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Formulation Development And Evaluation Of Novel Drug Delivery Systems For Enhanced Solubility And Bioavailability Of Poorly Soluble Antifungal Drugs

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Abstract:
SLN will be an alternative drug delivery system for poorly water-soluble drugs Efinaconazole to enhance the bioavailability and therapeutic response of drug. The poorly water-soluble drugs Efinaconazole was successfully incorporated into SLN by the hot homogenization and sonication process. The in-vitro test confirmed the drug retention and prolonged the drug dissolution with slow release. Drug release from the SLN was highly influenced by the type and concentration of lipid and surfactant. Based on the in vitro and in vivo results, it was observed that SLN incorporated in combination of Efinaconazole with palmitic acid (A5andA6) was physiologically safe and also exhibited sustained release until 12 hours. The selected formulation of Efinaconazole (EF1-EF8) which was formulated using Palmitic acid and Tween-80 newline.
Keywords: *Development, Evaluation, Nanoparticle-Based Drug Delivery Systems, Enhanced Solubility and Bioavailability.*

INTRODUCTION

Currently, one of the primary challenges faced by the pharmaceutical industry is the poor water solubility and insufficient bioavailability of drugs. Current data suggest that approximately 40% of commercially available pharmaceuticals, as well as a significant majority of investigational drugs, struggle with low solubility. The difficulties in dissolving and releasing poorly soluble drugs have restricted the bioavailability of oral solid dosage forms the most widely used and patient-compliant method of drug delivery hindering the development and application of many new compound drugs. Due to low bioavailability, patients need to consume higher drug dosages to achieve the desired therapeutic effects. However, increasing the dosage can result in more side effects, potentially harming the physical and mental health of patients and decreasing their medication compliance. The issue of low water solubility not only poses significant challenges to medical development but can also lead to various clinical problems, such as variability in patient responses, difficulty in maintaining a safe therapeutic index, increased costs, and the potential risk of toxicity or inefficacy (1, 2).

Therefore, effectively addressing the poor solubility and low bioavailability of drugs has always been a focal point and a significant challenge in pharmaceutical and medical research. To overcome these issues, the development of Nanomedicine delivery systems, as an innovative drug delivery strategy, has emerged, breaking through the traditional bottlenecks associated with the solubility and bioavailability of drugs. Nanomedicine delivery systems primarily encompass two fundamental aspects: Firstly, based on pathological changes, these systems can precisely transport drugs to the specified lesion sites, thereby maximizing therapeutic effectiveness and significantly reducing damage to healthy tissues. Secondly, they can control the rate of drug release, ensuring that drug concentration in the blood remains within a safe and effective range, thus mitigating or avoiding toxic and adverse reactions (3-5). Composed of nanoparticles smaller than 100 nanometers, these delivery systems feature high permeability and potent retention effects, enhanced drug solubility, multifunctionality, controlled drug release mechanisms, and specific targeting capabilities towards diseased cells. Through nanotechnology-based structural modifications of drugs, these systems not only achieve precise control over drug release and increase drug stability but also prevent premature

degradation of the drug molecules before reaching the lesion, thereby enhancing bioavailability and prolonging circulation time of the drug (6).

MATERIAL AND METHODOLOGY

1.1 Preformulation Study

Preformulation study, Nano particle preparation, bio availability study design and data handling, optimization of bio analytical methods for the estimation of Efinaconazole in rat plasma samples, standard and sample solutions, in vitro dissolution methods, in vivo data analysis, and statistical analysis of pharmacokinetic data are covered in this chapter. General Preformulation includes all actions and investigations needed to transform an active pharmacological ingredient into an appropriate dosage form. The physical and chemical characteristics of a drug substance alone and with excipients are studied. Thus, Nano particle assessment, in vitro dissolving technique development, and drug-excipient compatibility were determined in this study (7).

1.2 Formulation Development of Efinaconazole SLN

High-shear hot homogenization and ultra-sonication produced Efinaconazole-loaded SLN. Stearic acid, Glycerylmonostearate, and palmitic acid were mixed with surfactants (1% and 2%). To dissolve medicinal fat, Efinaconazole was combined with lipid and soya lecithin in an organic phase and heated to 70^0C. Similar temperatures were applied to the surfactant-containing aqueous phase. Later, heated lipid solution was added and homogenized with a mechanical stirrer for 30 minutes to create a transparent solution. Sonicating the solution for 25 minutes produced equally sized SLN. This standard process was used to create SLN with variable lipid and surfactant amounts as shown in table 1. Cosurfactant concentration was constant throughout formulations.

Table 1 The formula for the preparation of Solid lipid Nanoparticles of Efinaconazole

Formula	Drug % w/w	Lipid	The concentration of Lipid % w/w	Co surfactant %w/w	Emulsifying Agent name	Concentration of Emulsifying Agent %w/w
F1	0.1	Stearic Acid	1	0.5	Tween 20	1
F2	0.1	Stearic Acid	1	0.5	Tween 20	2
F3	0.1	GMS	1	0.5	Tween 20	1
F4	0.1	GMS	1	0.5	Tween 20	2
F5	0.1	Palmitic Acid	1	0.5	Tween 20	1
F6	0.1	Palmitic Acid	1	0.5	Tween 20	2
B1	0.1	Stearic Acid	1	0.5	Tween 40	1
B2	0.1	Stearic Acid	1	0.5	Tween 40	2
B3	0.1	GMS	1	0.5	Tween 40	1
B4	0.1	GMS	1	0.5	Tween 40	2
B5	0.1	Palmitic Acid	1	0.5	Tween 40	1
B6	0.1	Palmitic Acid	1	0.5	Tween 40	2
A1	0.1	Stearic Acid	1	0.5	Tween 8 0	1

A2	0.1	Stearic Acid	1	0.5	Tween 80	2
A3	0.1	GMS	1	0.5	Tween 80	1
A4	0.1	GMS	1	0.5	Tween 80	2
A5	0.1	Palmitic Acid	1	0.5	Tween 80	1
A6	0.1	Palmitic Acid	1	0.5	Tween 80	2

1.3 Characterization of SLN of Efinaconazole

1.3.1 Infrared studies (FTIR)

Efinaconazole and lipid compatibility was investigated by FTIR spectroscopy of their physical combinations. Infrared investigations were done on physical combinations at 4000–400 cm-1. Efinaconazole basic functional group skeleton was investigated (8).

1.3.2 Particle size and zeta potential

The Efinaconazole-loaded SLN particle size was measured by DLS in a Zetasizer 9DTS. To assess preparation uniformity, SLN Polydispersity index (PDI) was investigated. Particle size analysis by zeta sizer included surface charge (9).

1.3.3 Entrapment efficiency

Centrifugation measured free unloaded medication in the formulation. The formulation was centrifuged at 10,000 RPM to separate the supernatant. The supernatant contains the formulation's unloaded drug, which was measured spectro-photometrically, and entrapment efficiency was examined (10).

1.3.4 Morphology of SLNs

SLNs' exterior topography was studied using scanning electron microscopy (Hitachi, Japan). Samples were distributed on the conducting stub for electron-focused imaging.

