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Fabrication, Characterization and *In vitro* Evaluation of Luliconazole Enriched Nanosuspension Topical Gel

Running Title: Luliconazole Nanosuspension Gel for Topical Application

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Abstract This research aims to formulate, optimize, and evaluate a Luliconazole-loaded nanosuspension gel for topical administration. Using the Solvent evaporation/ultrasonication technique, Luliconazole nanosuspensions were fabricated with glyceryl monostearate (GMS) as a lipid. Six different nanosuspensions were formulated by varying the GMS concentration and sonication time. The formulation was optimized by assessing the particle size (nm) and entrapment efficiency (%). The smallest particle size and the highest efficient entrapment (%) formulation was chosen. The optimized nanosuspension was then combined with a 1% Carbopol 934 gelling solution to obtain the topical nanosuspension gel. The formulated gel was assessed for zeta potential, appearance, pH, spreadability, viscosity, drug content, drug release, and *in vitro* skin irritation using the HET-CAM technique. The nanosuspension gel had a particle size of 122.6 nm with PDI of 0.318, and an entrapment efficiency of 78.4%. The zeta potential was -26.9 mV, indicating good stability. The pH, viscosity, and spreadability were found to be satisfactory. An 8-hour sustained release with a maximum release of 83.46% was observed in the drug release study. The formulation's dermatological safety was further confirmed by the HET-CAM method *in vitro* skin irritation testing, which showed no evidence of irritation. The research concluded that Luliconazole nanosuspension gel holds potential as an effective drug delivery for treating fungal infections.

Keywords Luliconazole, Nanosuspension Gel, Particle Size, Zeta Potential, HET-CAM Test

1. Introduction

Skin fungal infections are common worldwide, impacting approximately 20–25% of the population. Fungal infection of the skin is a major health issue, with an estimated 1.73 billion reported cases in 2021 globally, according to the Global Burden of Diseases study. Superficial cutaneous mycoses (SCM) cover several fungal infections, of which the most frequent one is tinea, which is mostly affected by dermatophytes such as *Trichophyton rubrum, Trichophyton mentagrophytes, and Epidermophyton floccosum.* More efficient and patient-friendly treatment options are needed due to the rise in resistant fungal infection cases and the shortcomings of traditional therapy [1].

Topical treatments are effective methods for managing these infections, as they directly target the affected area, minimize systemic side effects, improve treatment efficacy, and enhance patient compliance. This approach also

reduces the risk of systemic absorption and its associated complications [2]. Due to their local action and reduced systemic toxicity, topical formulations like creams, ointments, gels, and lotions are still the drug of choice for cutaneous fungal infections. Some of the limitations of these traditional formulations include poor drug retention at the site of infection, poor penetration through skin, and high rates of drug elimination, which result in more frequent dosing and inadequate patient compliance [3]. In addition to this, many antifungal drugs are poorly soluble in water, which decreases their bioavailability and therapeutic activity in conventional formulations [4].

Solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), liposomes, niosomes, and other newly emerging drug delivery systems have proved to be effective alternatives for these limitations [5]. Amongst these, liposomes are the least chemically as well as physically stable and tend to aggregate and release the drug while in storage. Their poor skin retention and high, complicated production costs limit their large-scale usage [6]. Batch-to-batch consistency and relatively low encapsulation efficiency are issues for Niosomes. Patient tolerability may be compromised due to the potential of surfactant components to cause localized skin irritation and hypersensitivity reactions [7].

NLCs are plagued by issues such as poor aqueous solubility of luliconazole, decreased skin retention, and incomplete penetration, which compromise optimal dermal bioavailability. Formulation and storage stability can also be an issue. Whereas SLNs exhibit improved biocompatibility, the capability to encapsulate lipophilic drugs, controlled release of the drug, and increased skin permeation. The solid lipid matrix of SLNs shields the drug from degradation, and the nano-sized particles enhance drug permeation across the stratum corneum, and hence exert an excellent therapeutic effect [8].

Nano emulsions are physically unstable and tend to phase separate, so viscosity enhancers are necessary for proper residence time in the skin. Surfactants employed may sometimes cause mild skin irritation [9]. Multistep synthesis pathways and changing drug release patterns make it difficult to scale and achieve batch-to-batch reproducibility. Manufacturing issues may restrict Luliconazole polymeric nanoparticle commercialization [10]. As they enhance drug penetration, spanlastics can be susceptible to formulation instability and need careful optimization. Regulatory and manufacturing challenges limit their wider use on the skin [11].

Nanosuspensions are colloidal dispersions containing small nanoparticles that efficiently deliver insoluble drugs. Their simple preparation process allows for higher drug loading and passive targeting, addressing the challenge of low bioavailability commonly seen with poorly soluble drugs, particularly those categorized as BCS class 2 [12]. Nanosuspensions not only enhance solubility but also pharmacokinetics, efficacy, and safety, leading to more effective hydrophobic drug delivery. In addition, they enhance bioavailability and skin permeability, with sustained drug release and local concentrations. This is a result of their special characteristics, such as high water content, good adhesion, biocompatibility, and biodegradability [13].

Topical antifungal agents, including polyenes and azoles, are commonly used for treating skin infections. Azole antifungals inhibit ergosterol synthesis by interfering with the ability of the fungal cell membrane to maintain its integrity, thereby making it more permeable. Luliconazole, being an imidazole analogue, is highly effective against dermatophytes and belongs to the Biopharmaceutical Classification System (BCS) - Class 2 drug due to the low solubility and high permeability [14]. With its addition to gel formulations derived from nanosuspensions, the solubility is enhanced. Compared to conventional formulations, it yields a formulation of enhanced stability with sustained release, which maximizes drug bioavailability at the site of infection [15].

