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FELBAMATE LOADED SOLID LIPID NANOPARTICLES: *IN VITRO* AND *IN VIVO* EVALUATION

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ABSTRACT

Felbamate is chemically a phenylcarbamate derivative with PEGylation and it is pharmacologically an antagonist of *N*-methyl-D-aspartate receptor (NMDA) receptors. It is used primarily as an anticonvulsant for the treatment of severe refractory epilepsy. It is slightly soluble in water with $t_{1/2}$ of 4-6 hours. Felbamate loaded Solid Lipid Nanoparticles (SLN) have been developed using stearic acid as lipid, poloxameras surfactant, polysorbate 80 as cosurfactant by microemulsion technique. Prepared SLNs were evaluated for particle size, drug content, in vitro release profile, release kinetics, in vivo acute toxicity and in vivo bioavailability. It was concluded from the study that the formulation prepared with lipid concentration of 50 mg, surfactant concentration of 75 mg, co-surfactant concentration of 0.75 ml, aqueous phase volume of 5 ml, stirring speed of 400 rpm, sonication time of 30 minutes in 500mL beaker and volume of cold aqueous phase 30 ml has shown the improved *in vitro* physic chemical properties and hence have chose as the best formulation. The relative bioavailability of this formulation was found to be 9.69 times higher than plain suspension.

KEYWORDS: ***Solid Lipid, Nanoparticles, Particle Size, Sonication, Felbamate***

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INTRODUCTION

About 40 % of the new chemical entities (NCE) which are commercially available in the market are poorly water soluble due to which sufficient amount of drug absorption from the gastrointestinal tract (GIT) is being a challenge for research scientists. Low solubility and/or low permeability lead to oral bioavailability issues which ultimately affect drug safety and efficacy. Previously, different colloidal carrier systems have been investigated to overcome this problem. But certain disadvantages are associated with them such as drug expulsion upon storage, limited stability, low drug loading, and polymers cytotoxicity[1-3]. This leads to the rise of fabricating solid lipid based nano drug delivery system termed as solid lipid nanoparticle. Solid lipid nanoparticles (SLNs) were developed in the end of the 20th century. The use of SLNs is a striking improvement because the solid matrix of the lipids presents high flexibility in controlling the drug release and protects the encapsulated drugs from gastric degradation. SLNs are generally composed of biodegradable and biocompatible solid lipid as solid core, coated by nonhazardous surfactant/cosurfactant as the outer shell. Use of solid lipids increases drug absorption mainly through enhanced drug dissolution and solubilization in the intestinal-milieu, improved lymphatic-transport, enhanced gastrointestinal permeability, and decreased gastric-emptying rate. Particle size and PDI are key characteristics and are critical parameters in the stability and fabrication of SLNs. These characteristics mainly depend upon particles composition and different fabrication techniques[4-9]. The main aim of the current research work is to develop solid lipid Nanoparticles of felbamate (antiepileptic drug) using placket and burman design of experiments. Felbamate is a PEGylated phenylcarbamate derivative that acts as an antagonist of NMDA receptors. It is used as an anticonvulsant, primarily for the treatment of seizures in severe refractory epilepsy. It is slightly soluble in water with the logP value of 0.56[10-15].

MATERIALS AND METHODS

Materials

Felbamate was received as gift sample from AurobindoPharma. Stearic acid (Arjun Industries, India), Poloxamer 407 (Signet, Mumbai), Polysorbate 80 (Sisco Research Laboratories, Chennai), Chloroform and Methanol (Rankem, Chennai), Dialysis Membrane 50 – LA 387 (Himedia, Mumbai) were purchased from the local market. All the reagents used were of analytical grade.

Methods

Development of Felbamate loaded solid lipid nanoparticles

Solid lipid nanoparticles of felbamte were fabricated by oil in water microemulsion technique. Procedure followed was briefly explained here. The lipid phase containing stearic acid was melted at its melting point of 69-70ºC and the drug felbamate was added to this molten lipid. In another vessel, surfactant (Poloxamer 407) and Co-surfactant (polysorbate) were dissolved in 10 ml of aqueous phase and heated to same temperature. Then the lipid phase was added dropwise to aqueous phase by maintaining the same temperature and then subjected to magnetic stirring at 200 rpm-400rpm for 15-30 minutes. The obtained o/w microemulsion was dispersed in cold water under probe sonicator for 30 minutes to solidify the nanoparticles in a volume ratio of 1:1 hot microemulsion to cold water. The fabricated Felbamate loaded nanoscale solid lipid particles were frozen and dried on a lyophilizer at -40°C temperature and operating pressure 0.4 bar. The dried powder was stored in a desiccators. Composition of prepared SLNs is given in table 1.

