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Research Article

Development and characterization of Luliconazole Loaded Solid Lipid Nanoparticles for Topical Delivery

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A B S T R A C T

Superficial fungal infections in immunocompromised patients can lead to various disorders and complications. There is a critical need for new topical treatment options for these fungal infections. Luliconazole (LUZ) is a topical antifungal medicine used to treat fungal infections. This paper aims to develop a new topical gel incorporating Luliconazole SLN (LUZ-SLN). The study suggests that LUZ-SLN embedded in a gel could serve as an effective drug delivery system for topical antifungal treatments. Initial experiments were conducted to characterize the LUZ-SLN and compare it with the raw drug. The prepared gel was found to be homogeneous, safe for human use, and non-irritating. The nano-systems demonstrated a 5-fold enhancement in solubility, a s4-fold increase in dissolution velocity, greater skin retention, and improved antifungal activity. The LUZ-SLN gel showed the highest drug retention in different skin layers within 8 hours. Additionally, both LUZ-SLN and Control exhibited higher ZOI (Zone of Inhibition) values (93mm and 87mm, respectively) compared to marketed cream (83mm). This suggests that the LUZ-SLN-loaded gel was more effective in combating the fungus. Therefore, the LUZ-SLN-loaded gel presents a new approach with improved activity and enhanced dermal delivery for drugs with poor aqueous solubility, compared to traditional drug-containing gel formulations.

Keywords: Luliconazole, Solid Lipid Nanoparticles, Nanotechnology, Emulsion method, Controlled release, Antifungal

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INTRODUCTION:

Fungal infections are one of the most common skin diseases, affecting approximately 25% of the population. It is estimated that 40 million people in developing and developed countries are affected by fungal infections. Studies have shown that vaginal mycosis is one of the three most common infections in humans. The number of fungal infections increases with changes in age, climate and disease. People taking antibiotics, corticosteroids, immunosuppressive drugs, and birth control pills are more susceptible to fungal infections[1]

Until now, fungal infections were fought with oral antibiotics. While antifungal drugs are commonly used to enhance the effect of the drug in the treatment of rare fungal infections, oral therapy is often associated with side effects such as nausea, vomiting, headache, and nephrotoxicity and hepatotoxicity. Therefore, primary care is a suitable treatment method for infectious diseases, which has the advantages of targeting the site of infection, reducing systemic side effects, improving treatment effectiveness, and improving patient compliance. The effectiveness of antifungal treatment depends onkey factors such as penetration of the drug into the target area and residence time for effective absorption of the drug through the skin. In central administration of anti-inflammatory drugs, the drug must penetrate the stratum corneum. In this context, selectivity may play an important role in drug penetration into the skin. This method of treating infections involves the use of ointments, creams, gels, & lotions that require large quantities, and frequent use due to the short residence time on the skin and long duration of use. Therefore, there is a need for an innovative delivery system that can accurately deliver drugs to the target site and effectively distribute them to different parts of the skin.

Solid Lipid Nanoparticles (SLN)

SLNs were introduced in the late 20th century. They have been used to replace traditional drug carriers such as emulsions, liposomes, microemulsions, and other polymer-

containing formulations. Solid lipid nanoparticles were first developed for oral administration [2]. They are not without the problem of lipid toxicity and industrialization. It is a nano-sized drug contained in lipid that remains solid at room/body temperature. They can be produced in small sizes from 50 nm to 500 nm. Their size increases their surface area, causing them to exhibit more drug. They provide the potential for diffusion of chemicals and nutrients. Additionally, solid lipid nanoparticles produce less toxicity than other methods due to their biocompatibility [3].

Luliconazole is a novel, broad-spectrum, imidazole antifungal agent primarily used for the topical treatment of superficial fungal infections, including tinea pedis (athlete's foot), tinea cruris (jock itch), and tinea corporis (ringworm). Approved by regulatory agencies for its potent antifungal activity, luliconazole demonstrates a high level of efficacy against dermatophytes and certain non-dermatophyte fungi, offering advantages over traditional antifungal agents. Luliconazole exerts its antifungal effects by inhibiting the enzyme **lanosterol 14-α-demethylase** (a cytochrome P450-dependent enzyme). This inhibition disrupts the biosynthesis of ergosterol, a critical component of fungal cell membranes. The depletion of ergosterol leads to increased membrane permeability and ultimately results in fungal cell death. Luliconazole is characterized by its high lipophilicity, which facilitates rapid and deep penetration into the stratum corneum and dermis. It has a prolonged retention time in the skin, allowing for once-daily dosing and improved patient compliance.When applied topically, systemic absorption is minimal, and drug levels in plasma remain negligible, reducing the risk of systemic side effects. Luliconazole's localized action minimizes its impact on the body's other biological processes, making it highly selective and effective against fungal pathogens. In this study, luliconazole was loaded into solid lipid nanoparticles (SLNs) to increase its penetration into the skin owing to the lipidic nature of SLNs. The drug-loaded SLNs were absorbed into a gel to enhance skin retention time. This development could potentially improve the effectiveness of luliconazole as a topical antifungal drug.

MATERIAL AND METHOD:

Luliconazole API was supplied by Maithri Drugs Private Limited, Hydrabad, India, as a gift sample. Steric acid was purchased from Merck Chemical Company (Mumbai, India). Carbopol 934 was purchased from Loba Chemie, Mumbai, India. Tween 80 was purchased from S D Fine-Chem Limited, Mumbai. Thermo Fisher Scientific India Pvt. Ltd. Mumbai purchased methyl paraben and propyl paraben. All other chemicals and solvents were used without further purification and were of analytical grades.

Preformulation Studies

1. **Morphological Characterization:**

The physical characteristics of luliconazole, including color, odor, taste, and nature, were evaluated.

2. **Melting Point Determination**:

The melting point of luliconazole was determined using a capillary tube sealed at one end and placed in a paraffin-filled melting point apparatus. The temperature was recorded from the start to the complete melting of the drug.