By enhancing drug delivery, patient compliance, and ensuring sustained antifungal activity, nanosuspension-based gel systems provide a new means of overcoming the drawbacks of traditional topical preparations. Therefore, the present work aims to eliminate such barriers and enhance the therapeutic efficacy of mycotic skin infections [16].

The work encompasses the fabrication and evaluation of a nanosuspension gel of Luliconazole for local administration in the treatment of skin fungal infections. Luliconazole undergoes a 15% decrease in oral bioavailability as a result of first-pass metabolism, and thus its inclusion into nanosuspensions in a topical gel presents an efficient drug delivery option. With its high lipophilicity and low aqueous solubility, optimization of colloidal carriers for Luliconazole would remarkably increase its solubility and enhance topical delivery. In addition, utilization of nanosuspensions might facilitate penetration of the stratum corneum, enhance topical diffusion, ensure safety of the drug, intensify therapeutic efficacy, and facilitate absorption in deeper layers of the skin [17].

2. Materials and Methods

2.1. Materials

Pure Luliconazole API was sourced from Micro Labs Limited, Bengaluru. Glyceryl monostearate (GMS) and Carbopol 934 were procured from Hi Media Lab, Mumbai, India. Methyl paraben, propyl paraben, and triethanolamine were obtained from Loba Chemie, Mumbai, India.

2.2. FTIR Spectroscopy

FTIR spectral analysis was conducted using an Alpha Bruker Spectrometer. Spectra were recorded for both the

pure Luliconazole, GMS and the physical blend of the Luliconazole and GMS. After acquiring the spectra, and the main peaks, the FTIR analysis was carried out to assess the compatibility of the drug with the lipid [18].

2.3. Preparation of Luliconazole Nanosuspensions

Luliconazole nanosuspensions were developed by the solvent evaporation/ultrasonication method. A mixture of 30 mg of Luliconazole and glyceryl monostearate (used in three different concentrations: 30 mg, 45 mg, and 60 mg) dissolved in equal volumes (1:1) of chloroform and methanol. The drug-lipid solution was then added dropwise to a 5% poloxamer 407 solution, and the mixture was stirred magnetically at a temperature of 50-60ºC. The heating was stopped once the solvent evaporated, and stirring persisted for six more hours. The nanosuspensions were then subjected to sonication for 10, 15, and 20 minutes using a probe sonicator set to a fixed amplitude and frequency to achieve the desired particle size. The resulting nanosuspension dispersions were filtered through 0.22 µm sterile syringe filters. GMS concentration and sonication time were systematically varied during formulation optimization, and their effects on particle size and entrapment efficiency were assessed. The preparation with a smaller particle size and higher entrapment efficiency was found to be selected as the optimized formulation. Additionally, the optimized formulation was transformed into a topical gel and evaluated for other parameters [19].

The formulation composition of all the nanosuspensions, along with sonication time is given in Table 1.

Table 1. Formulation composition of Luliconazole nanosuspensions

Formulation code	Luliconazole (mg)	GMS (mg)	Poloxamer 407 (%)	Sonication Time (min)
LN-1	30	30	5	10
LN-2	30	30	5	15
LN-3	30	45	5	15
LN-4	30	45	5	20
LN-5	30	60	5	20

2.4. Evaluation of Luliconazole Nanosuspensions

2.4.1. Particle Size and Polydispersibility Index (PDI)

The particle size and PDI of all the formulated nanosuspensions were measured using the Malvern Zetasizer, which employs dynamic light scattering at 25ºC. Prior to analysis, every sample was diluted with ultrapure water at a 1:10 ratio [20].

2.4.2. Percentage Entrapment Efficiency

The entrapment efficiency of LUL-NS was measured by the centrifugation method in a 10 ml volumetric flask, where the sample was diluted with phosphate buffer at pH 7.4. The mixture was sonicated for 15 minutes at 15 °C before centrifugation. The supernatant was collected after centrifugation at 12,000 rpm for 40 minutes using a cool centrifuge. The drug concentration in the supernatant was measured with a UV-visible spectrophotometer at 299 nm [21]. The entrapment efficiency (EE%) of the drug was determined by using the following formula.

$$\textit{Entrapment Efficiency}\ (\%) = [(Ct - Cf)/Ct] X\ 100$$

Where
Ct is the amount of total drug.
Cf is the concentration of unentrapped drugs.

2.5. Evaluation of Luliconazole Nanosuspension Gel (LUL-NSG)

2.5.1. Physical Appearance

The optimized LUL-NSG formulation was evaluated visually for its colour, appearance, and consistency [21].

2.5.2. Zeta Potential

Malvern Zetasizer was used to determine the zeta potential of the optimized LUL-NSG at 25°C, which utilizes the dynamic light scattering (DLS) method [22].

2.5.3. pH

The pH of the optimized formulation was measured with a digital pH meter by immersing the electrode in a beaker with 1 g of LUL-NSG [23].

2.5.4. Spreadability

1 g of LUL-NSG was placed between the glass slides, and a weight of 50 g was set on the top slide for 5 min. The top slide and 50 g weight were expected to detach. The time elapsed was measured for the top slide to travel 10 cm and come off the bottom slide under the load [24].

