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SOLID LIPID NANOPARTICLES FOR ENHANCEMENT OF ORAL BIOAVILABILITY OF CEFPODOXIME PROXETIL

U. A. Nimbalkar, M. V. Dhoka* and P. A. Sonawane

AISSMS College of Pharmacy, Kennedy Road, Pune, Maharashtra, India

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Correspondence to Author:

M. V. Dhoka

AISSMS College of Pharmacy, Kennedy Road, Pune, Maharashtra, India

ABSTRACT

Solid lipid nanoparticles (SLNs) have been proposed as suitable colloidal carriers for delivery of drugs with poor bioavailability. The objective of this study was to develop and evaluate solid lipid nanoparticles of Cefpodoxime Proxetil (CP) for enhancement of bioavailability via its lymphatic absorption. Solvent evaporation technique was adopted to prepare Cefpodoxime Proxetil loaded SLN with Precirol ATO 5 as a carrier with narrow size distribution. The mean particle size, drug entrapment efficiency (%), zeta potential and long term physical stability were investigated in detail. Drug release from Cefpodoxime Proxetil- Solid lipid nanoparticles (CP-SLN) was studied using a Franz diffusion cell. A pharmacokinetic study was conducted on male rats after oral administration of CP and CP-SLN. It was found that the relative bioavailability of CP with SLNs was significantly increased as compared with oral CP suspension. FTIR and DSC study revealed that drug is completely encapsulated in lipid matrix. Dry powder for reconstitution was selected as dosage form for the oral administration of CP-SLNs. These results indicated that bioavailability of CP was improved when formulated as SLNs due to its lymphatic absorption.

INTRODUCTION: Cefpodoxime Proxetil (CP) (1-[(isopropoxycarbonyl) oxy] ethyl ester of (Z)-7-[2-(2-amino-1, 3-thiazol-4-yl)-2- methoxyiminoacetamido]-3-methoxymethyl-3- cephem-4-carboxylic acid) is the orally active ester prodrug of third generation Cephalosporin. CP is used orally for the treatment of mild to moderate respiratory tract infections, uncomplicated gonorrhea and urinary tract infections.

Cefpodoxime Proxetil is a prodrug and gets hydrolyzed to its parent moiety Cefpodoxime Acid (CA) by non specific Cholinesterase enzyme in the intestinal wall/plasma [1]. It has 50% oral bioavailability. The reasons for this poor bioavailability of CP are low aqueous solubility and preabsorption luminal conversion of CP into CA by action of digestive Cholinesterase [1].

Bioavailability of CP can be improved simply by eliminating preabsorption conversion of CP to CA [2, 3]. One of the ways to eliminate CP to CA conversion is by protecting CP from cholinesterase attack by using lipid carriers because cholinesterases are unable to hydrolyze triglycerides. Hence formulation needs to be prepared for CP, which can bypass the passage of drug through epithelial cells and provide sufficient protection to the drug from the luminal cholinesterase.

Hence, in order to improve bioavailability formulation, enabling lymphatic absorption such as nanoparticles, nanoemulsions can be prepared [2]. Several means and mechanisms of delivering bioactives to or through lymphatic regions following the oral route have been investigated and documented.

These include paracellular mechanism, exploitation of M cells and transcellular mechanism of drug and nanocarrier absorption [3]. The most promising mechanism is transcellular absorption which operates for dietary lipids. The co-administration of lipid vehicle along with bioactives thus enhances stimulation of chylomicrons formation by enterocyte which dissolves and assimilate lipophilic molecules into their non polar core and thus promote the absorption of water insoluble drugs into intestinal lymphatics and organs [4, 5].

This avoids presystemic hepatic metabolism and thus enhances the concentrations of orally administered drugs in the systemic circulation. At the capillary level, the intracellular junctions between endothelial cells of lymphatic capillaries are more open compared with blood capillaries that results in molecular sieving of colloidal particles of large size directly into lymphatics, avoiding the blood capillaries. By utilizing this property of lymphatic system, absorption of long chain fatty acids could be facilitated via chylomicrons formation, thus bypassing the portal circulation [2].

Such a lymphatic targeting can be achieved through lipid based carrier systems such as lipid solutions, micellar solutions, microemulsions, nanoemulsions, liposomes, self-emulsifying drug delivery systems and recently SLNs [5, 6].

Solid lipid nanoparticles (SLNs) introduced in 1991, have attracted increasing attention as an alternative colloidal carrier system to traditional polymeric nanoparticles for controlled drug delivery because of their good tolerability and biodegradability, lack of acute and chronic toxicity of the carrier, physical stability, possibility of large scale production and feasibility to incorporate lipophilic and hydrophilic drug [6, 7].