3. **Solubility**:

Solubility was assessed by dissolving 50 mg of luliconazole in 3 mL of various solvents (methanol, ethanol, acetone, chloroform, water, PBS pH 7.4) and shaking for 24 hours. After centrifugation, the supernatant was analyzed for solubility.

4. **Partition Coefficient**:

The partition coefficient (Log P) was determined by shaking luliconazole (1 mg/mL in water) with octanol. The concentrations in both phases were measured using UV spectrophotometry at 296 nm, and Log P was calculated as the ratio of drug concentration in the organic phase to the aqueous phase.

5. **UV-Visible Spectroscopy**:

a. **λ max Determination**: Luliconazole dissolved in ethanol was analyzed using UV spectrophotometry to identify its maximum absorbance (λ max) in the range of 200-400 nm.

b. **Calibration Curve**: Calibration curves in methanol and phosphate buffer (pH 7.4) were prepared by measuring the absorbance of dilutions (2-12 µg/mL) at λ max 296 nm.

6. **Fourier Transform Infrared Spectroscopy (FTIR)**:

FTIR spectra of luliconazole were recorded over a range of 4000–400 cm^{-1}. The spectra were analyzed to confirm functional groups and assess interactions with excipients.

7. **Compatibility Studies**:

Compatibility studies were performed by comparing the FTIR spectra of pure luliconazole with physical mixtures of the drug and excipients. Characteristic peaks of luliconazole were observed at specific wave numbers.

Preparations of luliconazole loaded solid lipid nanoparticles (SLN)

Solid lipid loaded Luliconazole drug was prepare by using melt emulsification method. In the lipid phase, a known amount of drug and steric acid were taken and dissolved in small quantities of methanol in a beaker to obtain a lipid-drug matrix. Aqueous phase was prepared by taking tween 80 in 10 ml distilled water and heated to 70^0C under continuous stirring. Aqueous phase was poured dropwise to lipid phase using a magnetic stirrer at 1000rpm for 15 min. The resulting dispersion was probe sonicated for 10 min. The mixed solution was transferred in ice water bath and stirring for 4 hours at 3000 rpm. Different formulation of drug loaded SLN were prepared by varying concentration of steric acid and surfactant.

Table 1: Composition of Different Solid Lipid Nanoparticles.

Formulation	Drug (mg)	Steric acid (mg)	Tween80 (%)
SLN-1	100	1000	2.0
SLN-2	100	1250	2.0
SLN-3	100	1500	2.0
SLN-4	100	1000	2.5
SLN-5	100	1250	2.5
SLN-6	100	1500	2.5

Evaluation of SLN

a. Evaluation of entrapment efficiency

Drug EE of drug can be calculated by weight amount of luliconazole added SLN were added in phosphate buffer 7.4 and diluted with 100ml phosphate buffer 7.4 solution. And sonicate for 10 minutes, then centrifuged at 1000 rpm for 15min then the supernant was withdrawn, and further diluted by buffer 7.4 solution and analyses at wavelength max at 296 nm of luliconazole using UV spectroscopy.

The results are shown in **Fig No 7.**

EE % = W (Added drug) −W (free drug) / W (Added drug) x 100

Where, W (added drug) is quantity of drug added during preparation of SLN, and W (free drug) is quantity of free drug measured in supernatant after centrifugation.

b. Physicochemical property

Physicochemical Properties of SLN dispersions were characterized as colour, odour, pH, and solubility of SLN-6 in aqueous medium.

c. Particles Size analysis and PDI:

At room temperature, mean particle size and PDI of luliconazole-loaded SLN analysed using a nanoparticle analyser and (DLS). Sample dissolved in water and sonicated for 20 minutes. After that this solution can be diluted and analyse the size of solid lipid nanoparticles. The results are shown in **Figure No 8.**

d. Zeta Potential:

The charges on the surface of luliconazole-loaded SLN was determine at room temperature, by using Malvern nanoparticle analyser was determined using solid lipid nanoparticles. The ZP was determined after dilution of sample with Distilled water at room temp. the results are shown in **Figure no 9.**

e. Scanning Electron Microscopy:

SEM used to examine the surface structure of SLN (SEM). An SEM image of a solid lipid nanoparticles can also be used to show its structure. SEM used to examine the morphology of luliconazole SLN. The result is shown in **Figure no 10.**

Formulation of Solid lipid nanoparticles loaded topical gel:

The gel developed as per referenced protocol with slight modification. Briefly, Carbopol 934P placed in defined quantity of distilled water while constant stirring at 600 rpm and followed by adding of methylparaben (0.02% w/v) and propylparaben (0.1% w/v) and remained undisturbed with continuous stirring for 30 min. Prepared gel base set aside for 24 hrs. Next, SLN F6 disseminated with measured quantity of propylene glycol (5% w/w) and 1% ethanol (20% w/w) and far ahead it added to carbopol gel bases with continuous shaking at 1000 rpm and followed by churning for 30min. Tri-ethanol amine (TEA) subjected to the final stage to maintain pH (5.5 - 6.5) for drug stabilization and stirred thoroughly to obtain clear gel**.**

The same procedure applied to get three formulations having varying amount of carbopol and aim is associated to prepare different forms of gel is to obtain best homogeneous anduniform texture with stable physicochemical reliability in respect of % release of leading moiety. Different formulations of SLN gel are enlisted as in Table;

Table No 2: Preparation of different formulations of solid lipid nanoparticles containing gel

Formulation code	Carbopol 934 % (w/v)
G1	0.5%
G2	1%
G3	1.5%

Characterization of gel

a. Appearance:

The visual appearance, odour, texture, of the SLN-based topical gels were evaluated upon application, including grittiness, consistency, and uniformity. The results are shown in **Table No 11.**

b. pH determination:

pH of each SLN Gel was determined using digital pH meter. Each 50 mg formulation was added in beaker and pH of formulation was determined by using calibrated pH meter. The result is shown in **Table No 12.**

c. Gel strength:

20 ml of formulation was placed in 25 ml graduated cylinder and gelled in thermostatically controlled water bath at 37°C. A weight of 5 g was placed onto the gel. The time required to travel 2 cm distance for the 5 g weight through gel was determined.