1.3.5 Drug Content

Blank comparable to SLN common weight was used to assess drug content. Drug was extracted in water for 6 hours after weighing sample. Filtered solution absorbance at 238nm was used to measure Efinaconazole (11).

1.3.6 Powdered x-ray diffraction study

Continuous scan mode was used for SLN X-ray analysis, with a sample width of 0.010̦ (2) and a scanning speed of 10/min. Expert proanalytical diffractometer evaluated at 30kv and 15mA. The samples were tested from 0-1000 (12).

1.3.7 Transmission electron microscopy (TEM)

TEM measured particle exterior electron topography. To evaluate morphology, drug-loaded SLN were finely disseminated over phosphotungsic acid/2% conducting slab.

1.3.8 Stability studies

SLNs loaded with Efinaconazole were analysed for stability after 6 months of storage at room temperature (28±2°C) and refrigerated at 3-5° C. After storage, SLN average size, surface charge, EE, and PDI were examined (13).

1.4 Loading of SLNs in hard gelatin capsules

The selected Efinaconazole loaded SLN was chosen for further studies and lyophilized to form free flowing powder. The powdered SLN was filled into size 4 hard gelatin capsules containing 10mg/20mg equivalent of Efinaconazole (14).

1.5 Evaluation of optimized capsules (15-19)

1.5.1 Uniformity of weight

Twenty capsules filled with Efinaconazole loaded SLN was weighed individually and their mean was calculated. The standard deviation of the capsules was also calculated. The capsules were considered

to pass the test only if not more than two capsules exceed the mean weight over >10%, and none deviate over >20%.

1.5.2 Disintegration test

Disintegration test was conducted in standard disintegration apparatus. One capsule was placed in each tube and disc was added on top of it. The basket rack assembly suspended in the beaker containing the liquid medium and the time taken for the capsule to completely disintegrate was recorded.

1.5.3 Drug content

Five samples were selected randomly and their average weight was calculated. The contents of the capsules were completely transferred into volumetric flask containing pH 6.8 phosphate buffer and left over night. 1 ml of the solution was diluted to 100 ml in a separate standard flask and the amount of drug present in the solution was determined at UV spectroscopy at 238nm.

1.5.4 Drug Dissolution release studies

In vitro drug dissolution of capsules with an equivalent weight of 10mg and 20mg incorporated with Efinaconazole SLN was performed by placing the capsules basket apparatus. The dissolution was carried out at 37.5^0C at 50 RPM. Samples were taken from the dissolution jar at specific intervals and replaced with dissolution medium and API released was estimated by UV spectroscopy at 238nm.

1.5.5 Stability studies

The Efinaconazole loaded SLNs capsules were stored at ambient temperatures for 6 months and average particle size, zeta potential, EE and PDI have been determined.

1.6 In- Vivo Study

The Pharmacokinetic Behaviour of drug loaded SLN (Efinaconazole loaded) were investigated in rats. The formulations were orally administered and the comparison were made with respect to the API suspension of the respective drugs (20).

The rats were randomly divided into the following eight groups

Group I - Normal Control

Group II - Disease Control

Group III – SLN Formulation with Efinaconazole SLNs formulation EF2

Group IV - SLN Formulation with Efinaconazole SLNs formulation EF6

Group V – Free drug Efinaconazole as suspension

RESULT AND DISCUSSION

1.7 Preformulation Study

1.7.1 Physical description

Efinaconazole was observed for colour, Odour and physical state. It was observed that the sample was off white, odorless, and crystalline.

1.7.2 Melting point

Capillary technique determined Efinaconazole melting point. One-ended capillary tube with 3mm Efinaconazole was filled. Capillary was added to the digital melting point equipment. The melting point was measured from medication melting to sample melting. With breakdown, melts at 225 °C.

1.7.3 Determination of λmax of Efinaconazole Drug

The 10 mg medication was precisely weighed and dissolved in methanol, then filled to 100 ml with a volumetric flask. After pipetting 1 ml of this stock solution into two 10 ml volumetric flasks, volume was increased to 10 ml. A UV-visible spectrophotometer scanned the fluid between 200 and 400 nm. Fig 1 shows a λmax of 285nm.

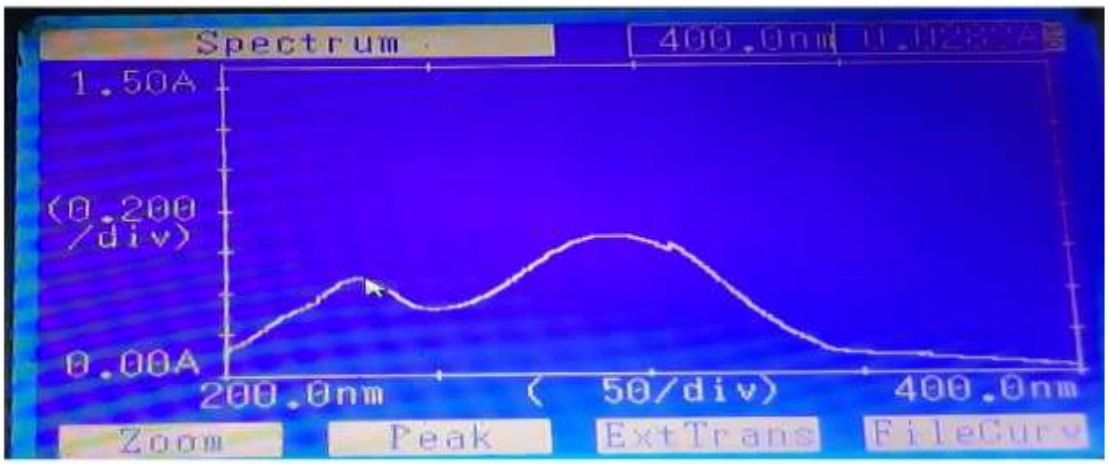

Figure 1 λmax determination by UV-Visible spectrophotometer

1.7.4 Drug-excipients compatibility

Compatibility study is one of the most important factors in determining polymeric delivery effectiveness. Compatibility between drug and polymers due to interaction with no changes chemical and physical properties of the drug because each drug has its unique chemical and physical properties. Compatibility between drug and polymers is determined by various methods, such as Differential Scanning Calorimetry (DSC), powder X-ray diffraction, Fourier Transform Infrared Spectroscopy (FTIR) etc.