The SLNs-based system possess characteristics of conventional carriers as well as some additional characteristics as elaborated above that obviate drawbacks associated and reported for conventional systems. Therefore they are considered to be a better alternative than liposomes, microemulsions, nanoemulsions, polymeric nanoparticles, self-emulsifying drug delivery systems and among others [8, 9].

SLNs have been documented as value added carriers for successful delivery of peptides and anticancer drug like doxorubicin through intestinal route. SLNs reportedly enhanced the oral bioavailability of cyclosporine A, vinpocetine, carvedilol, methotrexate and ketoprofen. It is also reported that SLNs were found to be stable at gastric physiological pH, even after 180 minutes of administration and suggested them as a suitable carrier system for lymphatic drug delivery [10].

Therefore, in this study CP-loaded SLNs were successfully prepared by solvent evaporation technique [11] and the physicochemical characteristics of the SLNs were investigated. SLNs were evaluated for various parameters like mean particle size [11, 12], drug content [12, 13], entrapment efficiency [12, 13], zeta potentials [14] and in vitro drug release study [12, 14].

Bioavailability studies were conducted in male Wistar rats after oral administration of CP-suspension and CP-SLNs [5].

MATERIALS AND METHODS:

Materials: Cefpodoxime proxetil and Precirol ATO 5 were obtained as a gift sample from Maxim Pharmaceuticals, Pune and Colorcon Asia Ltd. (Goa, India) respectively. All other chemicals and reagents were of analytical grade. This research work was carried out during year 2010-11.

Methods:

Preparation of Solid Lipid Nanoparticles:

Solvent Evaporation Method: Among the various techniques available CP-loaded SLNs were prepared by using solvent evaporation technique. Cefpodoxime Proxetil 100 mg was weighed accurately and dissolved in 10 ml of dichloromethane (DCM) AR grade. Different proportions of Precirol ATO 5 and lipophilic surfactant Span 60 was dissolved to this solution (organic phase). In aqueous phase 1 gm of Tween 80 was added to 100 ml of purified water.

Aqueous phase was stirred with speed of 2000 rpm for 15 mins. Then organic phase was added to aqueous phase and obtained pre-emulsion is stirred with 13000 rpm for 3 hrs. Composition of different trial batches is shown in **table 1**.

TABLE 1: COMPOSITION OF DIFFERENT TRIAL BATCHES OF SLNs

Formulation Code	CP (%)	Precirol ATO 5 (%)	Span 60 (%)	Tween 80 (%)	Organic solvent	Aqueous solvent
F1	1	3	2	1	DCM	Water
F2	1	5	2	1	DCM	Water
F3	1	10	2	1	DCM	Water
F4	1	15	2	1	DCM	Water
F5	1	20	2	1	DCM	Water

Characterization of CP-SLNs:

Compatibility Studies:

Fourier Transform Infrared Spectroscopy (FTIR): The CP and Precirol ATO 5 (1:1) were kept at room temperature for 30days. Then samples were subjected to the FTIR studies by using KBr as a blank. Prepared SLNs were evaluated for following tests;

Particle Size: The particle size analysis of the selected formulation was performed using Malvern Mastersizer 2000 MS (Malvern Instruments, Worcestershire, UK). Analyses were performed using a 90^{o} scattering angle at 25^{0}C. Measurements were obtained using a He-Ne laser of 633 nm.The average particle size and size distribution of each CP-SLN dispersion was recorded.

Zeta Potential: Zeta potential measurement was carried out by using Zeta potential analyzer (Delsa 4405X; BECKMAN COULTER) at 25^{o}C. The conductivity of the solution was adjusted to 50µS/cm by 0.1mmol/l sodium chloride solution for zeta potential measurement.

Drug Content: To CP-SLNs equivalent to 100 mg of CP 5ml of chloroform was added to dissolve Precirol ATO 5. It was evaporated to dryness and methanol was added to it. Then it was sonicated for 10 min in water bath sonicator and solution was filtered using Whatmann filter paper. Filtrate was diluted suitably with 0.1 N HCl and analyzed spectrophotometrically at 263 nm.

Entrapment efficiency: Drug entrapment efficiency (EE) in the SLNs was expressed as percent of the added drug actually entrapped into solid lipid nanoparticles. For this the 25% NaCl solution (5 ml) was added to the 100 ml of dispersion. This leads to aggregation and settling down of of SLNs. Settled lipid nanoparticles were separated and 10 mL of methanolic 0.1 N HCl was added to it, to solubilize free drug. After that solution was sonicated, filtered and analyzed with UV spectroscopy. % entrapment efficiency was calculated by following formula:

$$\text{EE (\%)}: \frac{\text{Total drug content - unentrapped drug}}{\text{Total drug content}} \times 100$$

***In vitro* release kinetics of CP from SLN:** *In vitro* release studies were performed on Optimized CP-SLN formulations using modified Franz diffusion cell. Dialysis membrane (Himedia, Mumbai) having pore size 2.4 nm, molecular weight cut off between 12,000–14,000, was used. Membrane was soaked in double-distilled water for 12 h before mounting in a Franz diffusion cell. SLN formulation containing 10 mg of CP was placed in the donor compartment and the receptor compartment was filled with dialysis medium (0.1 N HCl) (7 ml). At fixed time intervals, 0.1 ml of the sample was withdrawn from receiver compartment through side tube. Fresh dialysis medium was placed to maintain constant volume. Sample was diluted suitably and analyzed by UV spectrophotometry at 263 nm.

