Formulation and evaluation topical Gel Containing Luliconazole Nanoparticles

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***Abstract*—New topical pharmaceutical options are critically needed for the treatment of fungal infections for prolonged therapeutic action. Luliconazole is a topical antifungal medicine for the treatment of fungal infection but bioavailability barriers of luliconazole approached to develop effective topical luliconazole solid lipid nanoparticles (SLN) gel formulation with prolonged therapeutic potential against tropical fungal infection.SLN of luliconazole was prepared by the solvent diffusion method using stearic acid & poloxamer 188. The preformulation studies were conducted for the authenticity of the leading moiety. Thereafter, the prepared SLN followed by gel formulations were subjected to physicochemical evaluation, *in-vitro* release profile of drug with kinetics studies. Thereafter, FTIR spectroscopy and scanning electron microscopy of the optimized formulation was done successfully. The results reveal that SLN F6 shows a significant entrapment efficacy with the highest entrapment of 92.13%±0.975. In particle size, size distribution and zeta potential analysis, SLN exhibit a mean particle diameter of ~344.3 nm, with unimodal size distribution, a polydispersity index of 0.168, intercept value 0.98 with 92% peak intensity and zeta potential ~18.8 mV.Further, G3 gel shows a higher entrapment efficacy with 91.39%±0.187 as compared to other formulation. The *in-vitro* drug release profile of the G3 gel with 1.5 % carbopol 934 w/v shows a sustained release profilewith79.57%±0.213ofthedrugreleaseevenafter24hr softhetime. It is concluded that the Luliconazole loaded SLN based gel formulation containing carbopol 934 1.5%w/v is suitable for topical application and may show a much better result of anti-fungal activity.**

***Index Terms*—Solid lipid nano particles loaded Gel, Drug Content, pH of the Gel, In-vitro drug release study**

I. INTRODUCTION

Fungal infections of the skin and subcutaneous tissues are among the most common infectious conditions worldwide, particularly affecting immunocompromised individuals such as patients with hematological disorders, organ transplant recipients, and those undergoing prolonged immunosuppressive therapy. These infections are often progressive in nature and, if left untreated, may lead to severe morbidity and mortality. Conventional antifungal therapies face challenges such as poor skin penetration, limited bioavailability, frequent dosing, and reduced patient compliance.

Topical drug delivery remains the preferred route for treating cutaneous and subcutaneous fungal infections as it allows direct application of the drug at the site of infection, minimizes systemic side effects, and avoids first-pass metabolism. However, the stratum corneum acts as a major barrier to drug permeation, restricting effective drug transport into deeper skin layers. As a result, many conventional topical formulations such as creams, lotions, and ointments fail to maintain adequate drug concentration at the target site.

Nanotechnology-based drug delivery systems have emerged as a promising approach to overcome these limitations. Among them, solid lipid nanoparticles (SLNs) have gained considerable attention due to their biocompatibility, biodegradability, controlled drug release, enhanced skin permeation, and improved drug stability. SLNs, with particle sizes in the nanometer range, facilitate close contact with the skin surface, improve drug retention in the epidermal and dermal layers, and provide sustained antifungal activity.

Luliconazole is a novel, broad-spectrum imidazole antifungal agent approved by the US Food and Drug

Administration (FDA) for the treatment of dermatophytic and candidal infections. Despite its high antifungal potency, luliconazole exhibits limited skin penetration and short retention time when formulated in conventional topical dosage forms. Incorporation of luliconazole into nanoparticulate carriers such as SLNs can significantly enhance its permeation, prolong drug residence time in the skin, and improve therapeutic efficacy.

Gels are preferred topical vehicles due to their non-greasy nature, ease of application, good patient acceptability, and ability to release drugs in a controlled manner. Combining luliconazole-loaded SLNs with a suitable gel base offers an effective strategy to achieve enhanced antifungal activity with improved stability and patient compliance.

Therefore, the present study aims to formulate and evaluate a topical gel containing luliconazole-loaded solid lipid nanoparticles and to assess its physicochemical properties and antifungal efficacy, providing a promising approach for improved topical antifungal therapy.

II. MATERIALS AND METHODS

Materials

Luliconazole was obtained as a gift sample from SMS Pharmaceuticals (India). Carbopol 934P (Sigma-Aldrich, Italy), stearic acid and methanol (Fisher Scientific, India), ethanol (Merck, India), Poloxamer 188 (Central Drug House, India), n-octanol (S.D. Fine-Chem, India), and buffer reagents (Thomas Baker, India) were used. All chemicals were of analytical grade.