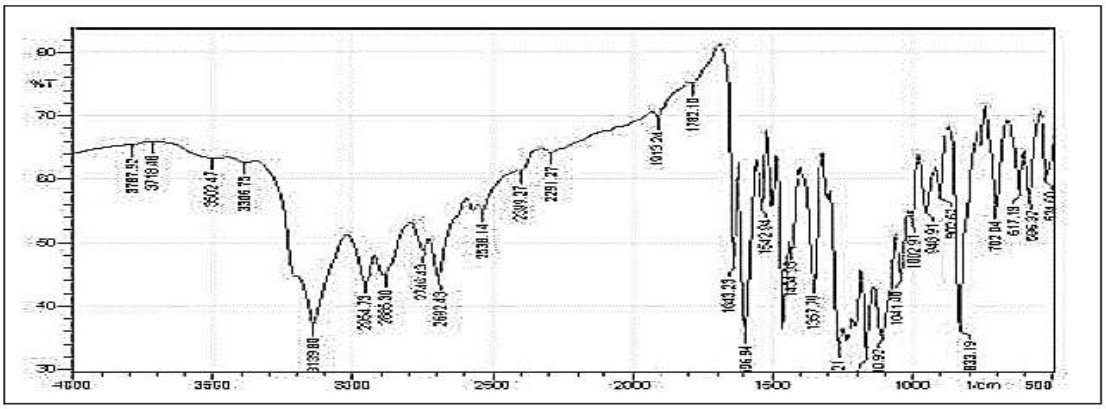

Figure 2 Reference FT IR spectra of Efinaconazole

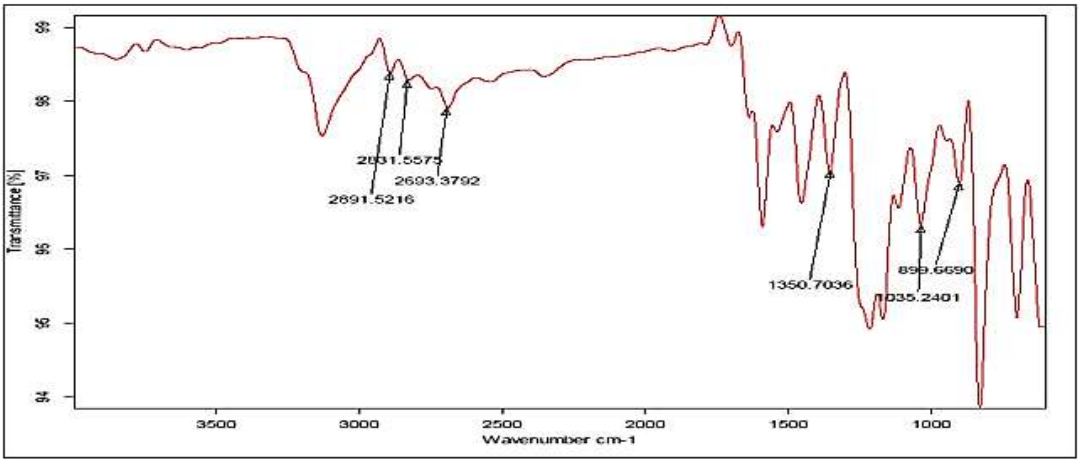

Figure 3 FTIR spectra of Efinaconazole (API)

The identification of pure drug (Efinaconazole) is performed with the help of FTIR spectroscopy. A comparative IR spectrum of pure Efinaconazole and reported reference spectrum Fig. 2 and 3 were found to be almost similar.

1.8 Preparation and Characterization of Efinaconazole SLNs

The selected Efinaconazole SLN formulations were formulated with varying concentration of Palmitic Acid and was shown in the table below

Table 2 Composition of Selected Efinaconazole SLN formulation of using Emulsifying Agent Tween 80 and Palmitic Acid

Formula	Drug % w/w	Lipid	Concentration of Lipid % w/w	Emulsifying Agent name	Concentration of Emulsifying Agent %w/w	Concentration of cosurfactant %w/w
EF1	0.10	Palmitic Acid	0.5	Tween 80	2	0.5
EF2	0.10	Palmitic Acid	1.0	Tween 80	2	0.5
EF3	0.10	Palmitic Acid	1.5	Tween 80	2	0.5
EF4	0.10	Palmitic Acid	2.0	Tween 80	2	0.5
EF5	0.20	Palmitic Acid	0.5	Tween 80	2	0.5
EF6	0.20	Palmitic Acid	1.0	Tween 80	2	0.5
EF7	0.20	Palmitic Acid	1.5	Tween 80	2	0.5
EF8	0.20	Palmitic Acid	2.0	Tween 80	2	0.5

1.8.1 FTIR study of selected Efinaconazole SLN Formulation

Table 3 FTIR study of selected Efinaconazole SLN Formulation

Observed(cm^{-1})	Reported (cm^{-1})	Inference
3319.64	3500-3100	N-H Stretching
2849	2850-2100	C≡C(Alkyne)
1737.9	1750-1730	C=O of Ester
1305.5	1350-1000	C-N

