 ±1.34

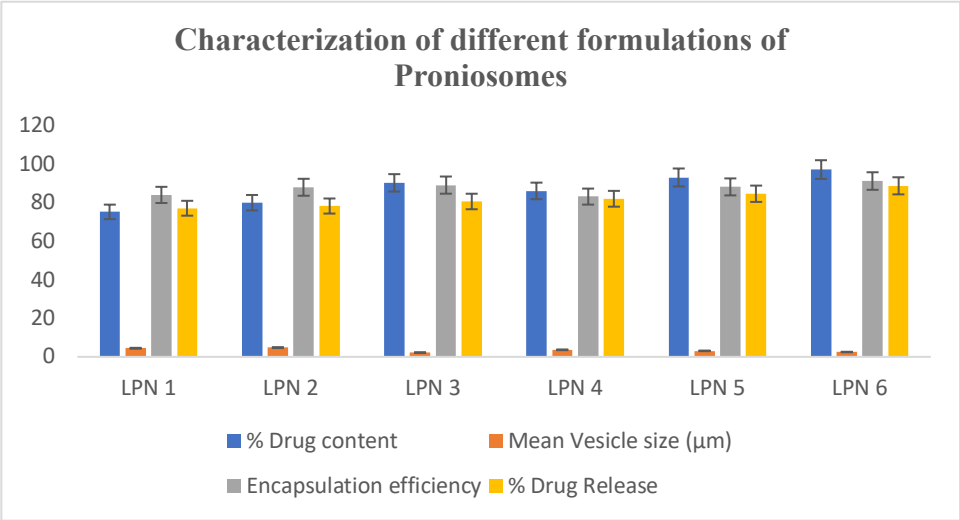

Figure 4. Characterization of different formulations of Proniosomes

4.4 Risk Assessment and Identification of Critical Quality Attributes

Risk assessment was performed to identify the formulation variables influencing the critical quality attributes (CQAs), particularly the percentage drug content and drug release. Soya lecithin and glyceryl monolinoleate were identified as major factors affecting formulation performance. The analysis revealed that the lipid composition played a significant role in controlling vesicle stability and release kinetics, thereby guiding the subsequent optimization process using design of experiments (DoE).

4.5 Optimization of Proniosomal Formulation Using Design of Experiments

A 3^2 factorial design was employed to systematically assess the effects of soya lecithin (X1) and glyceryl monolinoleate (X2) on formulation outcomes, as presented in Table 4. Nine experimental batches were prepared based on the coded and decoded levels of the independent variables. The dependent variables evaluated were drug content and percentage drug release.

Factorial analysis revealed that both soya lecithin and glyceryl monolinoleate significantly influenced the encapsulation efficiency and drug release profiles. An increase in lipid concentration generally improved drug encapsulation, whereas its impact on the release rate varied depending on the vesicle structure. This experimental design facilitated the determination of optimized formulation parameters that balance drug loading with controlled-release characteristics.

Table 4. 3^2 Factorial Design Approach

Independent variables of formulations			
Independent variables (X1)	**Low (-1)**	**Medium (0)**	**High (+1)**
Soya lecithin (mg)	900	1000	1100
Glyceryl Monolinoleate (mg)	1500	1600	1700
Dependent variables			
Y1= % Drug content			
Y2= % Drug release			

4.6 Characterization of Factorial Batches (LPN1–LPN9)

The factorial batches (LPN1–LPN9), prepared using a 3^2 factorial design, were evaluated for encapsulation efficiency and percentage drug release to assess the impact of formulation variables. Encapsulation efficiency ranged from 76.48% to 88.76%, while drug release varied between 74.47% and 86.67%,

demonstrating that changes in soya lecithin (X1) and glyceryl monolinoleate (X2) significantly influenced formulation performance, as detailed in Table 6 and presented in Figure 5. Formulations with balanced lipid concentrations showed enhanced drug entrapment and more controlled release profiles, confirming the appropriateness of these variables for optimization. Overall, these findings highlight the critical role of formulation composition in vesicle properties and drug release, with the optimized proniosomal system exhibiting strong potential for improved topical delivery of luliconazole.

Table 5. Compositions of Factorial Batches in Coded & Decoded Form

LPN 3^2 = batches				
Batches	**Variable level in coded form**		**Variable level in coded form**	
	Soya lecithin (mg) **(X1)**	Glyceryl Monolinoleate (mg) **(X2)**	Soya lecithin (mg) **(X1)**	Glyceryl Monolinoleate (mg) **(X2)**
LPN 1	-1	-1	900	1500
LPN 2	0	-1	1000	1500
LPN 3	+1	-1	1100	1500
LPN 4	-1	0	900	1600
LPN 5	0	0	1000	1600
LPN 6	+1	0	1100	1600
LPN 7	-1	+1	900	1700
LPN 8	0	+1	1000	1700
LPN 9	+1	+1	1100	1700

Table 6. Characterization of Batches LPN 1-LPN 9

Batch	**Encapsulation Efficiency**	**% Drug release**
LPN 1	88.76	78.71
LPN 2	86.48	74.47
LPN 3	81.89	82.48
LPN 4	80.71	84.48
LPN 5	76.48	86.67
LPN 6	82.46	76.96
LPN 7	87.48	77.46
LPN 8	80.57	81.86
LPN 9	78.76	77.74