Preformulation Studies

The absorption maximum (λmax) of luliconazole was determined in methanol by UV-visible spectrophotometry and observed at 299 nm. Aqueous solubility was evaluated using the saturation shake-flask method in distilled water and acetate buffer (pH 5.5). Lipophilicity (log P) was determined using the n-octanol/water partition system. All experiments were conducted in triplicate.

FTIR Analysis

FTIR spectra of luliconazole, stearic acid, SLN, and SLN-gel formulations were recorded using the KBr pellet method over a range of 4000–400 cm^{-1} to assess compatibility.

Preparation of Luliconazole-Loaded SLNs

SLNs were prepared by the solvent diffusion method. Luliconazole and stearic acid were dissolved in ethanol and injected into an aqueous Poloxamer 188 solution under stirring, followed by centrifugation and high-pressure homogenization to obtain stable nanoparticles.

Evaluation of SLNs

Entrapment efficiency was determined spectrophotometrically at 299 nm. Particle size and zeta potential were measured using a particle size analyzer after dilution with phosphate buffer (pH 7.4). Morphology was examined by optical microscopy.

Preparation of SLN-Based Gel

Carbopol 934P was hydrated in distilled water and preserved using parabens. Optimized SLNs were incorporated into the gel with propylene glycol and ethanol, and pH was adjusted to 5.5–6.5 using triethanolamine. Four formulations (G1–G4) were prepared by varying Carbopol concentration.

Characterization of Gel

Gel formulations were evaluated for pH, viscosity, spreadability, and entrapment efficiency using standard methods.

In-Vitro Drug Release and Kinetics

In-vitro drug release of the optimized SLN gel (G3) was studied using the dialysis bag method at 37 °C. Samples were analyzed at 299 nm, and release kinetics were evaluated using zero-order, first-order, Higuchi, and Korsmeyer–Peppas models

Scanning Electron Microscopy

Surface morphology of the optimized SLN gel was examined using SEM after gold-palladium coating.

III. RESULTS AND DISCUSSION

Pre formulation Study of Drug

Determination of Absorption Maximum of Luliconazole in Ethanol

The absorption maximum (λmax) of luliconazole was determined in ethanol using UV–visible spectrophotometry. Standard solutions in the concentration range of 2–10 µg/mL were analyzed, and the λmax was observed at 299 nm. The

calibration curve exhibited good linearity with a regression equation of $y = 0.0664x - 0.0478$ and a correlation coefficient (R^2) of 0.998. This method was validated and found suitable for the qualitative and quantitative estimation of luliconazole.