Spreadability was determined by using the following formula:

$$\textit{Spreadability} = M\ X\ L/T$$

Where,
M - Weight in the pan (tied to the upper slide)
L - Length moved by the glass slide.
T - Time (sec).

2.5.5. Viscosity

Brookfield viscometer with spindle no. 96 was used to measure the viscosity of LUL-NSG at shear rates of 5, 10, 12, 20, 50, and 100 rpm. The viscosity values were recorded in centipoise (cps). A plot of shear rate versus viscosity was created to assess the flow properties of the optimized formulation [25].

2.5.6. % Drug Content

The drug content of the optimized formulation was measured by dissolving an exactly weighed sample of the

gel in approximately 10 ml of phosphate buffer of pH 7.4. 1 ml of this solution was then diluted to 100 ml with the same phosphate buffer and was analyzed by a UV spectrophotometer at 299 nm [26].

2.5.7. Surface Morphology by Transmission Electron Microscopy (TEM)

The surface morphology of the optimized formulation was analysed by Transmission Electron Microscopy (TEM). A small drop of the optimized LUL-NSG was gently loaded on a carbon-coated copper grid (400 mesh), and then the excess liquid was blotted out with tissue paper for even sample distribution. The sample was subsequently stained with 2% w/v neutralized phosphotungstic acid to provide contrast. After staining, it was air-dried at room temperature to remove traces of the solvent. The dried sample was observed under a TEM at an accelerating voltage of 200 kV. TEM images were captured, allowing for detailed observation of the surface morphology and structural features of the formulation [27].

2.5.8. *In-vitro* Drug Release Study

The drug release study of the nanosuspension gel was carried out using a Franz diffusion cell apparatus, consisting of a donor and receptor chamber. The gel sample of 100 mg was placed on the donor chamber, covered by a dialysis membrane. The receptor chamber was loaded with phosphate buffer, pH 7.4, and a magnetic bead was placed inside. The system was kept at 37±0.5ºC with constant stirring at 100 rpm. At regular time intervals (0.5, 1, 2, 3, 4, 5, 6, 7, and 8 hours), 1 ml samples were drawn, and an equal amount of fresh buffer was added to keep the volume constant. The samples withdrawn were diluted to 10 ml with phosphate buffer pH 7.4 and scanned using a UV spectrophotometer at 299 nm. The percentage cumulative drug release (%CDR) was determined, and the resultant data were fitted into a kinetic model to further describe the drug release pattern [28].

2.5.9. Drug Release Kinetics

The drug release data were analyzed using various kinetic release models (zero-order, first-order, Higuchi, and Korsmeyer-Peppas) to determine the mechanism of drug release from the optimized formulation. The model that best fitted the release profile was selected according to the maximum regression value (R^2) obtained [29].

2.5.10. *In-vitro* Skin Irritation Study by HET-CAM Method

This study was conducted to assess the *in vitro* skin irritation of the optimized formulation using fertilized hen's eggs, with the chorioallantoic membrane (CAM) of chick embryos serving as the test surface, as their blood vessels closely resemble those of human skin. White Leghorn chicken eggs weighing 50-60 grams and not more than 7 days old were used, whereas damaged or cracked eggs were rejected. Eggs were divided into three groups: negative control, positive control, and test, with each group having three eggs. For the negative control, 0.3 ml of 0.9% NaCl (saline) solution was applied to eggs. The test group was treated with 0.3 ml of the optimized formulation, and the positive control group received 0.3 ml of 1% Sodium Dodecyl Sulphate (SDS) solution to induce irritation for comparison with the other groups. Placed on a tray, the eggs were maintained in an incubator at 37±0.5°C and relative humidity of 58±2%. The eggs were turned manually five times daily for about 8 days. On day 8, the eggs were candled to ensure that the development of the embryo occurred. Once confirmed, eggs were again incubated for 24 hours, positioned with the larger end upwards without any rotation. On day 9, a minor incision close to the air sac was made so that the membrane was left intact. Subsequently, the eggs were exposed to their respective solutions and observed for haemorrhage, coagulation, and lysis of blood vessels within five minutes [29,30].

The irritation score (IS) was calculated using the formula given below, and the corresponding values with their interpretations are presented in Table 2.

$$IS = (301 - H/300)X\ 5 + (301 - L/300)X\ 7 + (301 - C/300)X\ 9$$

Where,
H- Haemorrhage
L- Lysis of blood vessels
C- Coagulation

Table 2. Irritation score value and its inference for HET-CAM Test

Irritation Score	Inference
0-0.9	No irritation
1-4.9	Weak irritation
5-8.9	Moderate irritation
9-21	Severe irritation

3. Results and Discussion

3.1. FTIR Spectroscopy

The FTIR spectral images for Luliconazole pure drug, pure GMS, and physical mixture of Luliconazole with GMS are shown in Figures 1, 2, and 3.

In IR spectrum of pure Luliconazole, significant peaks were observed at 722.81, 2199.36, 3006.02, 1510, and 941.17 cm^{-1}, representing C–Cl (chloride) stretching, C≡N (nitrile) stretching, C–H stretching, C=C (aromatic) stretching, and C–S–C (sulphide) stretching, respectively. Pure GMS's IR spectrum had absorption bands at 3306.74, 1047.17, and 1729 cm^{-1}, which were assigned to O–H (alcohol) stretching, C–O–C (ether) stretching, and C=O

(ketone) stretching, respectively. In the physical blend of Luliconazole and GMS, major peaks were found at 3123.34, 1511.41, 1047.01, and 1729.80 cm⁻¹ for O–H (alcohol) stretching, C=C (aromatic) stretching, C–O (ether) stretching, and C=O (ketone) stretching, respectively. FTIR analysis indicated that the drug, the lipid, and their physical blend showed similar characteristic peaks without any new peaks appearing. This shows that there is no chemical interaction between the lipid and the drug, thus establishing their compatibility.