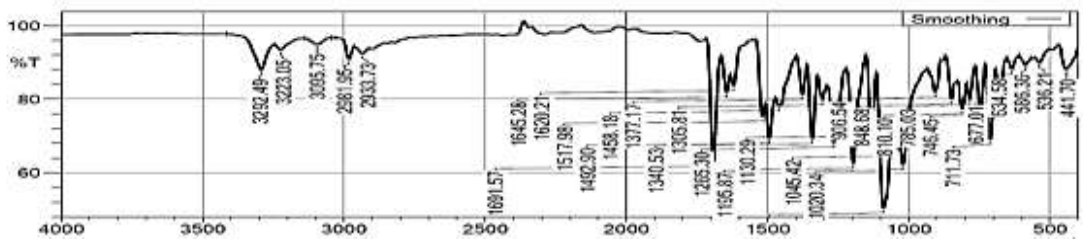

Figure 4 FTIR Spectrum of Pure Drug Efinaconazole

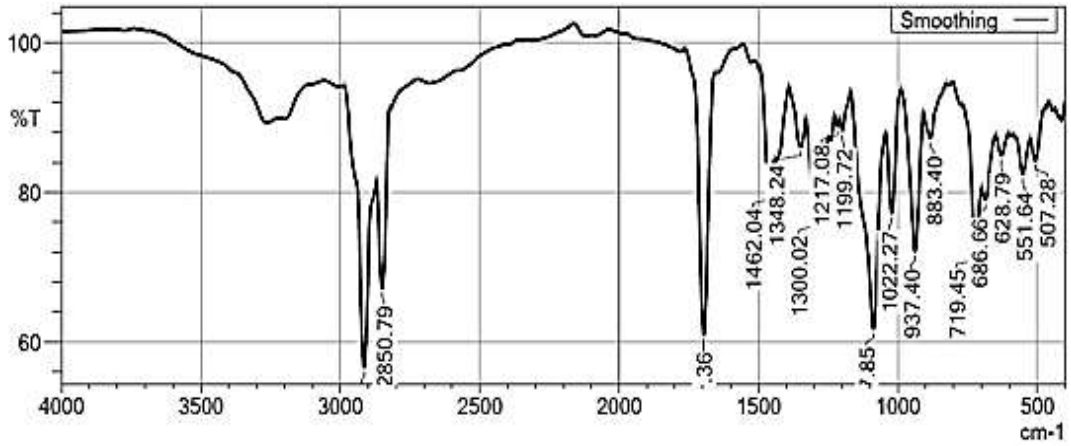

Figure 5 FTIR Spectrum of Efinaconazole SLN Formulation EF2

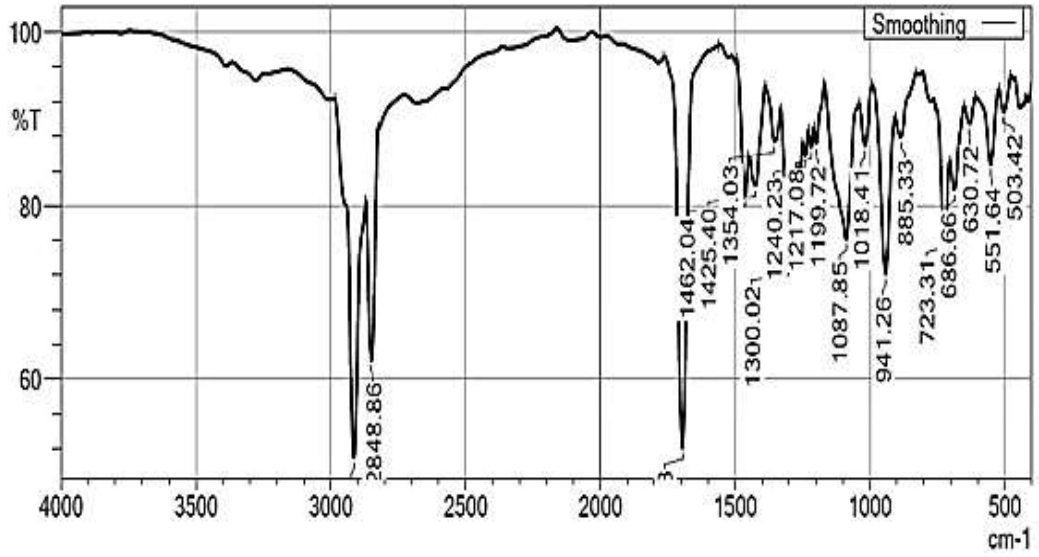

Figure 6 FTIR Spectrum of Efinaconazole SLN Formulation EF6

1.8.2 Particle size, Entrapment Efficiency, PDI, zeta potential of Efinaconazole loaded SLN formulations

The nanoparticle characterization parameters were mentioned in the table. The particle size was in the Nano range and was ranging from 191nm to 237 nm. Maximum EE was observed in the formulation EF6. All the particle exhibited negative surface charge around -36mV to -39mV. A similar trend was observed in the particle size and EE. The increased concentration of the tweens has increased the EE and decreased the particle size. Meanwhile, among the polysorbates used, tween 80 exhibited particles with smaller particle size and higher EE.

Table 4 Average particle size, zeta potential, Entrapment efficiency and PDI of Efinaconazole loaded SLN formulations

Formulation code	Particle size (nm)	PDI	Zeta potential (mV)	Entrapment efficiency (%)
EF1	238.61 ±2.95	0.262±0.062	-37.6 ± 1.024	73.8±1.55
EF2	233.70±3.13	0.274±0.045	-28.1 ± 2.035	76.8±1.35
EF3	235.11 ±0.93	0.369±0.036	-39.4 ± 1.330	72.4±4.35
EF4	236.3 ± 1.89	0.365±0.044	-37.6 ± 2.065	71.3±2.45
EF5	234.9 ± 3.96	0.371±0.052	-39.2 ± 2.064	72.5±0.45
EF6	191.9 ± 3.23	0.270±0.056	-31.1 ± 1.050	77.9±0.55
EF7	235.0 ± 1.89	0.363±0.058	-39.0 ± 2.350	73.7±2.30
EF8	237.6 ± 1.92	0.375±0.052	-39.0 ± 1.035	71.8±3.45

*Data expressed as mean ± SD n=3

1.8.3 In-vitro Release Profile of selected batches of Efinaconazole drug loaded with Tween 80 and Palmitic Acid

Selected batches of Efinaconazole drug loaded with Tween 80 and Palmitic Acid shown 30% of drug release for all the batches within 1hour. There was 60% drug release was released slowly over a period of 6 hours. The batch EF1 shows about 77% of the Efinaconazole drug released at the end of 12 hours. From the figure, it observed that EF2, EF6 shows a drug release of 75% at the end of 12 hours. The increased lipid content material decreased the cumulative release, which is in support with the earlier reports. The packing density of lipid molecules increased and as a result release is decreased. All the SLN formulations exhibited a burst type drug release in the first hour of dissolution and 30% of the release was observed. At the end of 6hrs 60% of drug release was observed from the formulations. Meanwhile, EF1 showed about 77% of Efinaconazole released at the end of 12 hours.

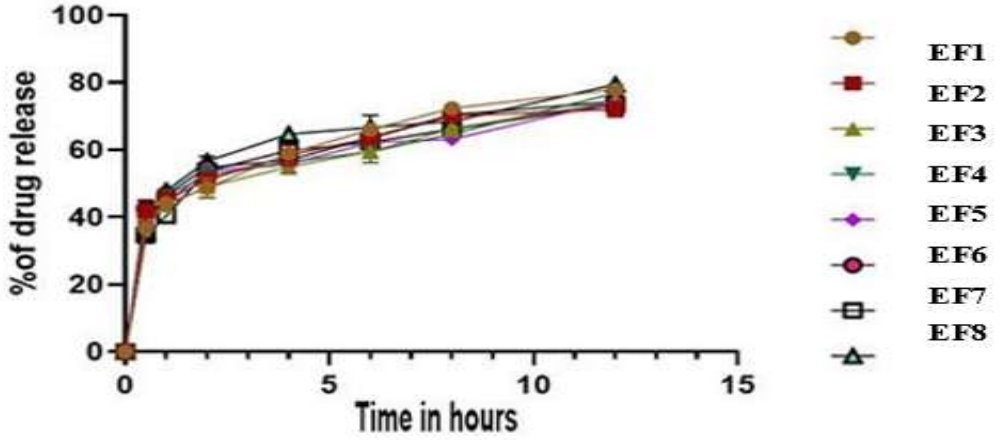

Figure 7 In-vitro Release Profile of Efinaconazole for selected batches of Efinaconazole loaded SLN formulations

1.8.4 Scanning electron microscopy (SEM)

The SEM studies were conducted to identify the topography of prepared SLN. Upon high resolution scanning, the SLN were observed to possess spherical morphology.

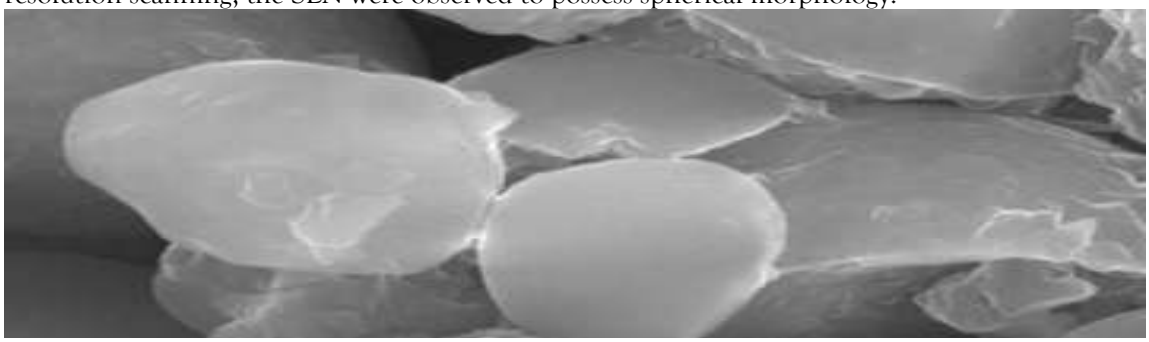

Figure 8 Scanning electron microscopy of Efinaconazole SLN EF2 (Containing Tween 80, Palmiic acid and drug concentration – 100 mg)