Freeze drying of CP-SLNs dispersion: Aliquots of above five batches of the optimized formulations were freeze-dried and converted into solid form to increase the stability of CP-SLNs and improve the palatability of dosage form. Lactose (5% w/v) was added as a cryoprotectant to 50 mL aliquots of samples, which were frozen in liquid nitrogen and lyophilized (Heto Drywinner, Thermo Scientific, USA) for 48 h at -70˚C, at a 0.05 mm Hg pressure. Freeze-dried samples were stored at room temperature. From the results of above parameters, optimized formulation was selected and evaluated for following tests.

Fourier Transform Infrared Study: A Jasco FTIR spectrophotometer (Jasco FTIR- 401, Japan) was used for infrared analysis of CP, CP-Precirol and CP-SLNs. About 1-2 mg of sample was mixed with 50 mg dry potassium bromide and the samples were examined at transmission mode over wave number range of 4000 to 400cm^{-1}.

Differential Scanning Calorimetry Study: The DSC thermogram of CP-SLN was recorded using Differential scanning calorimeter (DSC 823 Mettler Toledo, Japan). Samples were accurately weighed onto aluminum pans and then hermetically sealed with aluminum lids. Thermograms were obtained at a scanning rate of 10°C/min conducted over a temperature range of 30-300 °C in the environment of liquid nitrogen.

Particle Morphology: In the study, CP-loaded SLN dispersion was dried in a freeze dryer for 24 hrs. and sputtered with platinum in an ion sputter for 300 s. Images were collected at an acceleration voltage of 15 kV using a back scattered electron detector on Joel JSM 6360 SEM. Analysis was performed at 25±2^{0}C.

***In vivo* Studies:** Approval to carry out in-vivo study was obtained from Institutional Animal Ethics Committee, AISSMS College of Pharmacy and their guidelines were followed for the studies. The optimum SLNs formulation was screened from above studies and taken for the in-vivo studies. The animals used for in-vivo experiments were male albino rats (250-300gms). Two groups were made for the study and six rats were kept in each group. After administration of CP dispersion and CP-SLN formulation, plasma was withdrawn at fixed intervals and analyzed by HPTLC method.

Following parameters were used for analysis of plasma sample:

Instrumentation: The samples were spotted on Merck TLC aluminium plates, precoated with silica gel 60F $_{254}$ (10 cm by 20 cm with 250 µm layer thickness) using a Camag Linomat V applicator (Camag, Switzerland). The samples were applied onto the plates in the form of narrow bands of 5 mm width with a Camag 100 microlitre sample syringe (Camag, Switzerland) under a nitrogen atmosphere.

The length of the chromatographic run was 9 cm and the time required for each run was approximately 25 min. Linear ascending development was carried out in a twin trough glass chamber (10 cm × 10 cm). Densitometric scanning of the developed plates was performed using Camag TLC scanner III, operated with winCATS software (Version 1.4.2, Camag) in the absorbance mode at 263 nm. Scanning speed was kept at 4 mm/s.

Mobile Phase: The solvent system of chloroform-toluene-methanol (3:4:3), which developed in house, was used.

Calibration curve of Cefpodoxime Proxetil in Plasma: To each 0.5 ml dilution of CP, 0.5 ml plasma and 1 ml ACN were added in a glass tubes. Each sample was vortex mixed for 3 min and centrifuged (2500 rpm for 20 min). After centrifugation 20 µl aliquot was spotted on to the TLC plate to get concentration in the range of 100-600ng/spot. The densitometric scanning at wavelength 263 nm was done and the concentration of Cefpodoxime Proxetil in each sample was calculated using the areas obtained by densitometry scanning.

Preparation of formulations for Animal Studies: Suspension of CP-SLN of Cefpodoxime Proxetil and Pure drug were prepared using dose of 10 mg/kg.

Administration of Drug: Bioavailability studies were carried out for SLN of Cefpodoxime Proxetil. Dose for rats was calculated based on the weight of the rat. The rats were anesthetized using ether and the blood samples were withdrawn from retro-orbital region at 0 (pre-dose), 0.5, 1, 2, 4, 6 and 8 hrs in tubes containing anti-coagulant, mixed and centrifuged at 3000 rpm for 20 min. The plasma was separated carefully and stored at 2-10 ^{0}C until drug analysis was carried out using HPTLC.