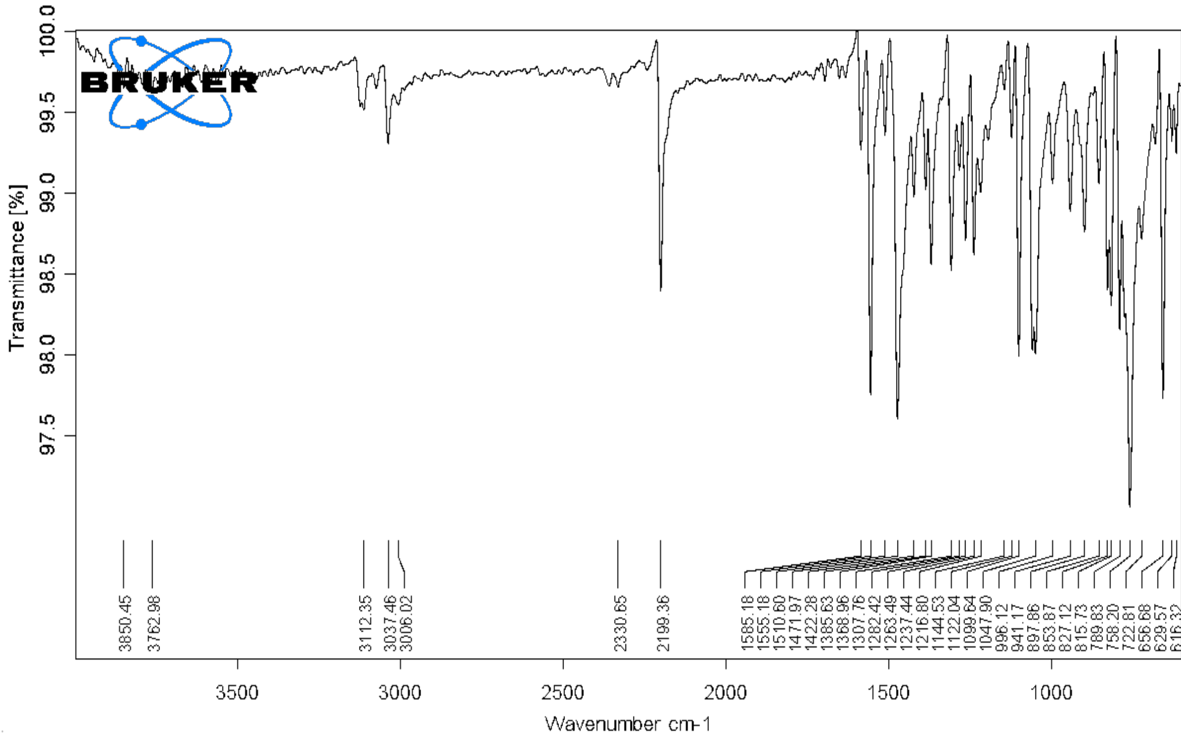

Figure 1. FTIR spectrum of Pure Luliconazole

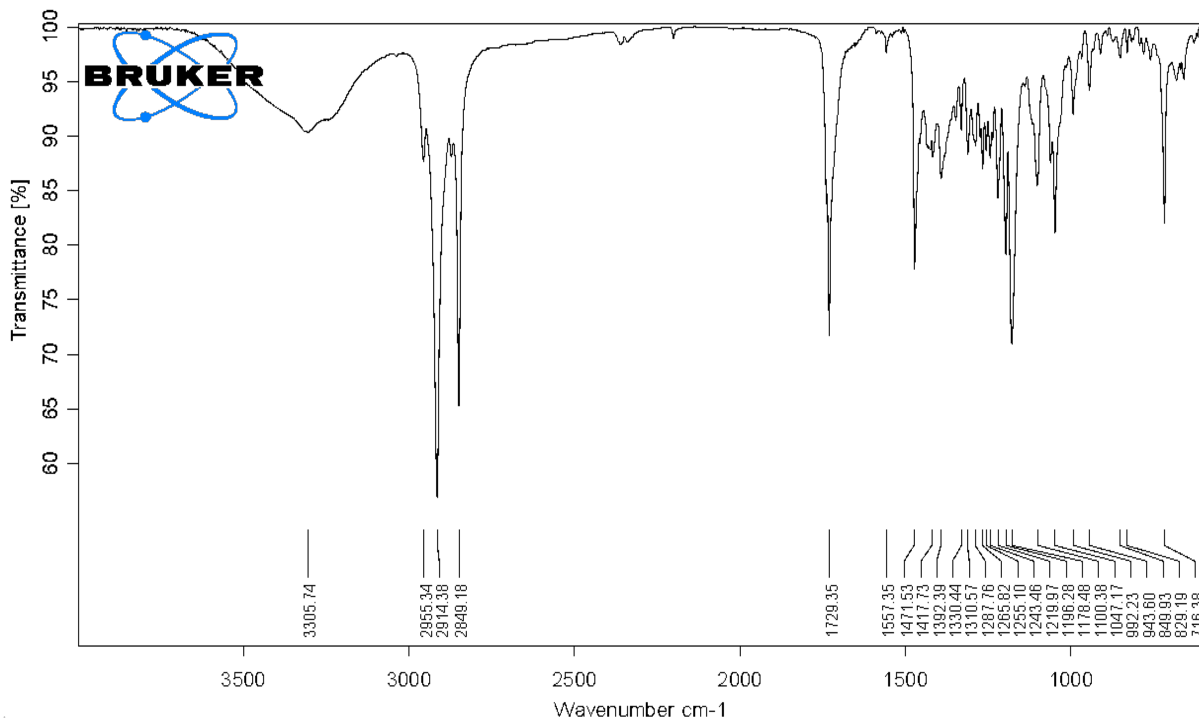

Figure 2. FTIR spectra of pure GMS

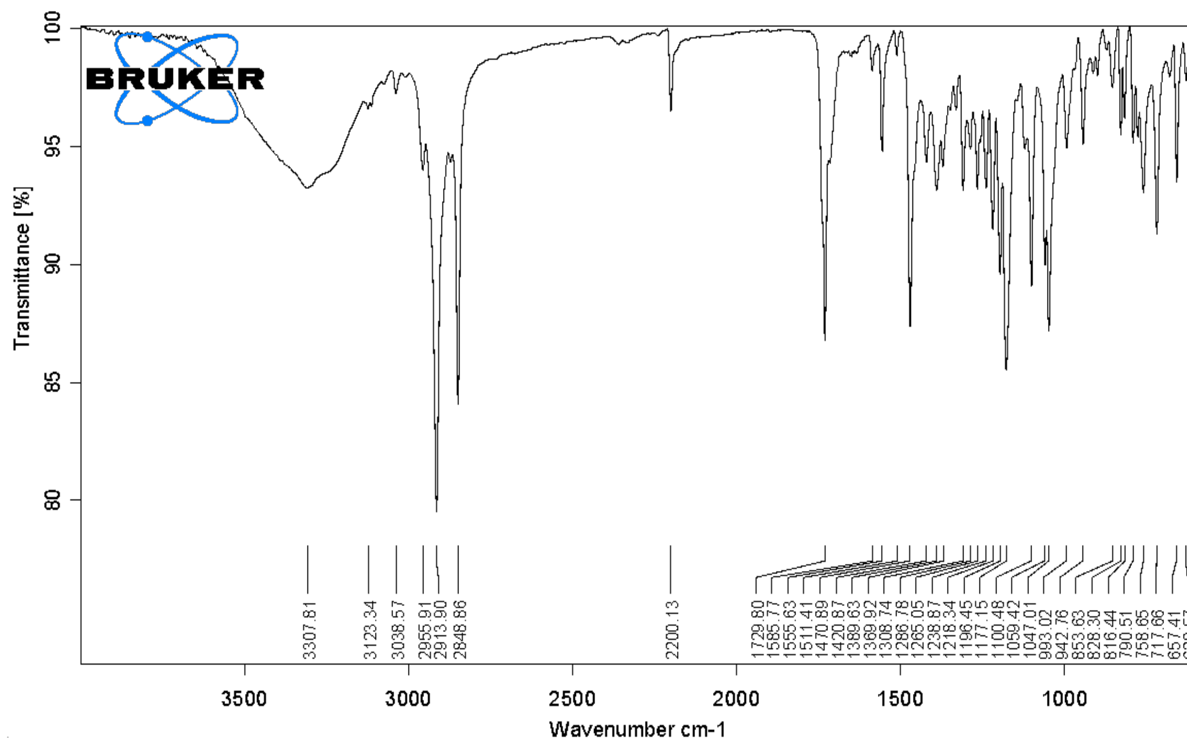

Figure 3. FTIR spectrum of Luliconazole and GMS physical mixture

3.2. Evaluation of Particle Size, PDI, and Entrapment Efficiency (%) of Luliconazole Nanosuspensions

All the Luliconazole nanosuspensions were assessed for particle size, PDI, and entrapment efficiency (%) to optimize the formulations and identify the one with the smallest particle size and highest entrapment efficiency. The results showed that the particle size varied between 122.6 and 203.1 nm, the PDI ranged from 0.233 to 0.449, and the entrapment efficiency ranged from 63.6 to 78.4% (Table 3). LN-4 formulation had a particle size of 122.6 nm and an entrapment efficiency of 78.4%, and was considered to be the most ideal formulation, as it possessed a smaller particle size and increased entrapment efficiency when compared to the other 5 formulations. The result is likely attributed to the optimum level of GMS, leading to efficient encapsulation of luliconazole into the lipid carrier. The lipid core was, in turn, enveloped by a surfactant layer, resulting in drug retention and leakage prevention. Increased sonication time also significantly contributed to particle size reduction, thereby resulting in nanoparticles with a small particle size distribution with a monodisperse system. Additionally, gel incorporation improves the skin penetration and provides sustained action. The particle size, PDI, and entrapment efficiency values of all the nanosuspensions are presented in Table 3, and the results of the particle size and PDI of formulation LN-4 are represented in Figure 4.