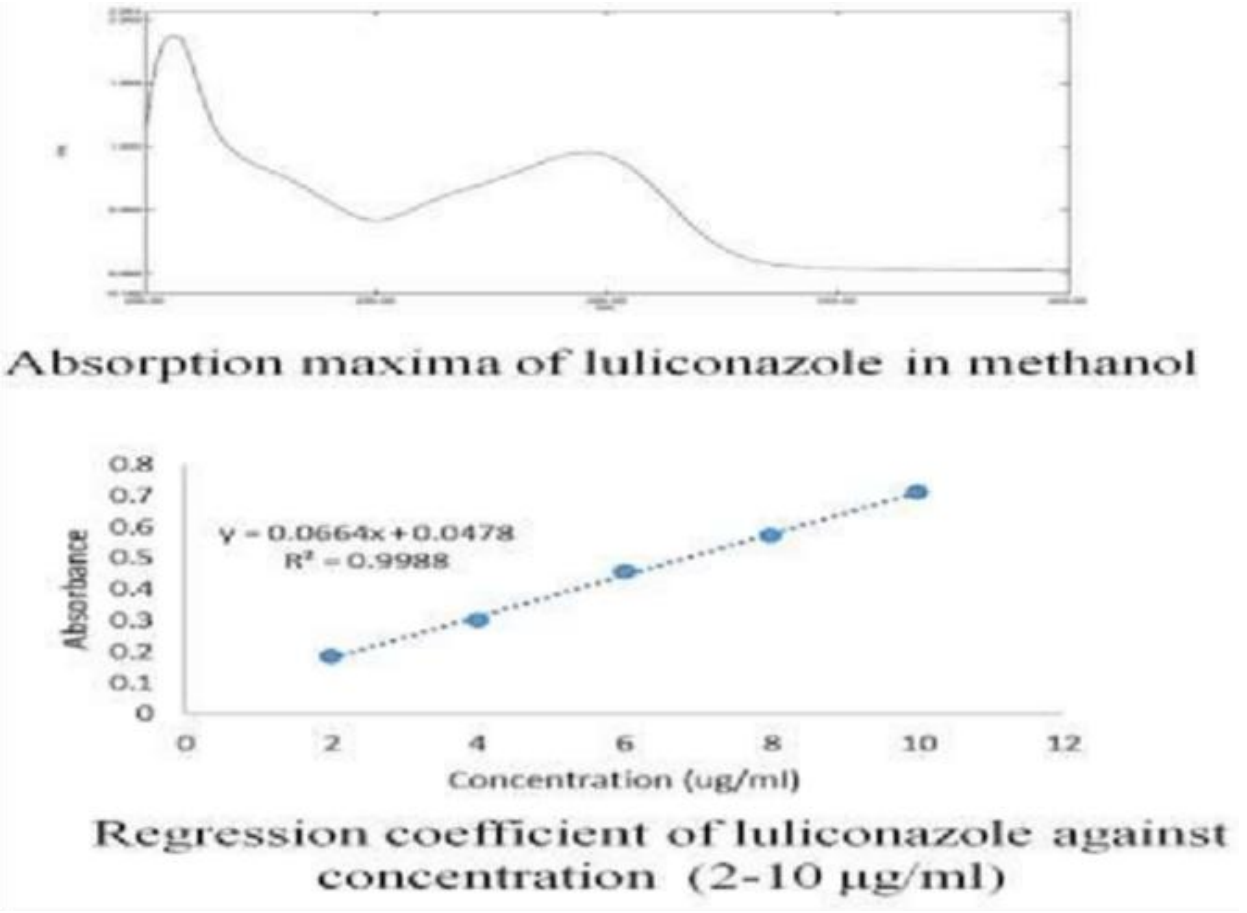

Figure1: Absorption maxima of luliconazole and regression coefficient against the different concentration of luliconazole (µg/ml)

FTIR analysis

luliconazole and stearic acid was performed to evaluate drug–excipient compatibility before and after formulation. The FTIR spectrum of luliconazole (Figure 7; Table 6) showed characteristic absorption peaks at 2979.43 cm^{-1} (C–H stretching), 2198.82 cm^{-1} (C≡N stretching), 1554.35 cm^{-1} (aromatic C–H stretching), 1471.35 cm^{-1} (aromatic C=C stretching), 820.41 cm^{-1} (para C–H bending), and 759.46 cm^{-1} (C–Cl stretching). The presence of these principal peaks confirmed the purity and authenticity of luliconazole and was consistent with reported literature, indicating no chemical interaction with the lipid used.

CharacteristicsPeaks	Reported(cm^{-1})	Observed(cm^{-1})
C-Hstretch	2850-3000	2979.43
C≡N Stretch	2100-2400	2198.82
C=Caromaticstretch	1450-1650	1554.35
C=C-CAromaticringstretch	1510-1450	1471.35
paraC-Hdistribution	860 -800	820.41
C-Clstretch	600 -800	759.46