HPTLC analysis of Cefpodoxime Proxetil in Plasma: Acetonitrile was added to plasma. Acetonitrile precipitates the plasma proteins, which were then vortex for 3 min and separated by centrifugation at 3000 rpm for 20 min. The solution was then spotted over TLC plate and was subjected to development using the procedure as mentioned for calibration curve.

The densitometric scanning at wavelength 263 nm was done and the concentration of Cefpodoxime Proxetil in each sample was calculated using the areas obtained by densitometric scanning. The concentration of the Cefpodoxime Proxetil was calculated using the calibration curve prepared in plasma. Noncompartmental analysis was employed for calculating pharmacokinetic parameters like T_{max}, C_{max}, and AUC_{0-t}.

RESULT AND DISCUSSION:

Compatibility studies: After 30 days sample was observed for physical changes but there were no physical changes observed in the mixture of CP and lipid combination. **Figure 1** shows infrared spectrum of CP (M1) and CP-Precirol (M2).

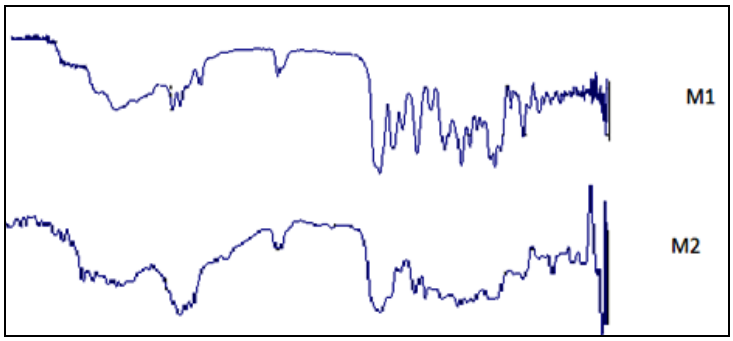

FIG. 1: COMPATIBILITY STUDIES

Preparation of Solid Lipid Nanoparticles: Various methods are available for the preparation of SLN which include Hot homogenization and Cold homogenization, micro emulsion and Solvent emulsification/ evaporation methods. Except emulsification/ evaporation method all other methods involve melting of lipids and drug. But as CP is heat sensitive drug which may be degraded at melting temperature of lipid, is Solvent emulsification/evaporation method wherein no heat is involved is a method of choice.

Particle Size: The effect of Precirol ATO 5 concentration on the particle size of SLN was determined. The mean particle size of the SLN was found to increase with increasing concentration of Precirol ATO 5 and it was in the range 115 nm to 320 nm (**Table 2**). The viscosity of the medium increases at a higher Precirol ATO 5 concentrations resulting in enhanced interfacial tension.

Shearing efficiency is also diminished at higher viscosities. This results in the formation of larger particles. Among five batches F2 batch shows smallest particle size. Though F1 batch having lower lipid concentration still it showed larger particle size than F2 this may be due to insufficient lipid concentrations to encapsulate complete drug.

Zeta Potential: Zeta potential is key factor to evaluate the stability of colloidal dispersions. In general particle could be dispersed stably when absolute value of zeta potential was above 30 mV due to the electric repulsion between particles. As shown in Table 2 all of zeta potential of obtained SLNs was about -25 mV to -22 mV which indicate instability of SLNs in aqueous system.

Due to lower zeta potential, surfactant molecules rearrange onto the surface of particles to form loops and tails leading to the bridging between the nanoparticles, which leads aggregation of particles. Freeze drying of SLNs dispersion overcomes the above problems of instability.

Entrapment Efficiency: The drug entrapment efficiency of CP-SLNs varied from 76.83 to 91.2% (**Table 2**) Results demonstrated that increase in concentration of Precirol ATO 5 increased the entrapment of the CP. A high amount of drug could be incorporated in nanoparticle dispersion.

Such high incorporation was possible because of lipid solubility of CP and also Span 60 as a lipid surfactant helps to solubilize the CP in to lipid which further increases entrapment of drug. Among five batches F1 having poor entrapment due to lower lipid content whereas on increasing lipid content SLNs showed good entrapment

Drug Content: Drug content studies of freeze dried formulations were done to detect the actual concentration of CP present in freeze dried powder. It will help further for calculation to formulate oral dosage form. The drug content of F1 to F5 formulations were varied from 70.11 % to 89.09%. It showed that F1 formulation having poor drug content due to lesser concentration of Precirol ATO 5. But from F2 to F5 drug content drug content increases initially and then again decreases. This is mainly due to increase in lipid content.