Table 3. Results of Particle size, PDI, and % EE of Luliconazole nanosuspensions

Formulation	Particle size(nm)	PDI	%EE
LN-1	203.1	0.352	63.6
LN-2	183.6	0.348	67.4
LN-3	155.6	0.233	73.4
LN-4	122.6	0.318	78.4
LN-5	138.7	0.449	75.6

3.3. Preparation of Optimized Nanosuspension Topical Gel

The optimized Luliconazole nanosuspension (LN-4) was entrapped in gel using 1% carbopol-934 as the gel base. Initially, 1% carbopol-934 was hydrated in 100 ml of distilled water at room temperature overnight. The hydrate mixture was then stirred using a mechanical stirrer until a uniform gel consistency was obtained. To this gel, 30 ml of the optimized Luliconazole nanosuspension was added to the Carbopol gel base and mixed gently to ensure even distribution. Methyl and propyl parabens (0.02%) were then added and thoroughly mixed. Triethanolamine was introduced dropwise to adjust the gel's pH. Lastly, distilled water was added up to the desired consistency and yielded a smooth, translucent, whitish topical nanosuspension gel. The optimized Luliconazole nanosuspension gel composition is shown in Table 4, and the prepared gel is depicted in Figure 5.

Figure 4. Particle size and PDI of optimized nanosuspensions LN-4

Table 4. Formulation composition of Luliconazole nanosuspension gel

Ingredients	Quantity
Luliconazole nanosuspension dispersion	30 mL
Carbopol-934	1% w/v
Methyl paraben	0.02%
Propyl paraben	0.02%
Triethanolamine	q.s. to adjust pH
Distilled water	Upto 100 ml

Figure 5. Luliconazole nanosuspension gel (LUL-NSG)

3.4. Evaluation of Luliconazole Nanosuspension Gel (LUL-NSG)

3.4.1. Zeta Potential (ZP)

Zeta potential is one of the primary parameters for assessing the physical stability of nano-formulations. The zeta potential of the LUL-NSG was -26.9 mV, showing good stability. In general, zeta potential values between -25 mV and +40 mV are said to be indicative of stable formulations. The electrostatic repulsion noted, as indicated by the zeta potential, is a result of the negative surface charges on the nanoparticle, and with time, hydrolysis can release fatty acids, with the possibility of further increasing the negative charge. LUL-NSG's ZP data is illustrated in Figure 6.

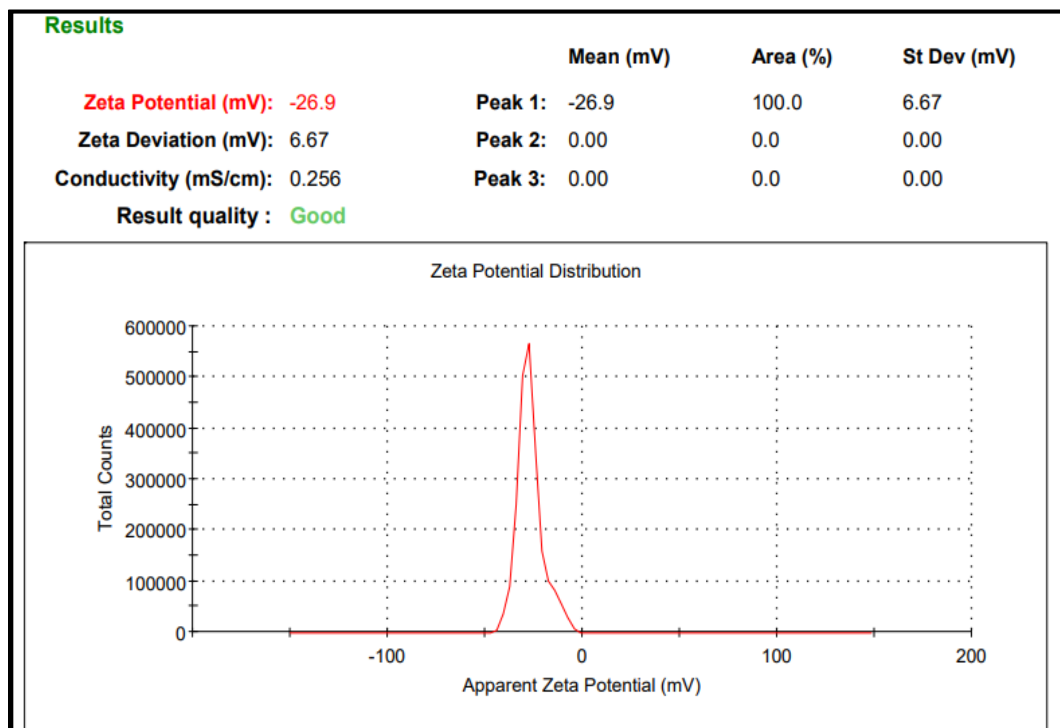

Figure 6. Zeta potential of LUL-NSG

3.4.2. Physical Appearance

The optimized formulation of LUL-NSG was visually examined for general appearance and found to be a white, clear, translucent gel.

3.4.3. pH, Spreadability, and Drug Content

The pH of the optimized formulation was found to be 5.8 ± 2.65. Spreadability of LUL-NSG was 11 ± 3.54 gm.cm/sec, and the drug content was 94.56 ± 2.33%. All the parameter results proved that LUL-NSG exhibited a remarkable physical appearance with a pH level appropriate for safe skin use. Its spreadability was in an acceptable range, which guarantees even distribution and a good spreading coefficient, which favours the effective diffusion of the drug across the skin layers. Table 5 summarizes the pH, spreadability, and content of LUL-NSG.