Table1 : FTIR interpretation of luliconazole

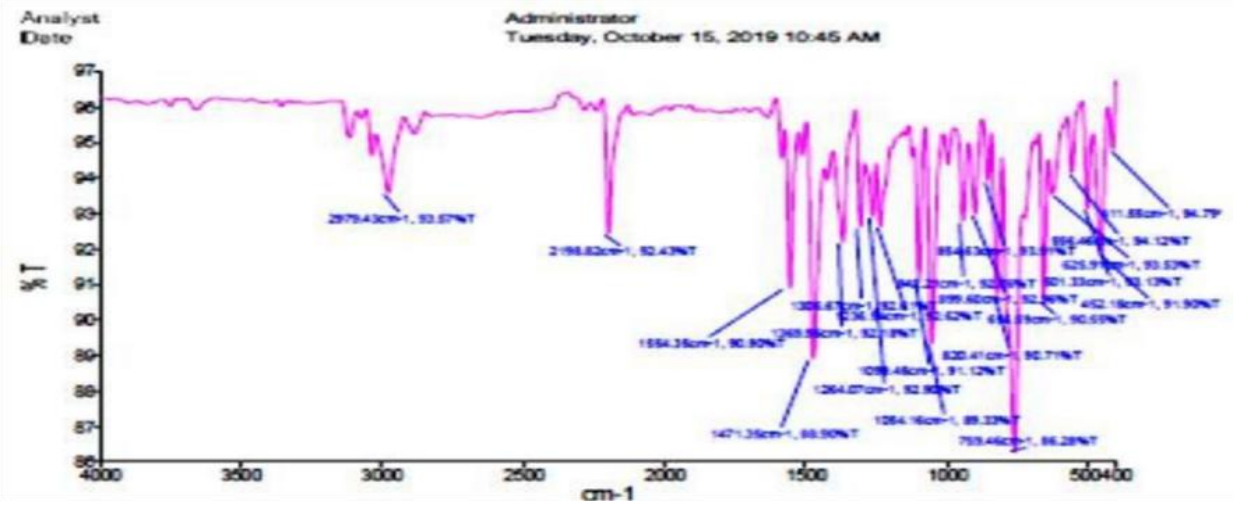

Figure 2: FTIR spectrum of luliconazole

Table2: FTIR interpretations t earic acid

CharacteristicsPeaks	Reported(cm^{-1})	Observed(cm^{-1})
C–Hstretchalkanes	2850-3000	2915.20
C-Hstretchaldehyde	2800-2860	2848.02
C=Ostretchsaturated	1700– 1730	1700.89
C-Cstretch	1400-1500	1471.59
C-Ostretch,aromaticaster	1250-1310	1295.47
O-Hbend	910 – 950	936.42
C=Cbend	665 -730	719.89
C-Istretch	500 -600	547.03

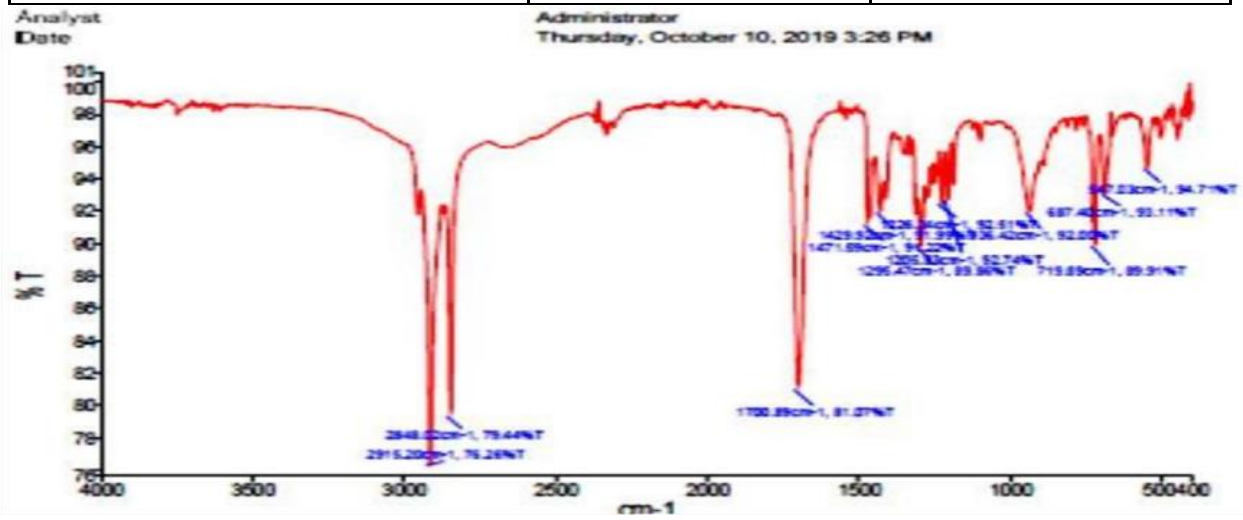

Figure 3 FTIR spectrum of stearic acid

Evaluation of SLNs: Entrapment Efficiency

In preformulation studies, luliconazole was characterized physicochemically and spectroscopically. After preparation of various SLN batches, the percentage entrapment efficiency (%EE) was determined spectrophotometrically at 299 nm. Results showed that SLN F6 exhibited the highest %EE (92.13% ± 0.98), while SLN F1 had the lowest

(53.78% ± 1.05). These findings are consistent with the study by Ige et al., which reported %EE values of 90–95%. Based on maximum drug entrapment, SLN F6 was selected as the optimized formulation for further evaluation, including physicochemical characterization and gel formulation. The %EE of all SLN batches is presented in Figure 3.