***In vitro* Release Kinetics of CP from SLN:** Franz diffusion cells with dialysis membrane (pore size 2.4 nm) were used in this study. Dialysis membrane retained nanoparticles and allowed the transfer of the drug immediately into the receiver compartment. **Figure 2** shows the % release of CP from five formulations. There exists an inverse relation between the percent drug released and particle size. Because large particle size causes increase in diffusion path for release of drug leads to lower drug release.

In-Vitro drug release parameters of five formulations are shown in **table 2**. F1 batch shows 85 %drug release upto 3hrs indicating poor EE while increase in Precirol ATO 5 concentrations results into the slow release of CP from SLN suggests that CP homogeneously dispersed in the lipid matrix. Generally CP dissolves in lipid diffuses to the surface and undergoes partitioning between lipid and aqueous phase.

TABLE 2: EVALUATION PARAMETERS OF SLNS

Formulation Code	Drug: lipid	Particle Size (nm)	EE (%)	Drug Content (%)	Drug Release (%)	Zeta potential (mV)
F1	1:3	118.87	76.83	70.11	84.34	-22.90
F2	1:5	**115.32**	**90.9**	**89.09**	**82.55**	**-23.12**
F3	1:10	201.05	91.20	88.12	75.07	-24.56
F4	1:15	275.73	90.56	84.33	70.89	-.25.55
F5	1:20	320.41	89.56	83.67	66.21	-.25.82

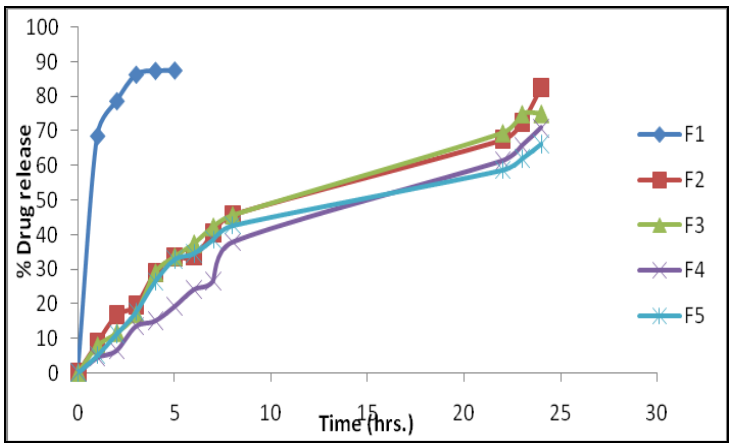

FIG. 2: % DRUG RELEASE PROFILE OF F1-F5 FORMULATIONS

Freeze drying of CP-SLNs dispersion: The particle size of the above five formulations after re-dispersion were from 118-321 nm which does not shown significant difference in it than before freeze drying. The cryoprotectant effect of Lactose observed here, may arise from the formation of a protective capping layer around the SLNs, sustained by hydrogen bonds between the polar function of the drug molecules, exposed at the surface of the SLNs, and the hydroxyl functions of the sugar. The formation of a hydrosoluble matrix, where the particles are embedded in, may facilitate the reconstitution of the dispersions. This solved the issue of instability of SLNs dispersion. Variations observed in the size of the SLNs after reconstitution of freeze dried product were shown in **Table 3**.

TABLE 3: PARTICLE SIZE BEFORE AND AFTER FREEZE DRYING BY AQUEOUS RE-DISPERSION

Optimized formulation	Before Freeze drying	After Freeze drying
	Particle size(nm)	Particle size(nm)
F1	118.87	120.98
F2	115.32	118.30
F3	201.05	205.55
F4	275.73	278.14
F5	320.41	325.05

From the result of above evaluation test Formulation F2 showed smallest particle size with better EE, drug content and controlled drug release than other four formulations. So it was considered as optimum formulation and selected for further evaluation.

Fourier Transform Infrared Study: Interaction between drug-lipid in SLN was studied by infrared spectroscopy by finding any change in frequency of functional group in SLN with respective functional group of CP. The spectral observations indicated that there is no strong interaction between the drug and the Precirol ATO 5. But IR spectra of CP-SLN showed no such a characteristic peak which indicates that drug is completely entrapped in the lipid matrix. Combined IR spectra of CP, CP-Precirol and CP-SLN are shown in **Figure 3**.