Table 5. Results of pH, spreadability, and drug content of LUL-NSG

Name of Parameter	Result value
pH	5.8 ± 2.65
Spreadability (gm.cm/sec)	11± 3.54
Drug content (%)	94.56% ± 2.33

3.4.4. Viscosity

The viscosity of the LUL-NSG was determined using a Brookfield viscometer with spindle T-95 at the shear rates of 5, 10, 20, 50, and 100 rpm. Rheological analysis revealed viscosity between 588.2 and 4238.4 cps, which is suitable for semisolid products. The rheogram also showed shear-thinning behaviour, wherein the viscosity decreased with increased shear rate, revealing pseudoplastic, non-Newtonian flow behaviour, which is highly suitable for topical applications. This property enhances manufacturing productivity and spreadability on the skin. Additionally, the formulation recovered its viscosity quickly upon application, meaning improved retention in the skin. The rheogram of LUL-NSG is presented in Figure 7.

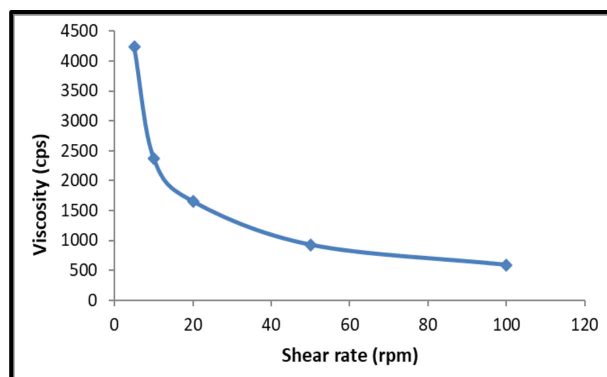

Figure 7. Viscosity of optimized LUL-NSG

3.4.5. Surface Morphology by TEM

Clear spherical nanoparticles with smooth, homogenous surfaces could be seen in TEM images, and the particle size values obtained from TEM were closely similar to the PS values from DLS analysis, as a measure of uniform distribution and lack of agglomeration. This, in turn, verifies the accuracy of size distribution data and nanoparticle formulation stability. The homogeneous size

distribution and uniform surface morphology indicated by Figure 8 imply that the drug is uniformly encapsulated within the polymeric matrix, leading to sustained release behaviour. Such studies employing nanoparticles have also found identical morphological features, in which spherical shape and homogeneity indicate successful entrapment of drug within the lipid vesicles surrounded by a surfactant layer [15,16].

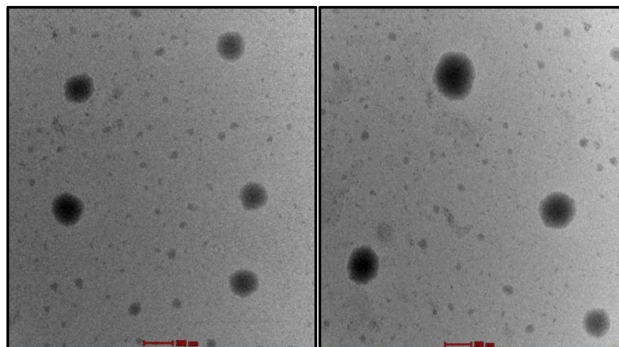

Figure 8. TEM analysis of optimized LUL- NSG

3.4.6. *In-vitro* Drug Release Study

The study was performed within a span of 8 hours, and proved that the optimum LUL-NSG formulation obtained an 83.46% maximum release of the drug, which is considered sufficient for topical delivery. An initial burst release was observed during the first 50 minutes, probably due to the rapid diffusion of the drug across the membrane. After this, the release profile shifted towards a more prolonged trend, perhaps because the drug was held in the solid lipid core of the nanoparticles, where it was buffered from ready diffusion. Further, the entrapment of the nanoparticles in a gel matrix retarded the release rate. The gel's viscous character resulted in a slow release of drug from 60% to 83% and the release was prolonged for about 8 hours to achieve the peak of 83.46%. This release profile, consisting of a burst followed by slow release, indicates the ability of the LUL-NSG gel formulation to provide therapeutic levels of the drug for an extended duration, lessening the frequency of application and improving compliance in patients for topical antifungal treatment [31]. The drug release profile of LUL-NSG is shown in Figure 9. In comparison to the previous study carried out by Bhoyar *et al.* on Luliconazole topical hydrogel, we observed that the study has shown a good drug release up to 79.49% in 8 hours, whereas our study claimed that the drug release can be further enhanced to 83.46% in 8 hours when incorporated into nanosuspension gel using GMS [32].

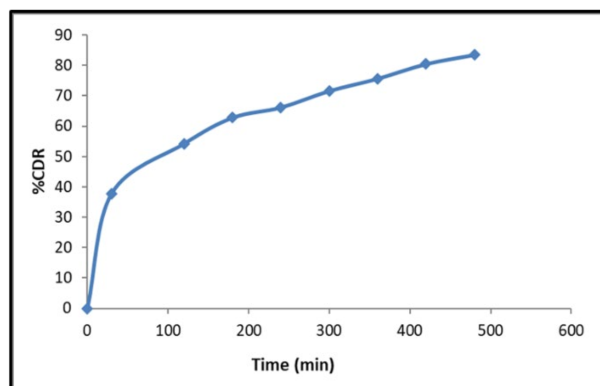

Figure 9. *In-vitro* drug release profile of LUL-NSG

3.4.7. Drug Release Kinetics

Among all the models tested, the Higuchi kinetic release model showed the highest regression value, indicating that the formulation followed this model. Higuchi model predicts that the drug release from the nano gel formulation is a diffusion-controlled process. The release rate is inversely proportional to the square root of time, which means that the release process is controlled by the drug molecules diffusion into the gel matrix. Moreover, as the nanoparticles can penetrate deeper layers of skin, the formulation can provide prolonged and effective drug delivery. The Higuchi drug release kinetics profile of LUL-NSG is shown in Figure 10.