Table 1
Composition of Felbamate loaded Solid Lipid Nanoparticles

Run	Stearic Acid (mg)	Poloxamer 407 (mg)	Polysorbate 80 (mg)	Volume of aqueous phase (mL)	Magnetic Stirrer rate (rpm)	Probe sonicator duration (min)	Volume of beaker used probe sonication (mL)	Volume of cold aqueous phase (mL)
FSN01	150.00	75.00	0.25	5.00	200.00	30.00	125.00	50.00
FSN02	50.00	75.00	0.25	15.00	400.00	10.00	250.00	50.00
FSN03	50.00	75.00	0.75	15.00	200.00	10.00	125.00	50.00
FSN04	50.00	25.00	0.25	15.00	200.00	30.00	250.00	30.00
FSN05	150.00	25.00	0.25	5.00	400.00	10.00	250.00	50.00
FSN06	150.00	75.00	0.75	5.00	200.00	10.00	250.00	30.00
FSN07	150.00	25.00	0.75	15.00	200.00	30.00	250.00	50.00
FSN08	50.00	25.00	0.25	5.00	200.00	10.00	125.00	30.00
FSN09	150.00	25.00	0.75	15.00	400.00	10.00	125.00	30.00
FSN10	150.00	75.00	0.25	15.00	400.00	30.00	125.00	30.00
FSN11	50.00	75.00	0.75	5.00	400.00	30.00	250.00	30.00
FSN12	50.00	25.00	0.75	5.00	400.00	30.00	125.00	50.00

Characterisation of Solid Lipid Nanoparticles of Felbamate Particle size, polydispersity index and zeta potential

Prepared solid lipid nanoparticles were maintained at room temperature for 30 days and they were characterized for particle size, polydispersity index and zeta potential. About 1 ml of prepared solid lipid nanoparticles were diluted appropriately using distilled water and then taken individually in a zeta cell and measured the average particle size, polydispersity index

and zeta potential using Zetasizer. The experiments were performed in triplicate.

Surface morphology analysis

Surface morphology of prepared solid lipid nanoparticles was done by scanning electron microscopy (SEM) and transmission electron microscopy (TEM).

Drug content, Encapsulation efficiency & Drug loading estimation

Assay (Drug Content estimation), % entrapment efficiency was done by developed RP_HPLC method.

HPLC Method to estimate samples of Felbamate:

RP-HPLC method was developed to estimate the in vitro samples of felbamate from solid lipid nanoparticles. Effective seperaton was done by using Phenomenex C18 column (ODS 250mm X 4.6mm, 5microns) . Mobile phase containing potassium dihydrogen phosphate buffer (50nM, pH 4.5), acetonitrile and methanol (65:26.2:8.8) in an isocratic mode elution. Flow rate was maintained at 0.8mL/min. The samples were analyzed by PDA detector.

Estimation of encapsulation efficiency and drug loading

Prepared solid lipid nano formulations were centrifuged using a refrigerated centrifuge (Remi) for 45 minutes at 19,000 rpm at -20°C and supernatant was separated and stored individually for further analysis. About 1 ml of supernatant was mixed with 1 ml of methanol, which was vortexed for 5 minutes and filtered through 0.22 µm membrane. Estimated amount of free drugs were expressed as W_{free}. The experiments were performed in triplicate

✓ Encapsulation efficiency (EE) and drug loading (DL) were estimated as follows

$$EE\ (\%) = \frac{[\text{Drug Content } (W_{total})] - [\text{Drug in the supernatant } (W_{free})]}{[\text{Drug Content } (W_{total})]} X100$$

$$DL\ (\%) = \frac{[\text{Drug Content } (W_{total})] - [\text{Drug in the supernatant } (W_{free})]}{[\text{Weight of the polymer used in the formulation } (W_{polymer})]} X100$$

***In-vitro* drug release study**

Drug release from felbamate loaded solid lipid nano particles was done by using dialysis bag method**.** In this method, accurately weighed quantity (equivalent to one dose) were carefully placed in dialysis bag (CUtoff size of 5kDa, Himedia), both ends were tightly sealed. The dialysis bag was positioned in a 100 ml phosphate buffer at pH 7.4 in a beaker, which was kept magnetic stirrer and stirred at 100 rpm (Remi, India). Temperature was maintained at 37°C ± 0.5°C. At scheduled time intervals (0, 1, 2, 4, 6, 8, 10, 12 and 24 hours), 1 ml of the release medium was withdrawn using micropipette and replaced with the same volume of fresh PBS. The samples were filtered immediately through a 0.45 µm membrane filter (Elix, Mill-Q) and the content of Felbamate was estimated after suitable dilution with a Thermo Scientific HPLC (Spectra system P-4000, USA) with UV detector (Kromasil 100) and C18 column (Particle size 5 µm, 250 mm×4 mm) at 265 nm.