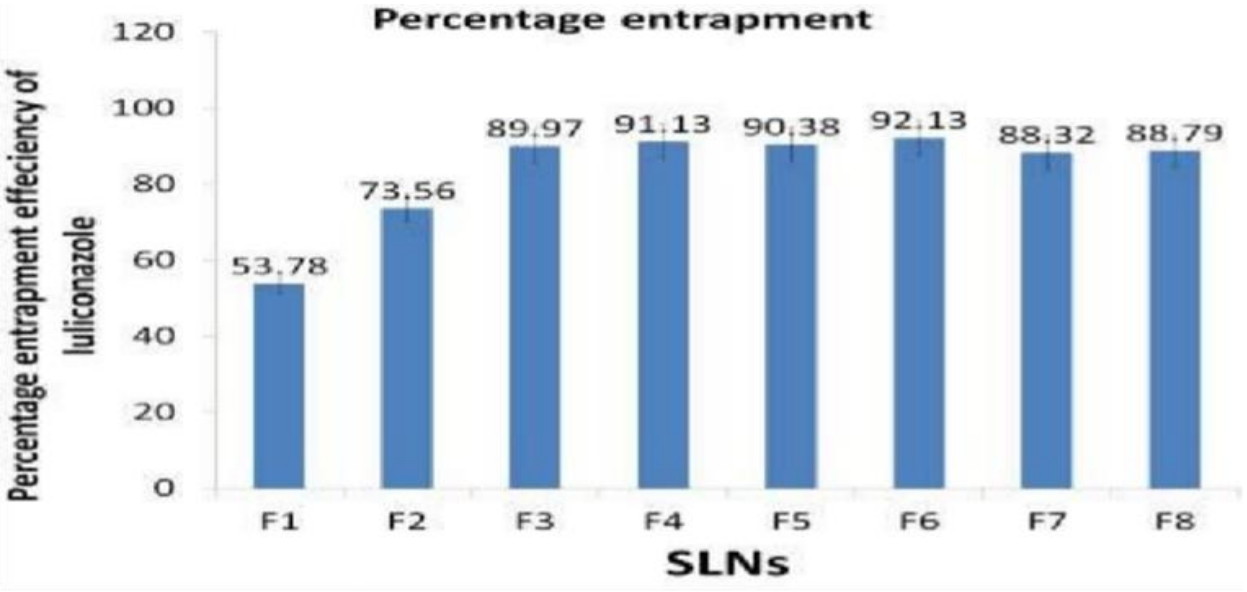

Figure 3: Percentage entrapment efficiency of luliconazole in SLN

Particle Size, Size Distribution, and Zeta Potential

The particle size and zeta potential of luliconazole-loaded SLNs were measured using a Nano ZS90 Zetasizer. Zeta potential is a key parameter for predicting the physical stability of nanoparticles, as higher values indicate stronger repulsive forces between particles and reduced aggregation. The SLNs exhibited a zeta potential of ~18.8 mV, indicating good stability. Particle size analysis showed a mean diameter of ~344.3 nm with a unimodal size distribution, a polydispersity index (PDI) of 0.168, an intercept value of 0.98, and 92% peak intensity. A PDI value below 0.5 indicates a uniform particle distribution with minimal aggregation.