3.4.8. *In-vitro* Skin Irritation Study by HET-CAM

The HET-CAM test was employed to determine the potential for *in vitro* skin irritation of the optimized formulation on the chick embryo chorioallantoic membrane (CAM). Irritation scores of the optimized formulation were compared with standard (0.9% NaCl) and positive control (1% SDS). Positive control (1% SDS) caused extreme irritation in the form of haemorrhage and vessel lysis with an average score of 12.38. On the other hand, the control (0.9% NaCl) also had a minimal mean value of 0.08 and was found to be irritation-free. The optimized formulation possessed a mean irritation score value of 0.07 and no ocular irritation. Such observations confirm that the optimized formulation belongs to the non-irritant group, confirming that it is safe for use on the surface of the skin. Representative images from the HET-CAM test are provided in Figure 11.

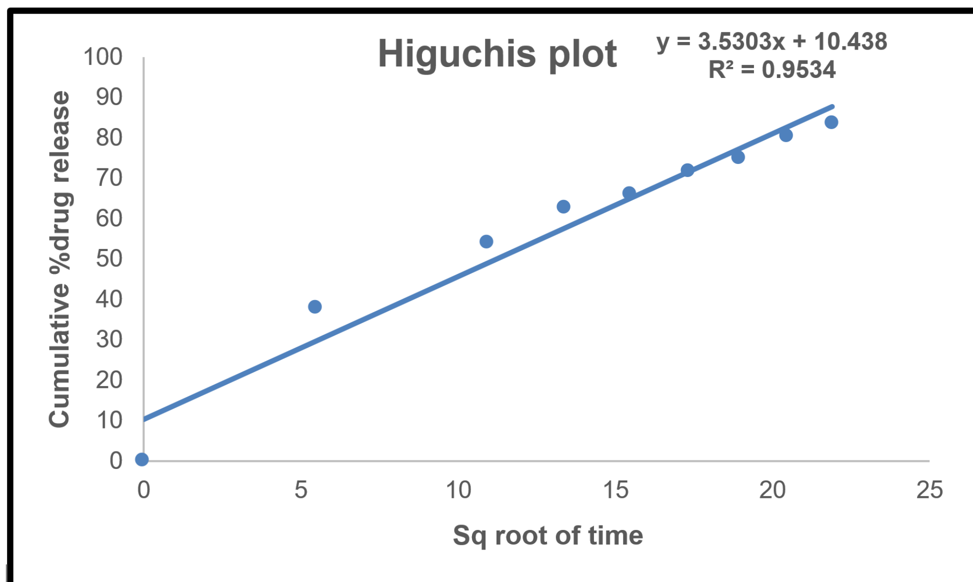

Figure 10. Higuchi release kinetics plot

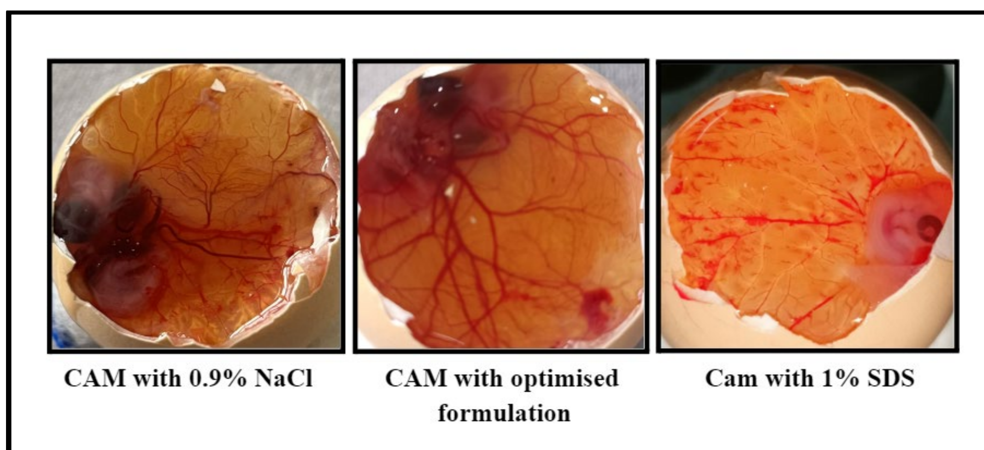

Figure 11. HET- CAM test images

4. Conclusions

This study focused on developing a Luliconazole nanosuspension gel for the treatment of skin fungal infections. Luliconazole nanosuspensions were prepared by the solvent evaporation technique and subsequent ultrasonication, with GMS being employed as the lipid. The best nanosuspension was chosen based on the smallest particle size and the highest entrapment efficiency. The LN-4 formulation was concluded to be the best and hence was formulated into a topical gel. The gel showed excellent zeta potential, indicative of better physical stability. Parameters, including pH, spreadability, and the viscosity of the gel, were within the acceptable values. The formulation was also found to sustain drug release for more than 80% after 8 hours. The HET-CAM test further indicated no irritation. In summary, the research suggests Luliconazole NSG may be a viable and effective option in treating topical fungal infections.

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Conflicts of Interest

The authors declare that there were no competing interests found.

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