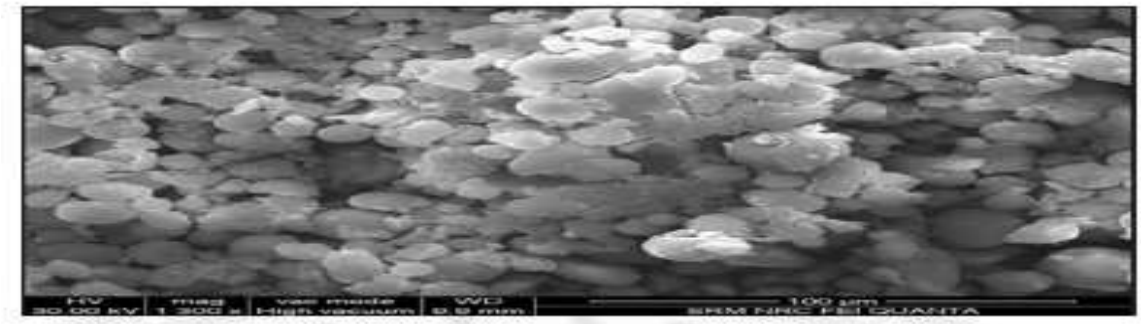

Figure 9 Scanning electron microscopy of Efinaconazole SLN EF6 (Containing Tween 80, Palmitic acid and drug concentration – 200mg)

1.8.5 Powdered X ray diffraction studies of selected Efinaconazole formulations

Powder X-ray analysis, of the Efinaconazole exhibited highly intense peaks and were characteristic of the API. Prominent peaks of pure drug Efinaconazole were observed at 2θ of 24, 93, 139, 162, 185, 208 and 231 were highly intense and indicated the crystalline nature. Whereas, in the prepared Efinaconazole SLN, the characteristic peaks of API were less intense. In addition, few low intense peaks were absent in the SLN, namely only one peak of pure drug at 162 to 350 was observed. These results clearly indicate the conversion of Efinaconazole to amorphous form. The similar results were observed in EF2, EF6 all the formulations of Efinaconazole indicating that the SLN preparation has resulted in the conversion of crystalline drug to its amorphous form.

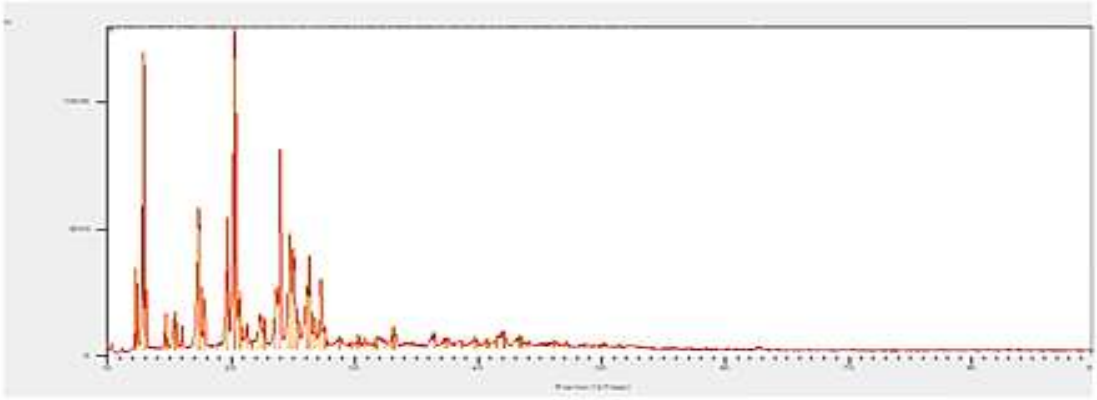

Figure 10 Powder X-ray Diffractions of Pure drug sample Efinaconazole

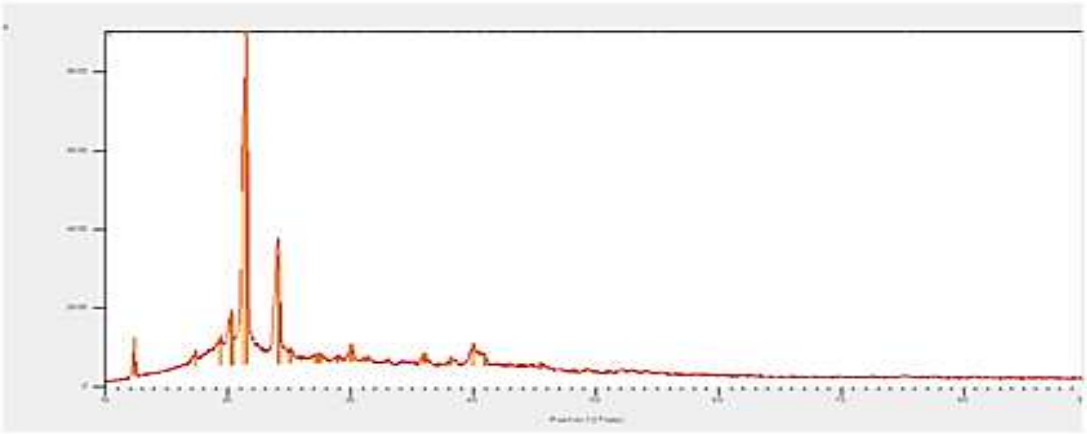

Figure 11 Powder X-ray Diffractions of selected Efinaconazole EF2 formulation

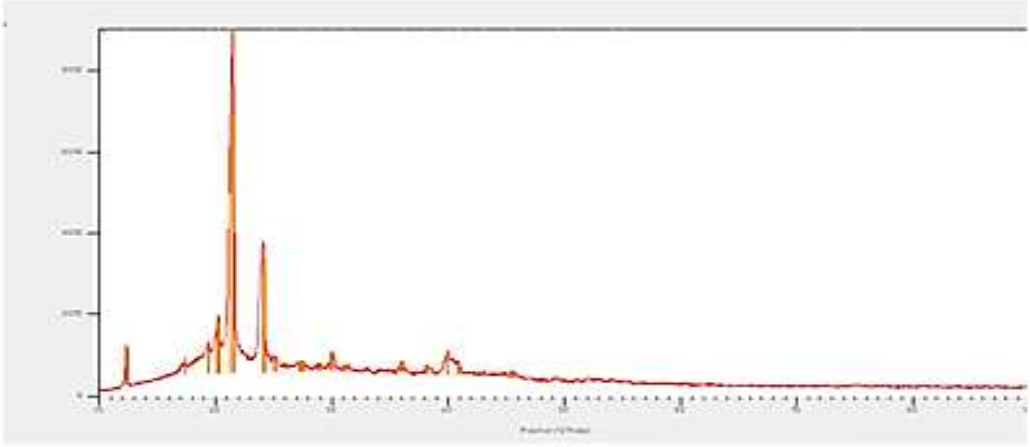

Figure 12 Powder X-ray Diffractions of selected Efinaconazole EF6 formulation

1.8.6 Transmission electron microscopy (TEM)

The TEM technique was used to analyses the morphology of prepared SLN. During TEM analysis, the particle was non-sticky to each other and were spherical shaped. It also confirmed that the prepared particles were of Nano range of 50-100 nm and in spherical shape.