d. Viscosity:

Viscosity of the gel formulation was calculated using a Brook-field viscometer and a suitable spindle number and RPM.T-bar spindle (Spindle-R/S, S-75) was lower perpendicularly into the gel in a beaker, being careful not to

touch the bottom of beaker. The spindle was rotted at 60 rpm, and the readings were taken after 60 seconds, when the gel level had stabilised. The results are shown in the **Table No 13**.

e. Spreadability:

Using the spread ability apparatus, spread ability was calculated. The device consists of 2 slides, one of which is fastened firmly in a wooden frame and the other of which may easily be placed on top of the fixed slide. Two grams of extra gel are sandwiched between the equipment' two slides. The slides can support a weight of 1 kg before being discharged. Slide edges that have extra gel are carefully cleaned off. The top slide is pulled by 80 gm of weight while the bottom slide is securely fastened. The top slide must travel 5 cm in the specified number of seconds. Better spread ability is indicated by a shorter interval. Following that, spread ability was determined using the following formula:

$$S = \frac{M \times L}{T}$$

Where,

S = is the Spreadability,

M = weight pan (tied in the upper pan),

L= length moved by the glass slide,

T = Time in seconds taken to separate the slide completely.

The result is shown in **Table No 14.**

a. Drug Content:

The drug content of SLN loaded gel was determined by diluting 1mL of the formulation with100 mL methanol, further diluted 10ml to 50ml with methanol followed by analysis with UV-visible spectrophotometer

b. *In-Vitro* drug diffusion Study:

In Vitro drug diffusion study was performed on the Franz diffusion cell using cellulose acetate membrane. Phosphate buffer pH 7.4 was used as diffusion medium and previously put in contact with membrane 30 min before placing the sample.Phosphate buffer pH 7.4 was placed in receptor compartment of franz diffusion cell. The receptor compartment was continuously stirred using magnetic bar and the temperature was kept at 37±0.5 °Cusing water bath. The experiment was started with the even application of 0.5 gm of SLN gel on the surface of cellulose acetate membrane from donor compartment side. Sampling was performed after 0.5, 1, 2, 6, and 12 hr and the fresh diffusion medium was added with each withdrawal of sample. The samples were diluted and analysed at 296 nm UV Visible spectrophotometrically.

c. *In vitro* antifungal activity

In vitro antifungal activity study was performed against *Candida albicans* species using modified agar diffusion method. Sabouraud's dextrose agar (SDA) was used for the preparation of cultures and incubation of fungal species. Cultivation/incubation media was prepared and sterilized (by autoclaving at 15 psig pressure, 121°C for 15 min). Fresh cultures of *C. albicans* were prepared and incubated at 37±2°C for 48 hr in dark condition. Sterilized SDA plates were prepared and a spherical well was made with a sterile borer in an aseptic area. Each formulation (SLN gel, and marketed formulation) was mixed thoroughly with the medium and poured into the wells on an agar plate under sterile conditions. The plates were dried and incubated at 37±2°C for 48 hr. The zone of inhibition was measured at the end of incubation.

d. Stability studies:

Optimized formulation was subjected to stability as per ICH guidelines at the following conditions (ICH, 2003).

Samples were kept in stability chamber at following conditions for 3 months-

1. 40± 2°C and 75 ± 5% RH (Accelerated temperature)
2. Room temperature

Formulations were analysed at 1, 2 and 3 months for following tests-

i. Visual appearance
ii. pH
iii. Gel Strength
iv. Spreadability
v. *In vitro* drug release

RESULT AND DISCUSSION

Preformulation Studies

1. Morphological Characterisation:

The pure API sample of luliconazole was found to be white, odourless, amorphous powder.

Table 3: Result of Organoleptic Properties

Sr No	Parameters	Specification	Observation
1	Nature	Amorphous	Amorphous
2	Colour	White	White
3	Odour	Odourless	Odourless

2. Melting point determination

Melting Point of luliconazole was found range of 149-151^{0}c, while as per literature standard it is reported to be 150-152^{0}c.As per practical value it could be concluded that luliconazole was in pure state.

3. Determination of Solubility:

The solubility of the drug in different solvents was studied and a solvent to be used in the final formulation was selected. The solubility was analysed using UV-VIS spectrophotometer at 296nm.

Table 4: Result of Solubility of luliconazole

Solvent	Solubility in (mg/ml)
Water	0.009±0.000
PBS 7.4	0.026±0.005
Ethanol	12.748±0.000
Acetone	17.794±0.038
Chloroform	19.963±0.519
Methanol	23.538±0.628

4. Partition coefficient:

Partition coefficient is normally used to determine the lipophilic and hydrophilic nature of a substance. Compounds with log p more than 1 are lipophilic in nature whereas those with less than 1 are hydrophilic.

.

Table 5: Partition coefficient of luliconazole

Partition coefficient of drug	Solvent system	Log P Values
Luliconazole	n-octanol: water	2.806±0.005 3.49

5. UV-VIS Spectrophotometric method for luliconazole:

Determination of λ max

The standard solution of luliconazole in different solvent media were scanned between 200- 400 nm in UV spectrophotometer. The maximum absorbance was observed at 296 nm in case of phosphate buffer. Thus, the working wavelength max was chosen as 296nm. The spectrum of luliconazole shows in **Figure No 1.**

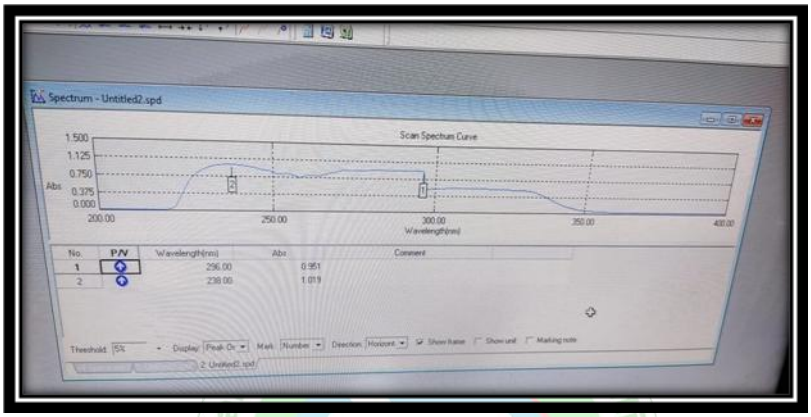

Figure 1: Wavelength max of Luliconazole

Preparation of Calibration Curve of Luliconazole:

Calibration Curve of Luliconazole in Methanol

The calibration of luliconazole in methanol was found to be linear in conc. range at 0, 2, 4, 6, 8, 10 µg/ml having a coefficient of regression (R2) value 0.9945.