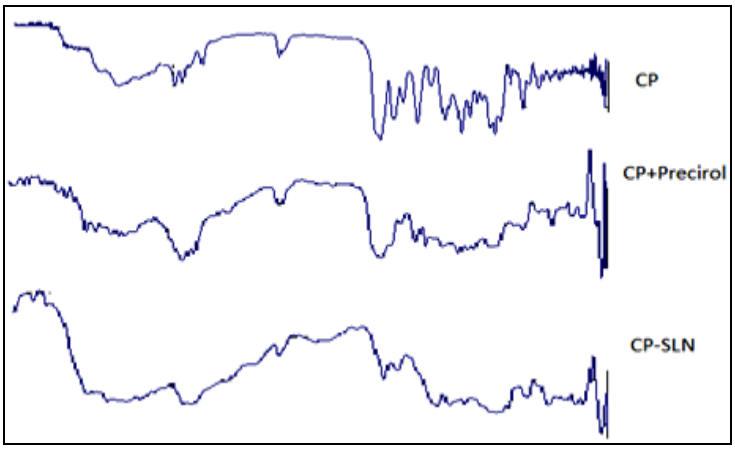

Figure 3: IR spectra of CP, CP-Precirol and CP-SLN

Differential Scanning Calorimetry Study: The DSC thermogram of CP recorded using Differential scanning calorimeter (DSC 823 Mettler Toledo, Japan), is the most widely used calorimetric techniques to characterize the physical state of drug in the lipid matrix. **Figure 4** depict the DSC thermogram of pure CP

(a) and CP-SLN (b). The DSC thermogram of CP exhibited a single sharp endothermic peak at 89° corresponding to its melting transition temperature. The thermograms of the CP-SLN showed no such characteristic peak, indicating that the drug was uniformly dispersed at the lipid matrix.

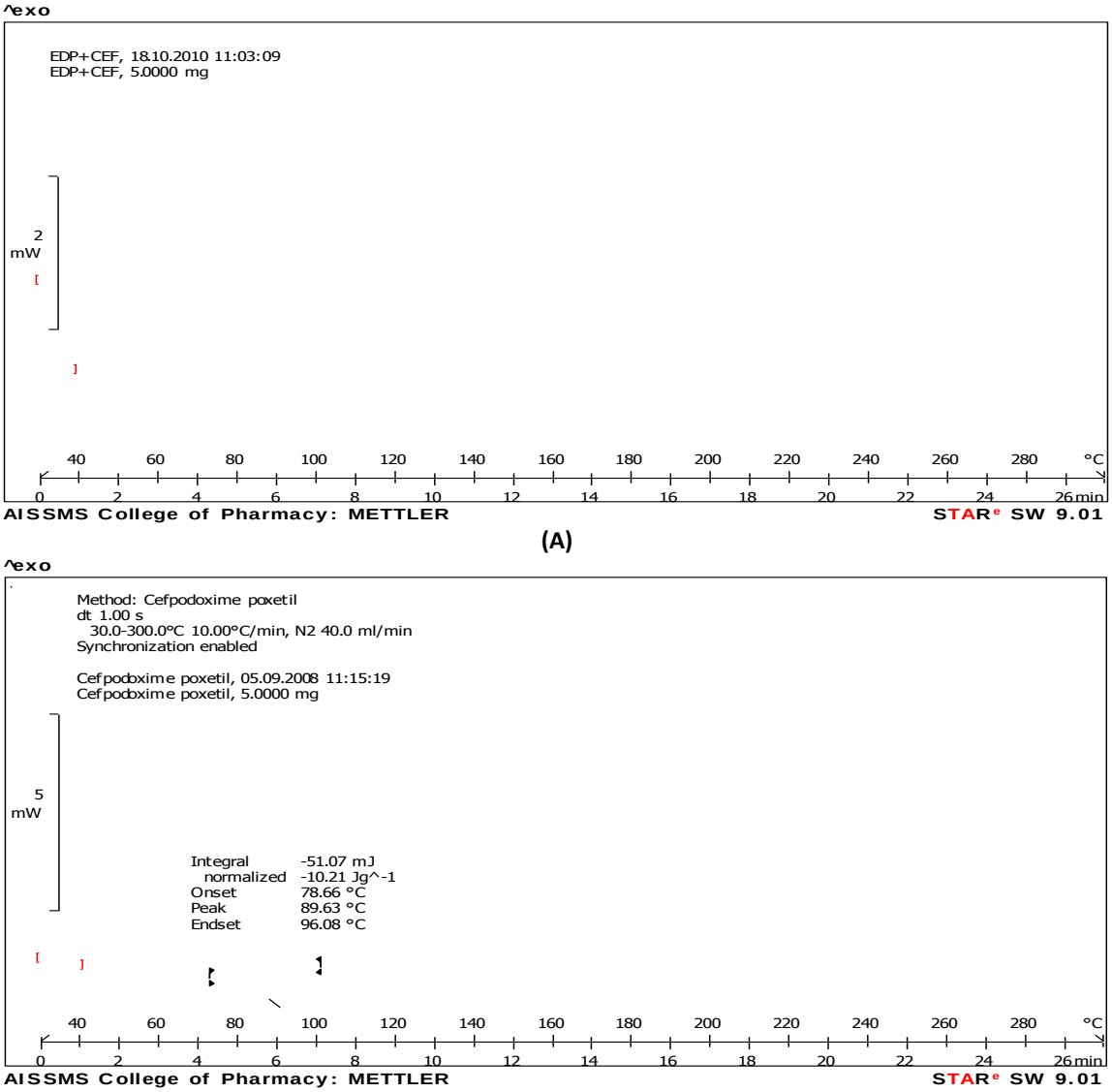

FIG. 4: DSC SPECTRUM OF A) CP AND B) CP-SLN

SEM Study: The SEM image of CP-SLN (**Figure 5**) revealed that the particle size was in nanometric range (110 nm) and the particles had spherical morphology.