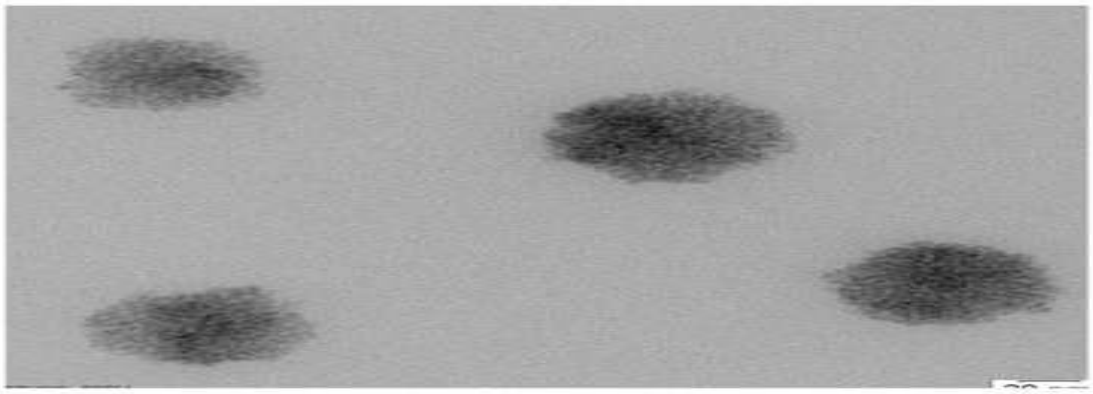

Figure 13 Transmission electron microscopy (TEM) of selected Efinaconazole EF2 formulation

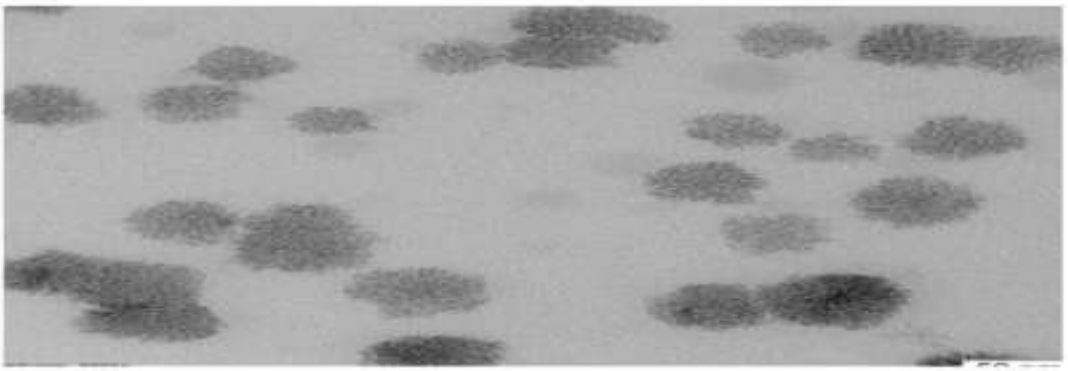

Figure 14 Transmission electron microscopy (TEM) of selected Efinaconazole EF6 formulation

1.8.7 Stability Study

The prepared SLN were stored at room temperature (28±2°C), refrigerated at 3-5° C for 6 months. To evaluate its stability. All the optimized formulations were stored in bottles and subjected to above mentioned temperatures at earlier mentioned temperature ranges. At the end of six months, the formulations were removed and evaluated for particle size and PDI. No marked difference in PDI and particle size was observed after 6 months and was mainly due to the lipid transition in the formulations and steric effect of Tween- 80 which enhanced the formulation stability.

Table 5 Stability Study data for the Formulation at initial, 3 and 6 months at room temperature and refrigerator temperature

Storage condition	Formulation code	Duration	Zeta size	Zeta potential	PDI	In-vitro drug release	Entrapment efficiency
Room tem	EF1	Day 1 Day 90 Day 180	238.71 239.87 245.87	-39.0 -39.4 -39.8	0.263 0.263 0.262	77.73 75.43 76.33	73.8 72.4 71.6
Room tem	EF2	Day 1 Day 90 Day 180	233.16 226.11 238.87	-34.40 -34.5 -34.87	0.369 0.383 0.394	75.80 74.44 73.21	76.8 75.4 75.02

Room tem	EF5	Day 1 Day 90 Day 180	234.41 235.22 236.87	-38.5 -38.7 -39.88	0.371 0.394 0.399	75.73 74.42 74.34	72.5 71.64 70.36
Room tem	EF6	Day 1 Day 90 Day 180	191.9 238.88 239.77	-30.2 -31.4 -32.87	0.270 0.273 0.281	75.22 74.12 73.36	77.9 76.4 75.2
Refri tem	EF1	Day 1 Day 90 Day 180	238.71 239.54 240.87	-39.2 -39.7 -39.87	0.263 0.263 0.261	77.73 76.43 76.33	73.8 73.04 72.69
Refri tem	EF2	Day 1 Day 90 Day 180	233.71 234.6 235.88	-32.44 -33.7 -34.87	0.274 0.276 0.278	75.80 75.44 74.21	76.8 75.7 74.9
Refri tem	EF5	Day 1 Day 90 Day 180	234.71 235.64 237.8	-38.0 -39.7 -39.87	0.371 0.373 0.385	75.73 74.42 74.34	72.5 71.8 71.11
Refri tem	EF6	Day 1 Day 90 Day 180	191.9 208.64 209.46	-31.9 -32.7 -32.87	0.274 0.280 0.281	75.22 75.12 74.36	77.9 77.46 76.24

1.9 Selected SLNs loaded in hard gelatin capsules

Considering the stability hurdles, the nanosuspension was converted to lyophilized powder. The dried SLNs powder of 166mg was filled into 4‖ size hard gelatin capsules containing 10 mg and 20 mg equivalent of Efinaconazole API.

1.10 Evaluation of loaded capsules

1.10.1 Uniformity of weight

Twenty number of prepared SLN filled capsules were individually weighed. The mean weight of the capsules was calculated and none of the capsules deviated more than 10% of mean weight.

1.10.2 Disintegration test

Capsules were introduced into the disintegration apparatus, the time for complete disintegration was recorded and was within permissible limits of 10 minutes and 5 seconds.

1.10.3 Drug content

The drug quantity of SLN filled capsules was investigated using UV method at 238 nm. The percentage drug content observed had uniformity in their drug content.

1.10.4 Dissolution drug release studies

In-vitro dissolution, of SLN loaded capsules, CN1, CN2, showed drug release of 30-40% in the first 30 minutes. At the end of 6 hours, 12 hours' drug release was observed to be 67% and 77%-78% respectively.

Table 6 Evaluation of capsules in SLNs (Mean ± SD n=3).