Table 6: Absorbance of Luliconazole in methanol

Concentration µg/ml	Absorbance
0	**0**
2	0.128
4	0.254
6	0.341
8	0.458
10	0.556

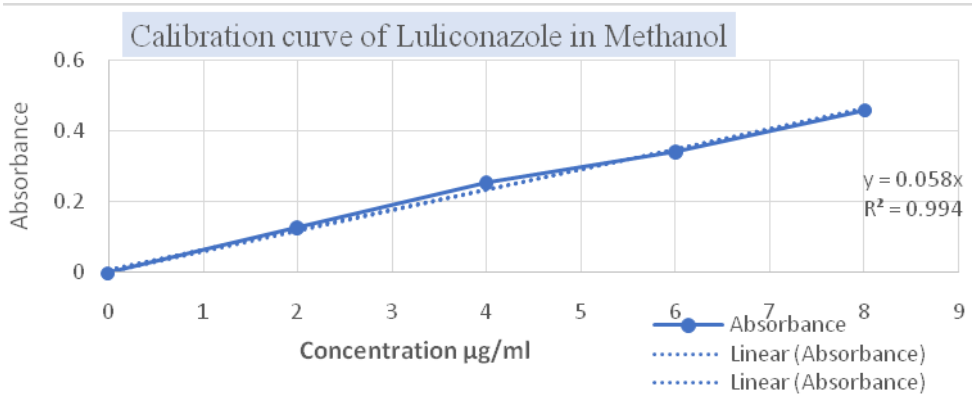

Figure 2: Calibration Curve of Luliconazole in Methanol

Calibration Curve of luliconazole in phosphate buffer 7.4

Table 7: Absorbance of Luliconazole in PBS

Concentration µg/ml	Absorbance
0	0
2	0.156
4	0.365
6	0.493
8	0.638
10	0.789

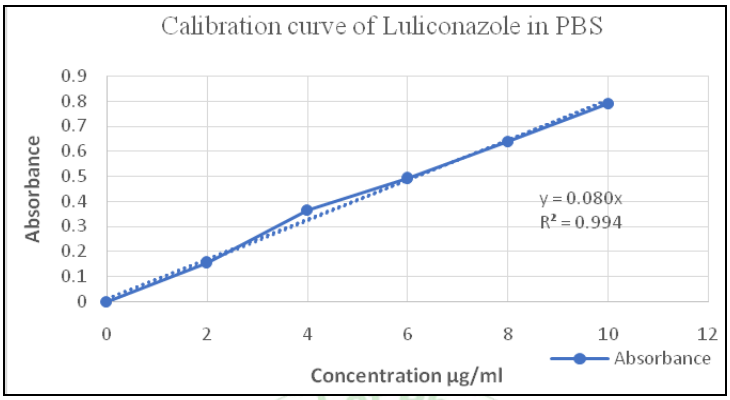

Figure 3: Calibration Curve of Luliconazole in PBS

6. Fourier Transform Infrared Spectroscopy (FTIR)

The infrared spectrum of pure luliconazole recorded by FTIR spectrometer is shown in fig 19 which was compared with standard functional group frequencies of luliconazole shows in table show that functional group frequencies of luliconazole were the reported range which indicate the purity of luliconazole.

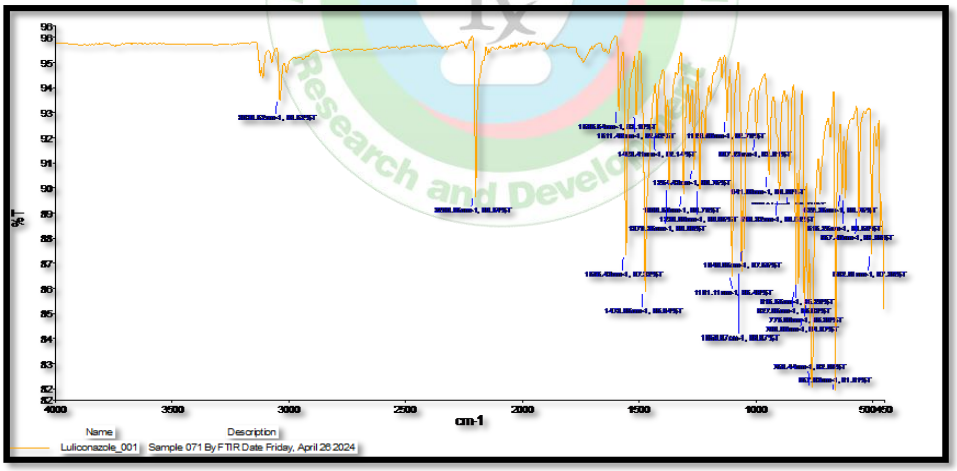

Figure 4: FTIR Spectrum of pure Luliconazole drug.