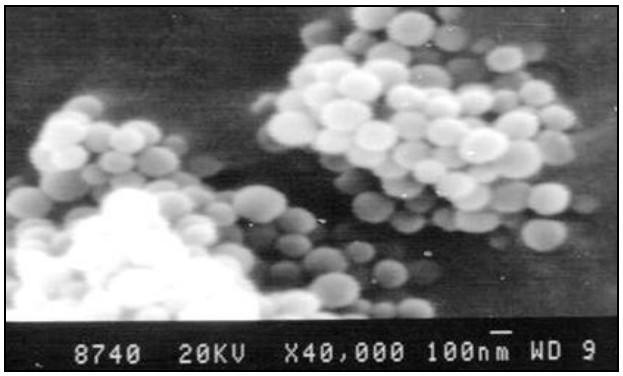

FIG. 5: SEM IMAGE OF SOLID CP-SLNS

***In-Vivo* Studies:** The rats were anesthetized using ether and the blood samples were withdrawn from retro-orbital region at 0 (pre-dose), 0.5, 1, 2, 4, 6 and 8 hrs in tubes containing anti-coagulant, mixed and centrifuged at 3000 rpm for 20 min. The plasma was separated carefully and stored at 2-10^{o}C. Acetonitrile was added to plasma.

Acetonitrile precipitates the plasma proteins, which were then vortex for 3 min and separated by centrifugation at 3000 rpm for 20 min. The solution was then spotted over TLC plate and was subjected to development.

Calibration curve of CP in Plasma: Table 4 shows the data for the calibration curve of CP in plasma and the calibration curve is represented in **Figure 6**. The values of slope, regression coefficient and intercept were found to be 5.563, 0.998 and 679.8 respectively. **Figure 7** shows chromatogram of blank plasma and CP which clearly indicates that there was no interference of plasma peaks at the R_f of the CP.

TABLE 4: LINEARITY OF CP IN PLASMA SAMPLE

Concentration (ng/band)	Area
100	1181
200	2338
300	2893
400	4066
500	5095
600	2338
800	2893

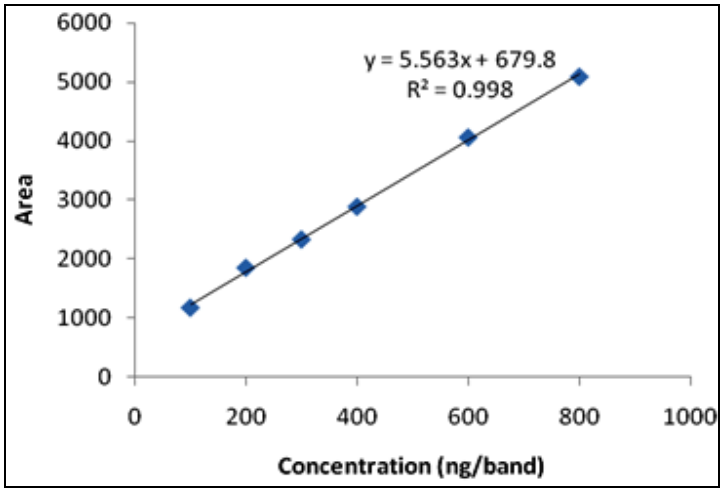

FIG. 6: CALIBRATION CURVE OF CP IN PLASMA SAMPLE

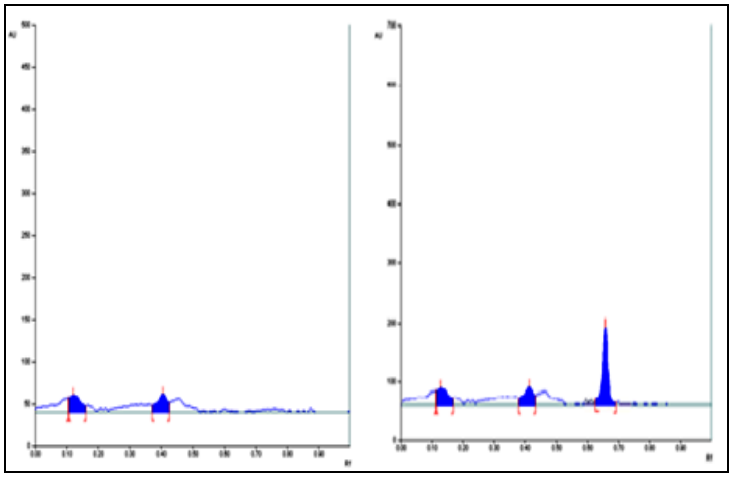

FIG. 7: TYPICAL CHROMATOGRAM OF (A) BLANK PLASMA (B) CP (100 ng/band, Rf- 0.65±0.05)