Formulation code	**Average weight of capsules (mg)**	**Drug content** (%)	**Disintegration time**
EF2 capsules (CN1)	98.7± 2.02	99.37±0.826	10 min 02 sec±0.032
EF6 capsules (CN2)	97.4 ±1.42	98.66±0.826	10 min 05 sec±0.045

Table 7 Dissolution profile of EF2 capsules (CN1) and EF6 capsules (CN2)

Time of Drug Release	CN1	CN2
0.5	30.66±1.33	30.65±3.42
1	43.73±1.64	42.18±2.54
2	54.81±2.56	51.14±2.26
4	60.96±0.13	58.23±3.04
6	66.07±0.48	67.55±1.62
8	74.35±0.44	75.15±1.16
12	78.92±0.52	77.14±2.37

*Data expressed as mean ± SD n=3

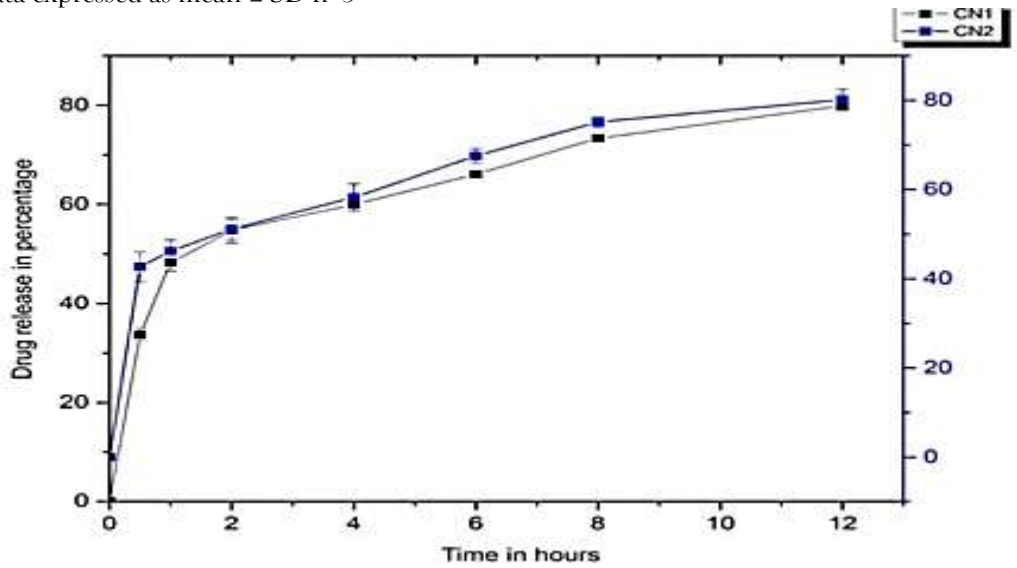

Figure 15 In-vitro Dissolution profile of EF2 capsules (CN1) and EF6 capsules (CN2)

Table 8 In-vitro release kinetics of Efinaconazole SLN's loaded in Capsules CN1 and CN2

Formulation code	Zero order	First order	Korsemeyer-peppas	Korsemeyer n (Release exp)	Hixon Crowell	Higuchi Equation
CN1	0.7425	0.8736	0.98	0.3693	0.9377	0.8389
CN2	0.6976	0.8361	0.9837	0.4190	0.9058	0.7961

1.10.5 Stability studies

The Efinaconazole loaded SLNs capsule were stored at different temperatures (28±2°C), refrigerated at 3-5° C for 6 months and average particle size, zeta potential, (EE) and Polydispersity index (PDI) were determined. The prepared capsules shown all the parameters within the limits of acceptance.

Table 9 Stability Study data for the SLN Formulation loaded in Capsules at initial, 3 and 6 months at room temperature and refrigerator temperature

Storage condition	Formulation code	Duration	Drug content	Disintegration time	In-vitro drug release
Room tem	CN2	Day 1	99.7± 0.02	10 min 08 sec±0.033	77.12± 0.52
		Day 90	99.07±0.82	10 min 02 sec±0.033	76.92± 0.52

		Day 180	98.44±0.83	11 min 04 sec±0.038	76.08± 0.54
		Day 1	98.7± 0.03	10 min 02 sec±0.033	78.92± 0.52
Room tem	CN1	Day 90	98.37±0.726	11 min 02 sec±0.042	78.14± 2.37
		Day 180	97.36±0.728	11 min 03 sec±0.032	77.14± 2.12
		Day 1	98.7± 2.02	10 min 02 sec±0.033	77.12± 0.52
Refri tem	CN2	Day 90	97.07±0.826	10 min 06 sec±0.032	77.02± 0.52
		Day 180	96.44±0.834	11 min 02 sec±0.041	76.69± 0.84
		Day 1	98.7± 2.02	10 min 02 sec±0.033	78.92± 0.52
Refri tem	CN1	Day 90	97.36±0.836	10 min 05 sec±0.032	78.14± 2.37
		Day 180	97.26±0.718	11 min 03 sec±0.022	77.84± 2.02

1.11 In-Vivo Study

The standard estimation curve method for HPLC corresponding to plasma drug concentration versus time profile was developed. The Pharmacokinetic parameters were studied using non-compartmental analysis and was shown in the table 5.30. The plasma samples were analyzed at the wavelength of 238nm. The plasma levels achieved by the SLN was higher than the drug suspension. Pharmacokinetic parameters were calculated by the software and the AUC observed for SLN has shown 2.1 and 2.5-fold increase when compared to free drug suspension. The Cmax was also higher for SLN and achieved in 5 hours. Mean residence time was significantly higher than that of free drug depicting sustained release over a long period of time. Elevated plasma concentrations of Efinaconazole and better pharmacokinetic properties of SLN was due to the Nanosized. In addition, controlled release from the formulation was also achieved. Hence these In-vivo results confirmed that SLN formulation could be successful in improving the oral bioavailability of poorly soluble drug Efinaconazole.

Table 10 Pharmacokinetic Profile for SLN Efinaconazole Formulation and drug Efinaconazole Suspension

Time (hrs.)	**SLN (EF2) (µg/ml)**	**SLN (EF6) (µg/ml)**	**Efinaconazole Suspension (µg/ml)**
0	0	0	0
1	0.50 ± 0.26	0.56 ± 0.54	0.37 ± 0.66
2	1.12 ± 0.76	1.23 ± 0.18	0.90 ± 0.56
3	2.14 ± 0.34	2.22 ± 0.44	1.24 ± 0.24
4	4.52 ± 0.24	4.58 ± 0.76	2.22 ± 0.74
5	4.78 ± 0.66	4.82 ± 0.42	2.03 ± 0.44
6	4.39 ± 0.62	4.63 ± 0.48	2.01 ± 0.54
8	4.24 ± 0.56	4.52 ± 0.72	2.00 ± 0.64
12	4.20 ± 0.72	4.43 ± 0.64	2.00 ± 0.28

*Data expressed as mean ± SD n=3

Table 11 Pharmacokinetic parameters for SLN Efinaconazole Formulation and drug Efinaconazole Suspension

Parameters	Efinaconazole suspension	Efinaconazole SLN Formulation EF2	Efinaconazole SLN Formulation EF6
C_{max} (µg/ml)	2.22	4.78	4.82
T_{max} (hrs.)	4	5	5.2
$T_{1/2}$ (hrs.)	2.804	9.28	19.52
AUC(µg/ml*h)	36.03	75.86	92.07
AUMC (µg/ml*h^2)	448.91	1754.48	6389.81
CL/F	21.98	0.0101	0.005
MRT (hrs.)	11.96	17.73	33.31

SUMMARY AND CONCLUSION

In summary, we developed SLN to entrap clinical drug Efinaconazole. It was prepared by a high-pressure homogenization method. The obtained SLN of Efinaconazole showed nanoscale, evenly distributed and excellent entrapment ability. Moreover, in vitro release research revealed that SLN of Efinaconazole showed an extended release capacity Efinaconazole without a distinct initial burst release consequence. The in vivo study of SLN of Efinaconazole indicated that the small intestine was the main absorption site and possessed a markedly improved oral bioavailability in rats. Overall, the SLN exhibited a tremendous application prospect for the oral delivery of low water dissolved drugs (21).