Table 8: Interpretations of Luliconazole (Pure Drug) FTIR Spectra

Functional Group	Standard frequencies cm-1	Observed frequencies cm^{-1}
C-H Aromatic stretch	3000-3100	3039.52
C=C stretching	1650-2000	1586.54
N-H Bend (Secondary amine)	1580-1650	1556.43 & 1511.48
C-N stretch (aromatic amine)	1000-1350	1370.26
C-N stretch (aliphatic amine)	1020-1250	1059.67
O-H bend (alcohol/phenol)	1310-1360	1309.60
C-Cl Stretching	600-800	790.96

7. Drug and Excipient Compatibility Study:

FTIR analysis of SLN-6 performed to determine possible interaction between drug and drug additives. spectral data reveal principal absorption peaks of luliconazole at 2955.75 cm-1 for C-H stretching, 2523 & 2647 cm-1 for S-H stretching, 2201.52 cm-1 for C≡N stretching, 1556.90 cm-1

for C=N stretching, 1471.88 cm-1 for C=C aromatic ring stretching and 720.33and 1101.29 cm-1 for C-Cl stretching. Whereas, principal absorption peaks of stearic acid were found at 2914.97cm-1& 2848.05 cm-1 in high-frequency region attributed to -CH2- band asymmetric and symmetric stretching vibrations, whereas and 1698.03 cm-1 for -COOH stretching is attributed in low-frequency region. Spectral analysis of optimized SLN confirmed that there are no more changes in luliconazole after successful formation of SLN. Spectral data strongly supports referenced values as reported.

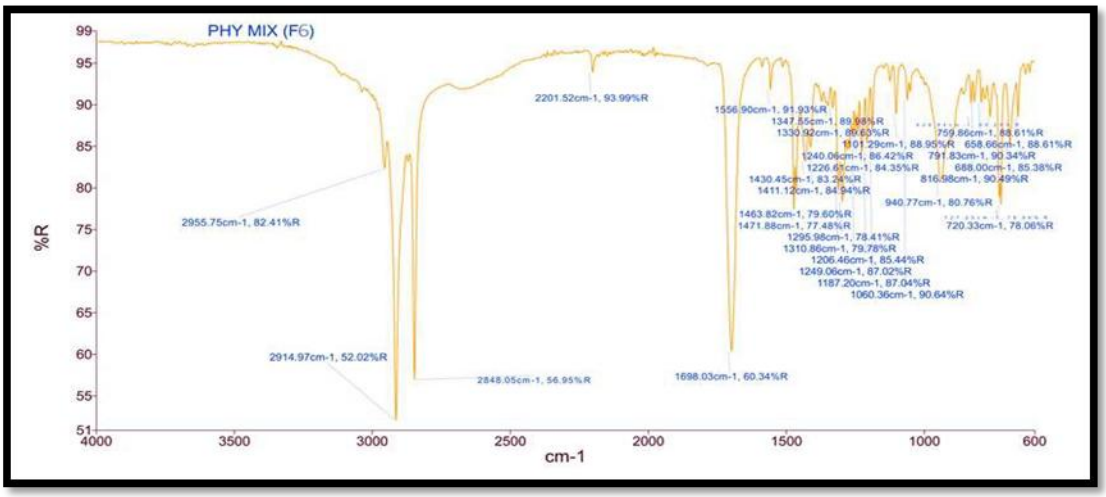

Figure 5: FTIR Spectrum of SLN-6

Table 9: FTIR interpretation of SLN-6

Functional Group	Standard frequencies cm-1	Observed frequencies cm^{-1}
C-H stretch	2850 - 3000	2955.75 2914.97 2848.05
C≡N Stretch	2100 - 2400	2201.52
C=C alkene stretch	1650 - 2000	1698.03
C=C Aromatic stretch	1450 - 1650	1463.82
C-Cl stretch	600 - 800	609.29

Preparation of SLN Dispersion:

The lipid selected was stearic acid according to the solubility studies of various lipids. The particular concentration of lipid was melted above at a low concentration, resulting in a smaller particle size. stearic acid was selected for further evaluation. its melting point, and the drug was added to form a clear mixture; this is the oil phase. The aqueous phase was prepared by dissolving the selected surfactant, *i.e.*, tween 80 in the required quantity of distilled water under the same temperature as the oil phase. The aqueous phase is incorporated into the oil-phase dropwise under magnetic stirring while maintaining the temperature constant. This solution was homogenized for 5 min under 8000 rpm and then sonicated for 5 min. This nano-dispersion was allowed to cool to room temperature to yield nanoparticles.Further, in optimization of SLN, method archived step by step with alternate changes in concentration of stearic acid and tween80 (w/v). All prepared groups of SLN were coded successfully and proceed to quantitate percent entrapment of active moiety spectrophotometrically at 296 nm. Obtained data were evaluated statistically. SLN which deal with high entrapment of luliconazole chosen as optimized SLN and proceed for further evaluation

.

Figure 6: Prepared SLN batches of Luliconazole

Evaluation of SLN

1. Determination of entrapment efficiency

Initially, in pre-formulation studies, luliconazole characterized physicochemically and spectroscopically. After successful formation of different batches of nanoparticles, percentage EE of luliconazole determined. Percentage of EE evaluated spectrophotometrically at 296 nm. Thereafter results reveal that SLN F6 and SLN F1 have highest and lowest % EE of luliconazole loaded SLN by 95.52% and 85.65% w/w respectively. Similarly, study cited by Ige et al. reported maximum % EE by 90–95% w/w. Therefore, based on percent drug entrapment, SLN F6 selected as an optimized SLN and proceed for further evaluation includes physicochemical properties and gel formation. Percent drug entrapment of all SLN groups have been shown graphically in **Figure No 7.**

Table 10: Entrapment Efficiency of SLN Formulation

Batch	Drug Entrapment Efficiency (%)
SLN-1	85.65
SLN-2	89.37
SLN-3	94.39
SLN-4	94.86
SLN-5	93.88
SLN-6	**95.52**

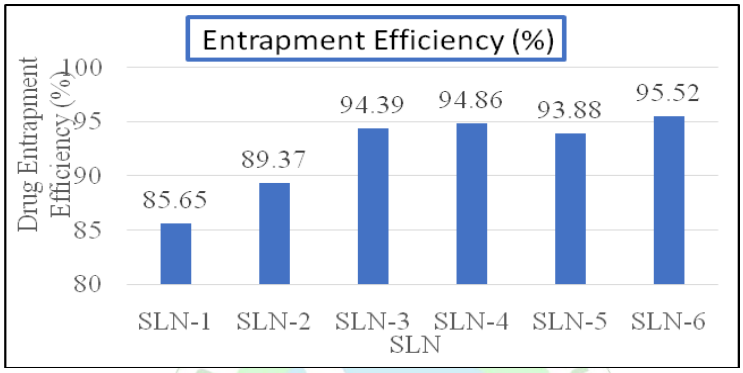

Figure 7: Percentage entrapment efficiency of luliconazole in SLN

2. Physicochemical property

The SLN-6 evaluated based on their physicochemical characteristics such as colour, odour, pH stability, and aqueous solubility. physicochemical results reveal that SLN has white transparent colour with homogeneous and uniform texture, aromatic odour, better stability at 7.4 pH, and water solubility found 0.153 ± 0.035 mg/ml, i.e. much enough than luliconazole solubility.