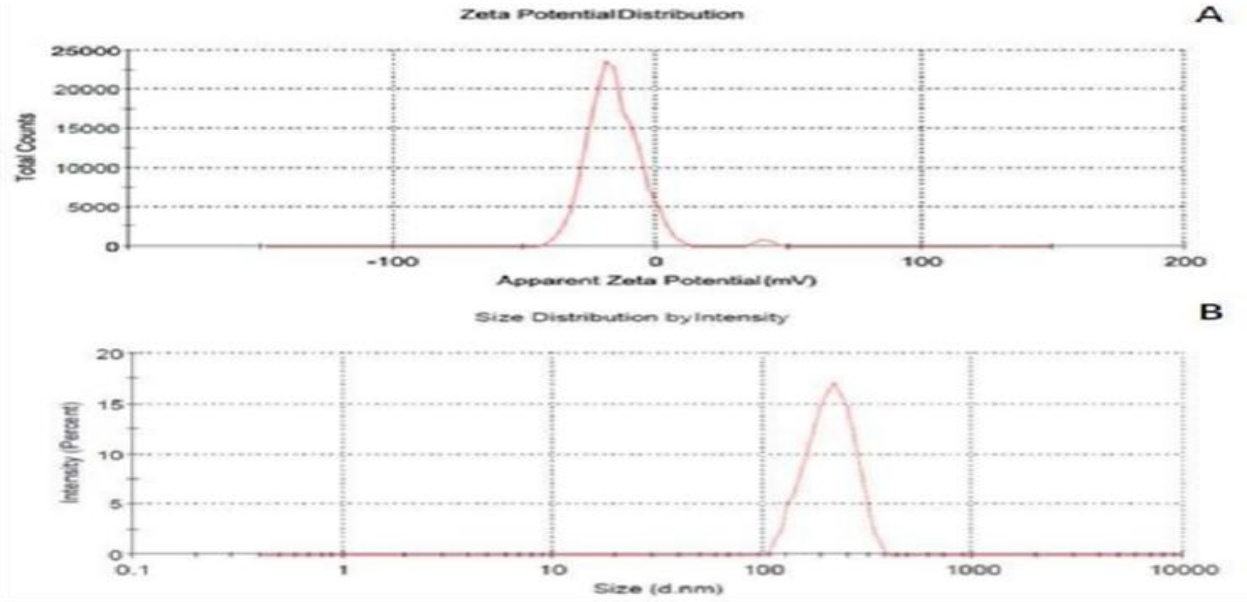

Figure 4 zeta potential, particle size and size distribution o fluliconazole SLNF6

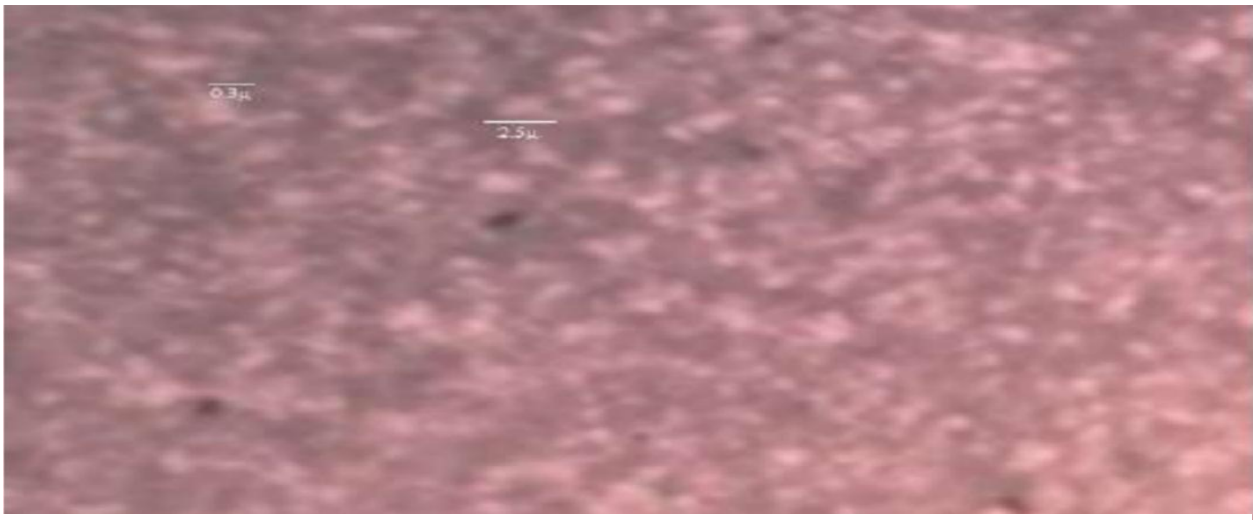

Figure 5: Optical microscopy images of luliconazole loaded SLNF6

IV. CONCLUSION

The purpose of topical drug delivery system is to allow therapeutic quantity of drug to correct place in body and to achieve and sustain desired effect of drug for while. Inpresent investigation, we have designed solid lipid nanoparticles (SLN) loaded with luliconazoleto enhance skin permeation and controlled drug release at targeted site and incorporate them in topical gel of carbopol 934 with good skin retention time. physicochemical property of prepared gel determined as per standards protocol to overcome compliance after patient use. Even spectroscopical analysis reveals no chemical interactivity between luliconazole and excipients. microscopic examination (optical microscopy and scanning electron microscopy) of gel showed uniform distribution of SLN inside gel with good order of kinetics of drug release. Hence, it can be concluded that SLN gel provides controlled release of drug and these systems can be good source as drug carriers for lipophilic drugs, bioavailability enhancer for poorly water-soluble drugs by nanoparticles, drug delivery system**.**

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