REFERENCES

1.Agarwal, R, Iezhitsa, I, Agarwal, P, Abdul Nasir, NA, Razali, N, Alyautdin, R & Ismail, NM (2015), 'Liposomes in topical ophthalmic drug delivery: an update', Drug Deliv, vol. 21, pp. 1-17.
2.Joseph, E., Saha, R.N. (2023) Advances in Brain Targeted Drug Delivery: Nanoparticulate Systems, Journal of Pharma Sci Tech. Volume 3, Issue 1, page 1-8.
3.Joy Tang et al, (2023). Erlotinib resistance in lung cancer: current progress and future perspectives, Frontiers in Pharmacology.
4.Balguri, SP, Adelli, GR, Janga, KY, Bhagav, P & Majumdar, S (2017), 'Ocular disposition of ciprofloxacin from topical', PEGylated nanostructured lipid carriers: Effect of molecular weight and density of poly (ethylene) glycol. Int J Pharm vol. 529, pp. 32-43.
5.Banerjee T, Mitra S, Singh AK, Sharma RK, Maitra A. (2022) Preparation and biodistribution of ultrafine chitosan nanoparticles. Int J Pharm, Volume 243, page 93-105. Baumgartner S, Vrecer F, and Zoroko B. (2022) Optimization of floating matrix tablets and evaluation of their gastric residence time, Int. J. Pharm, Volume 195, and Page 125-135.
6.Haresh Patel et al. (2023) Preparation and characterization of calcium phosphate coated vinblastine sulfate liposomes, IJPRBS; 2:2, 385-402.
7.Hippalgaonkar, K, Adelli, GR, Hippalgaonkar, K, Repka, MA & Majumdar, S (2023), 'Indomethacin-loaded solid lipid nanoparticles for ocular delivery: development, characterization and in vitro evaluation', J Ocul Pharmacol Ther, vol. 29, no. 2, pp. 216-28.
8.Değim Z, Özlem Çoban. Development of Nanocochleates Containing Erlotinib HCl and Dexketoprofen Trometamol and Evaluation of in Vitro Characteristic Properties. Turk J Pharm Sci (2018); 15(1):16-21.
9.Ekambaram P., Abdul HA. Priyanka K., (2022) solid lipid nanoparticles: a review. Scientific Reviews Chemical Communications, 2(1), 80-102.
10. Cavalli R, Bargoni A, Podio V, Muntoni E, Zara GP, Gasco MR. Duodenal administration of solid lipid nanoparticles loaded with different percentages of tobramycin. Journal of pharmaceutical sciences. 2003 May 1; 92(5):1085-94.
11. Chandra Boinpelly V, Verma RK, Srivastav S, Srivastava RK, Shankar S. α-Mangostin-encapsulated PLGA nanoparticles inhibit colorectal cancer growth by inhibiting Notch pathway. Journal of cellular and molecular medicine. 2020 Oct; 24(19):11343-54.
12. Ahiwale RJ, Chellampillai B, and Pawar AP. (2020) Investigation of 1, 2-Dimyristoylsn-Glycero-3-Phosphoglycerol-Sodium (DMPG-Na) Lipid with Various Metal Cations in Nanocochleate Preformulation: Application for Andrographolide Oral Delivery in Cancer Therapy. AAPS Pharm SciTech.; 21(279):1-18.
13. Fengzhen Wang, Mingwan Zhang, Dongsheng Zhang, Yuan Huang, Li Chen, Sunmin Jiang, Kun Shi & Rui Li (2018), 'Preparation, optimization, and characterization of chitosan coated solid lipid nanoparticles for ocular drug delivery', The Journal of Biomedical Research, vol. 32, no. 6, pp. 411-423.

14. Kessler, R. C., Angermeyer, M., Anthony, J. C., et al. (2017) Lifetime prevalence and age-of-onset distributions of mental disorders in the World Health Organization's World Health Survey Initiative. World Psychiatry, Volume 6, Page168-76. PMid: 18188442 PMCid: PMC2174588
15. Khalil RA., Ahmed A., Kassem MA., Ridi MS., Samra MMA., Awad G., Mansy SS., (2024). Preparation and in vivo Assessment of Nystatin-Loaded Solid Lipid Nanoparticles for Topical Delivery against Cutaneous Candidiasis. International Journal of Medical, Health, Biomedical, Bioengineering and Pharmaceutical Engineering. Vol: 8, No: 7.
16. Li S, Xu Z, Alrobaian M, Afzal O, Kazmi I, Almalki WH, Altamimi AS, Al-Abbasi FA, Alharbi KS, Altowayan WM, Singh T. EGF-functionalized lipid–polymer hybrid nanoparticles of 5-fluorouracil and sulforaphane with enhanced bioavailability and anticancer activity against colon carcinoma. Biotechnology and Applied Biochemistry. 2022 Oct; 69(5):2205-21.
17. Machín L, Tamargo B, Piñ A, (2019) RC. Bixa orellana L. (Bixaceae) and Dysphania ambrosioides (L.) Mosyakin & Clemants (Amaranthaceae) Essential Oils Formulated in Nanocochleates against Leishmania amazonensis. 24, 4222, (I): 1–10. doi:10.3390/molecules24234222
18. Mahato M, Sukumaran A, Mohamed M, Mir SR, Fouad H, Sadia A and Saima A. (2021) Science of Advanced Materials Box-Behnken Design Optimization of Etoposide Loaded Nanoemulsion: Formulation Development, Cellular Uptake Analysis and Pharmacokinetic Evaluation. Science of Advanced Materials. 13:1-10.
19. Mainardes, R.M., Evangelista, R.C. (2015), PLGA nanoparticles containing praziquantel: effect of formulation variables on size distribution. Int J Pharm. Volume 290(1–2), Page 137–144.
20. Lin CH., Chen CH., Lin ZC. Fang JY. (2017). Recent advances in oral delivery of drugs and bioactive natural products using solid lipid nanoparticles as the carriers. Journal of Food and Drug Analysis. Volume 25, Issue 2, Pages 219–234.
21. Gallarate, M, Chirio, D, Bussano, R, Peira, E, Battaglia, L, Baratta, F & Trotta, M (2023), 'Development of O/W nanoemulsions for ophthalmic administration of timolol', International Journal of Pharmaceutics, vol. 440, pp. 126-134.