3. Particle size and Polydispersity index

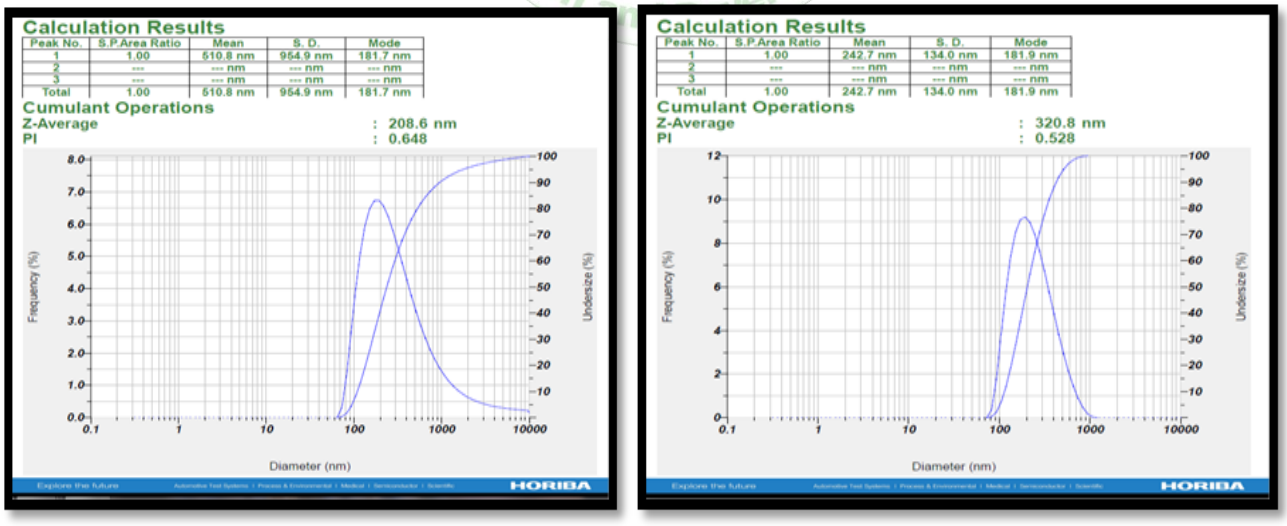

Figure 8: Result of Particle Size and PDI

The particle size, zeta potential and polydispersity index of the prepared SLN batches are reported in table. The particle size analysis of luliconazole SLN suspension revealed that the particle size measured by laser light method is around to 208 nm with low polydispersity index. All the SLN formulation shows particle sizes in the nano range (< 1 µm). The reduced particle size and polydispersity index could be attributed to the stabilization of colloidal system.

4. Zeta Potential

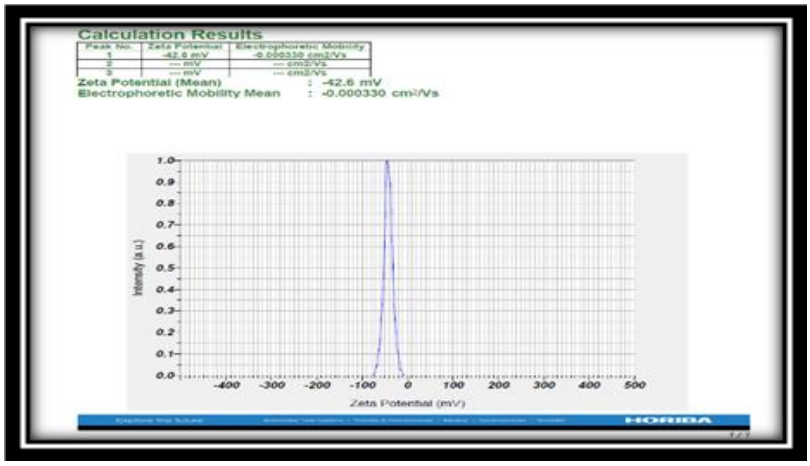

Figure 9: Result of Zeta Potential

The zeta potential is in the ideal range. The high zeta potential was found to reduce the tendency for particle aggregation due to higher magnitude of repulsive forces.

5. Scanning Electron Microscopy:

The SEM image of optimized SLNs (F6) is shown in Figure 5. The SLNs were observed to be spherical in shape, with a smooth surface. It was noticed that particles adhered together, probably due to the nature of the steric acid used in the formulation.