Plasma Concentration Profile of CP in rats: The *in-vivo* study was performed to quantify CP after oral administration of suspension of SLN and pure CP. **Table 5** shows the data of the plasma concentrations of CP after predetermined time analyzed by HPTLC. The plasma concentration time profile of CP and SLN formulation in rats is represented in **Figure 8**.

In the present study, the peak plasma concentration (C_{max}) is increased, as evident from the data in Table 6. The elevation of T_{max} represents delayed absorption of the drug due to slow release from the formulations. Increase in C_{max} and AUC suggests the improvement in bioavailability (**Table 6**). Relative bioavailability of CP-SLNs formulation was calculated by using following formula;

$$\text{Relative Bioavailability} = \frac{\text{AUC of Test}}{\text{AUC of Std.}}$$

TABLE 5: PLASMA CONCENTRATION PROFILE DATA FOR CP IN RAT FROM CP-SLN AND PURE DRUG (n=6)

Time (hr)	Pure drug Concentration	CP-SLN Formulation Concentration (µg/ml)
0	0	0
0.5	2.03	1.19
1	3.06	2.18
2	3.46	5.19
3	2.25	5.17
4	2.11	4.09
6	0.002	3.81
8	0	2.36

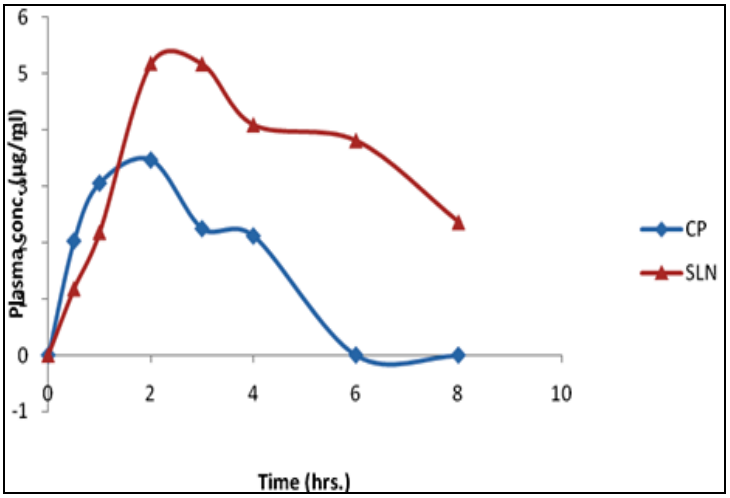

FIG. 8: PLASMA CONCENTRATION PROFILES OF CP AND SLN IN RATS

TABLE 6: PHARMACOKINETIC PARAMETERS OF CP AFTER ORAL ADMINISTRATION OF CP-SLN FORMULATION AND PURE DRUG IN ALBINO RATS

Formulation code	C_{max} (μg/ml)	t_{max} (h)	AUC_{0-8} (μg.h/ ml)
Pure drug	3.46	2	12.22
CP- SLN	5.18	3	28.69

$$\text{Relative Bioavailability} = \frac{\text{TEST AUC (0-8 h)}}{\text{Std. AUC (0-8 h)}}$$

$$= 28.69/12.22$$
$$= 2.35$$

These results suggest that there has been increase in the 2.35 folds bioavailability of CP due to incorporation in lipid formulation (CP-SLNs).

CONCLUSION: The present study has been a satisfactory attempt to formulate a solid lipid nanoparticles of an antibiotic i.e., Cefpodoxime Proxetil, with a view of its lymphatic as well as systemic absorption and controlled delivery of the drug. From the results, it can be concluded that biocompatible and cost-effective lipid i.e., Precirol can be used to formulate an efficient Solid Lipid Nanoparticulate system with smallest particle size with good percentage entrapment efficiency and practical yield. The particle size analysis revealed that the particles were of the size range of 110-130 nm and had lymphatic as well as systemic absorption due lipid coating. *In-vitro* drug release studies showed that release from the SLN get successfully retarded for over 24 hrs.

The *in-vivo* studies revealed that the relative bioavailability of the drug increased by about 2.35 times by formulating it into SLN form.

Thus, the current study attained the successful development and evaluation of a Solid Lipid Nanoparticles of an antibiotic i.e., Cefpodoxime Proxetil.

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