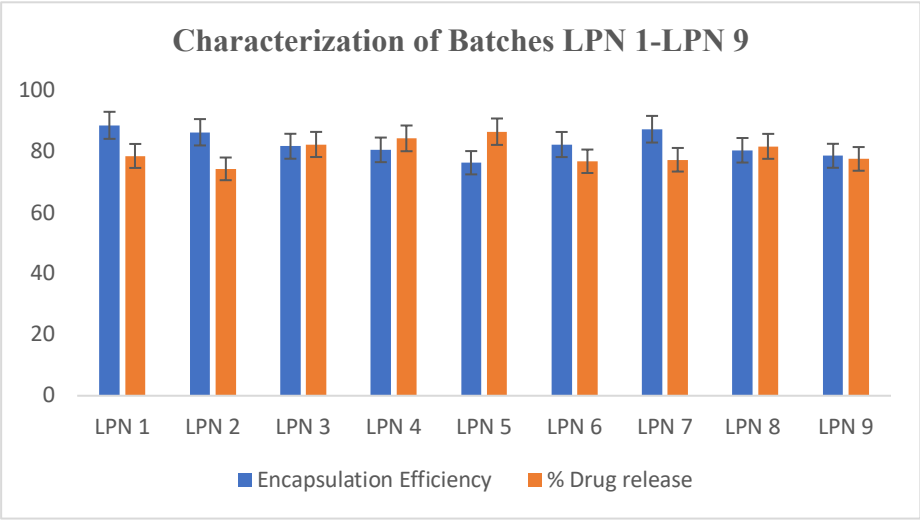

Figure 5. Characterization of Batches LPN 1-LPN 9

DISCUSSION

The present study successfully demonstrated the development and optimization of a luliconazole-loaded proniosomal gel to improve the topical delivery of a poorly water-soluble antifungal drug. Luliconazole possesses potent antifungal activity, but its limited aqueous solubility and restricted permeation through the stratum corneum can reduce the effectiveness of conventional topical formulations.[1-3] In the present work, preformulation studies confirmed the suitability of the drug for formulation development, and FT-IR and DSC analyses indicated the preservation of chemical integrity and thermal behavior. These findings support the compatibility of luliconazole with the selected excipients and are consistent with the reported suitability of vesicular drug delivery systems for lipophilic molecules.[3-7]

The prepared proniosomal formulations exhibited satisfactory drug content, appreciable encapsulation efficiency, and sustained drug release behavior. The high entrapment efficiency observed in the optimized formulations can be attributed to the lipophilic nature of luliconazole, which favors its incorporation within the hydrophobic bilayer of the vesicles. In addition, the combination of soybean lecithin, cholesterol, and glyceryl monolinoleate likely contributed to improved membrane stability and reduced drug leakage. Similar observations have been reported in previous studies on vesicular and topical carrier systems, where the composition of surfactants and lipid components played a major role in determining encapsulation efficiency and release performance.[6-8,11-14]

A major strength of the present work is the use of a 3^2 factorial design for formulation optimization. This approach enabled a systematic investigation of the influence of soya lecithin and glyceryl monolinoleate on the selected response variables. The results indicated that formulation composition had a significant effect on drug content and release behavior, highlighting the importance of rational optimization during proniosomal formulation development. These findings are in line with QbD- and DoE-based pharmaceutical development strategies, which emphasize structured experimental planning to achieve robust and reproducible dosage forms.[8-10] Recent studies on topical microsponges, nanoemulgels, and proniosomal systems have similarly shown that optimization-based design can markedly improve product performance and functional attributes.[11-14]

The sustained-release profile obtained from the optimized proniosomal gel may be explained by the bilayer architecture of the vesicular system, which acts as a diffusion barrier and permits the gradual release of the entrapped drug. The non-ionic surfactants used in proniosomal systems can also improve local drug disposition by altering membrane characteristics and facilitating close interaction of vesicles with the skin surface.[3,4,8,15] Furthermore, the incorporation of the optimized proniosomal dispersion into a carbopol gel base likely improved formulation residence time, spreadability, and convenience of topical application, thereby increasing its potential utility in dermal therapy.

The observed encapsulation efficiency and drug release pattern in this study were within a favorable range for proniosomal topical delivery systems and compare well with previously reported optimized vesicular formulations.[6,7,14] This suggests that the developed formulation could potentially enhance local drug retention and reduce the frequency of application, which may improve patient compliance during antifungal treatment. Such an approach is especially beneficial for superficial fungal infections, where prolonged treatment duration often contributes to poor adherence and therapeutic failure.[1,2]

LIMITATION

Despite these promising findings, the study has certain limitations. The evaluation was limited primarily to physicochemical characterization and in vitro release performance. Ex vivo skin permeation, antifungal activity testing, long-term stability studies, and in vivo therapeutic evaluation were not performed and are necessary to confirm the clinical utility of the optimized formulation. Future studies should therefore focus on these aspects to further validate the potential of proniosomal gels as topical delivery platforms for luliconazole. Nevertheless, the present investigation clearly demonstrates that proniosomal technology is a promising and rational strategy for improving the topical delivery of poorly soluble antifungal agents.

CONCLUSION

In this study, a luliconazole-loaded proniosomal gel was successfully developed and optimized using a design of experiments (DoE) approach, resulting in high drug encapsulation and sustained topical release with suitable physicochemical characteristics. These findings demonstrate that proniosomal technology effectively improves the delivery performance of poorly soluble antifungal drugs and holds promise for enhanced topical therapy. Notably, this study highlights the novelty of combining factorial design optimization with proniosomal engineering to achieve controlled release and improved topical delivery of luliconazole, offering a potential advancement in antifungal drug delivery systems.

CONFLICT OF INTEREST

The authors declare no conflicts of interest related to the publication of this study.

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