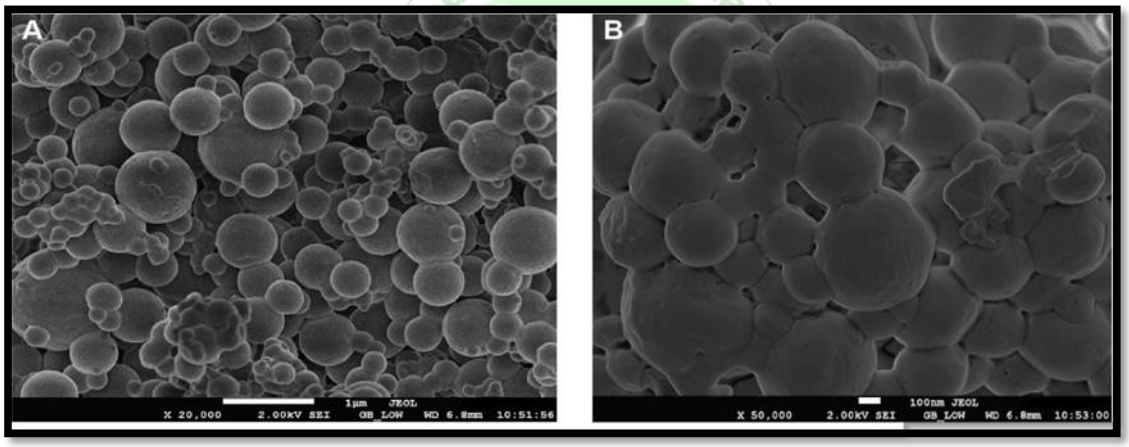

Figure 10: SEM images of optimized Luliconazole loaded SLNs

Evaluation of SLN loaded topical gel

SLN-6 batch was found to be optimized which is used further for preparation of gel from optimized SLN and evaluated for following parameters.

Figure 11: Visual appearance of SLN gel

a. Appearance:

Table 11: Physical evaluation of Luliconazole SLN based gels

Formulation	Appearance	Consistency	Grittiness	Uniformity
G1	Whitish	Smooth	None	Good
G2	Whitish	Smooth	None	Good
G3	Whitish	Smooth	None	Good

b. pH measurement:

pH of luliconazole-SLN based gels was found in range of 5.6 – 6.2 which is was near to the physiological pH of the skin. Hence it concludes that the gel formulation is safe to use topically. Results are shown in below table no 15.

Table 12: pH of LNZ-SLN based gel

Batch	G1	G2	G3
pH	5.8	5.6	6.2

c. Gel Strength:

Gel strength was determined by visually observing and measuring the time required for travel of 5 gm weight up to 2 cm distance through gel. These observations were graded as +++ if time required is more than 4 hr, ++ if time is 2.5 - 4 hr and + if time is less than 2.5 hr. + indicate low gel strength and the gel may get dissolved and cleared off faster from skin surface, ++ and +++ indicate good and very good respectively and will help to hold drug for prolonged period of time. The gel strength for the formulation was found to be ++ indicates good gel strength which will help desired drug release and may get easily cleared off from skin when required. The results are shown in table no--.

d. Viscosity:

The viscosity of luliconazole based SLN gel formulation was found to be in the range of 812 to 938 cps showing good consistency of the formulation. The results are shown in Table No --.

Table 13: Viscosity of luliconazole-SLN based gels

Batch	Viscosity (cps)	Gel Strength
G1	2325	++
G2	3975	++
G3	4087	+

+++ if time required is more than 4 hr, ++ if time is 2.5-4 hr and + if time is less than 2.5hr

e. Spreadability:

The value spreadability indicates that gel is easily spreadable by applying just a small amount of shear. Spreadability is inversely proportional to the viscosity of prepared gel. Spreadability decreased as the amounts increased. The Spreadability of the prepared carbopol 934 gel formulation was in the range of 2.9-3.7 gm.cm/sec. These values were represented in table no 17. All the formulations showed good spreadability.

Table 14: Spreadability of Luliconazole SLN based gels

Batch	Spreadability (gm.cm/sec)
G1	3.7
G2	3.4
G3	2.9

f. Drug content:

All the prepared LNZNS loaded batches shows good drug content, the drug content is within the range of 78% - 86.3%.

Table 15: Drug Content Luliconazole SLN formulation

Batch	Drug Content (%)
G1	92.47
G2	96.63
G3	85.43

g. *In-Vitro* drug diffusion study:

All the prepared batches show good drug release. Table no 19 shows the drug release of the SLN based gel batches.

Table 16: *In vitro* drug diffusion of gel

Time (Hr)	G1	G2	G3
0	0	0	0
1	5.41	7.2	6.84
2	9.38	11.53	10.48
3	12.75	16.4	14.13
4	17.2	22.32	19.64
5	23.15	29.22	25.62
6	31.78	39.08	34.8
8	48.47	55.21	50.68
10	58.32	67.84	62.19
11	66.92	79.1	71.69
12	78.32	**89.8**	83.49

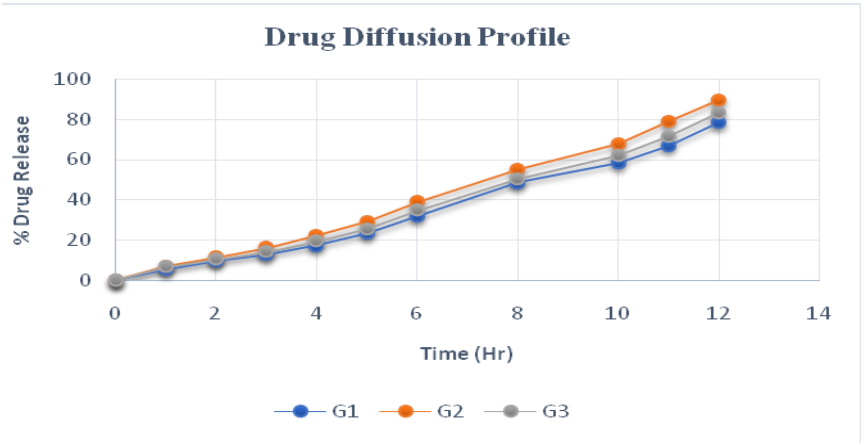

Figure 12: *In vitro* drug diffusion of gel

Table 17: Percentage drug diffusion profile of G2 and control gel.

Time(Hr)	% drug release of LUZ-SLN gel (G2)	% drug release of control gel
0	0	0
1	7.2	6.9
2	11.53	14.2
3	16.4	28.2
4	22.32	37.7
5	29.22	41.3
6	39.08	44.8
8	55.21	48.2
10	67.84	56.8
11	79.1	65.8
12	**89.8**	82.7

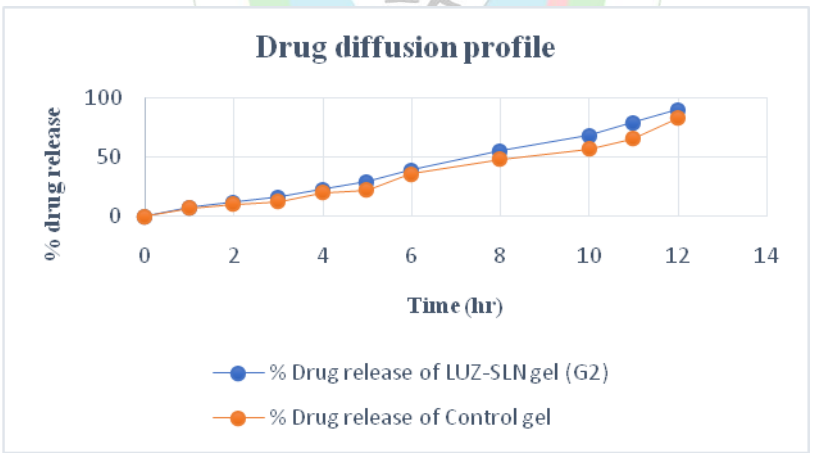

Figure 13: In-vitro drug diffusion profile of SLN gel (G2) and control gel

h. *In vitro* antifungal activity:

The antifungal activity was evaluated on the basis of zone of inhibition. Zone of inhibition interprets the effectiveness of formulation against the microbial species taken. Here *C Albican* is used as a reference as it is responsible for various skin infections. The zone of inhibition measured after 72 hr LUZ-SLN was found to be higher when compared with marketed preparation. This is due to the permeability of SLN to cross the fungal cell membrane and releases the drug inside the cell. The result reveals the enhanced potential of LUZ-SLN gel to act against *Candida* species as compared to marketed cream and the standard dilutions of luliconazole.

There was no significant difference between zone of inhibition of control and 1% luliconazole marketed cream. Whereas, optimized SLN gel exhibited larger zone as the small particle size of SLN results in better diffusion through membrane pores in the gel network. and (Table 20) A large amount of luliconazole was found to be localized within the same isotropic media, resulting in strong antifungal activity compared to commercial preparations. The zone of inhibition

for optimized SLN gel was greater than microemulsion based gel as reported by *Kansagra et al.*

In-vitro antifungal study clearly depicts that optimised SLN formulation exhibits better anti-fungal activity as it portrays larger zone of inhibition against *CAlbicans* in comparison to marketed luliconazole cream.

Table 18: Zone of Inhibition diameters for *In-vitro* antifungal studies

Sample	ZOI of C. Albicans diameter (mm)
Control	87
1% Luliconazole marketed	83
SLN Luliconazole Gel	93

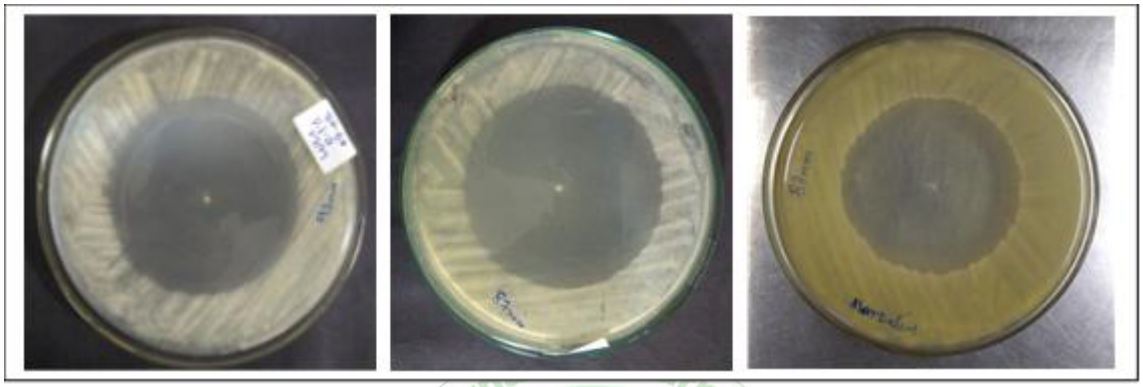

Figure 14: In-vitro antifungal studies: a) SLN luliconazole gel – 93mm b) Control-87mm c) Marketed Cream – 83mm

i. Stability studies:

As per ICH guidelines, the developed G2 topical gel was assessed for stability test for 90 days by exposing the sample at room temperature (25± 2°C) and accelerated condition (40± 2°C and 75± 5% RH) in Stability chamber, after 90 days' stability the gel is evaluated for Appearance, pH, viscosity, gel strength, Spreadability, % drug release etc.

Table 19: Stability Study

Month	Temperature	Appearance	pH	Viscosity	Gel Strength	% Drug Release
1	R.S.T.	No change	5.6	4012	++	89.6
	Acc. S.T.	No change	5.3	4122	++	89.2
2	R.S.T.	No change	5.4	4250	++	88.6
	Acc. S.T.	No change	5.5	4354	+++	88.3
3	R.S.T.	No change	5.9	4398	+++	88.2
	Acc. S.T.	No change	5.8	4495	+++	88

CONCLUSION

A topical drug delivery system is designed to ensure that the targeted area of the body receives an appropriate therapeutic dose of medication while maintaining the desired effects for a specific period. Our research has led to the development of solid lipid nanoparticles (SLN) containing luliconazole, which improves skin permeation and allows for targeted, controlled drug release. These nanoparticles were incorporated into a carbopol 934 topical gel with excellent skin retention properties. Standard protocols were followed to assess the gel's physicochemical properties and ensure its compliance after patient use. Spectroscopic analysis indicated no chemical interactions between the drug and the excipients. Additionally, optical microscopy and scanning electron microscopy examinations demonstrated that the SLN was evenly distributed throughout the gel and that the drug release kinetics were well-ordered.

In conclusion, the SLN gel system provides controlled drug release and serves as an effective drug carrier for lipophilic drugs, as well as a bioavailability enhancer for poorly water-soluble drugs through nanoparticle drug delivery.

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