Stability studies

Stability studies of optimized formulation were carried out according to international conference on harmonisation (ICH-QIA (R2) guidelines, 2003) for six months. The study conditions were 25°C±2°C/60%RH±5%RH (Long term), 30°C±2°C/65%RH±5%RH (Intermediate) and 40°C±2°C/75%RH±5%RH (Accelerated condition). The samples were evaluated at 0, 3 and 6 months for their particle size, polydispersity index, zeta potential, entrapment efficiency, drug content and release rate. In addition, samples were visually examined for any physical instability (separation and aggregation).

In vivo Acute Toxicity Study

In vivo acute oral toxicity study was performed to evaluate the toxicity of single dose administration of prepared plain and Felbamate Solid lipid nano formulations. The study was performed as per the approved institutional animal ethical committee (1171/PO/Re/S/08/CPCSEA). Total numbers of animals were divided into three groups each containing five healthy wistar rats weighing 250 - 350 g. All the animals were randomly assigned to polypropylene cages layered with husk and maintained at controlled room temperature (22 ± 2°C), light (12 hrs light/dark cycle). Animals were allowed free access to water “ad libitum” and standard pellet diet. Animals were treated in accordance with the “Guide for the care and use of laboratory animals”. The animals were kept in their cages for at least 5 days prior to dosing and were withheld of food overnight prior to dosing and 3-4 hrs after dosing but not the water. Following the period of fasting, animals were weighed and treated orally as per the treatment schedule. The animals were assigned to the following three test groups namely Group I (Distilled water); Group II (Plain nanoparticle) and Group III (Felbamate solid lipid nanoformulation). One animal in each group was gavaged once with respective doses (equivalent to 5 mg/kg of body weight) by oral gavages, using a curved and ball tipped stainless steel feeding needle. Thereafter, the animals were monitored for 48 hours for clinical signs of toxicity or mortality. Since, there was no mortality, remaining four animals in each groups were gavaged once with respective doses. Animals were observed individually for total of 14 days for clinical signs of toxicity or mortality after dosing, periodically during the first 24 hours, with special attention given during the first 4 hours. Body weight of the animals was also observed at regular intervals. Daily observations include changes in skin colour, fur, eyes, mucus membrane (Nasal), vital signs (Heart beat and rectal temperature), autonomic nervous system activity (Salivation, lacrimation, piloerection, urinary

incontinence and defecation consistency) and central nervous system activity (Drowsiness, gait, tremors and convulsion).

Statistical analysis

Results of the treatment groups were compared with control group for all the toxicological evaluations. Data was expressed as mean ± S.D. and was analysed using one way analysis of variance (ANOVA). Differences were considered significant at $P < 0.05$.

***In vivo* Bioavailability Studies**

The availability of the drug to the biologic system is integral to the goals of dosage form, design and paramount to the effectiveness of the medication. To achieve the anticonvulsant effect, it is necessary to reach the drug in the blood from the dosage form. Bioavailability study of the prepared Felbamate solid lipid Nano formulations was assessed. .

Evaluation of Parameters

The blood samples (0.5 mL) were collected from the retro-orbital plexus under mild ether anaesthesia into heparinised micro centrifuge tubes (containing 20µL of 1000 IU heparin/mL of blood) at 0 mins 1, 2, 4, 8, 10, 12, 24, 36 hrs after drug administration. After each sampling, 1 mL of dextrose-normal saline was administered to prevent changes in the central compartment volume and electrolytes. Plasma samples were obtained by centrifugation of each blood sample at 3000 rpm at 4°C for 10 mins and were stored at -20°C and the concentration of drug was determined by HPLC analysis (Zhong Da-Fang *et al.,* 2003). The chromatographic separation was performed with Shimadzu HPLC system with the best chromatographic conditions equipped with C18 column (ODS 250 mm X 4.6 mm with 5 micron pore size, Phenomenex) using a mobile phase combination of potassium dihydrogen phosphate buffer (50mM,pH4.5), acetonitrile and methanol (65:26.2:8.8, v/v/v) in an isocratic mode elution with the flow rate set at 0.8 mL/min. The samples were analysed by PDA detector. The pharmacokinetic parameters were determined from plasma concentration data by non-compartmental model. Kinetica software (Version 5.1) was used to determine the pharmacokinetic parameters such as area under the plasma concentration-time curve (AUC_{0-t}), maximum plasma concentration (C_{max}) and the time taken to reach the maximum plasma concentration (T_{max}). The relative bioavailability (Fr) of Felbamate was calculated using the following equation:

$$\text{Fr}\ (\%) = \frac{AUC\ (Felbamate\ Nanoparticle)}{AUC\ (pure\ Felbamate\ suspension)}$$

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS 18.0 (SPSS, Inc, Chicago, IL) statistical package. Data were expressed as mean ± standard deviation. One way analysis of variance (ANOVA) followed by Duncan multiple comparison method was used to correlate the difference between the variables. Data were considered statistically significant if P value was < 0.001, < 0.01 and < 0.05.

RESULTS & DISCUSSION

Development of solid lipid Nanoparticulate drug delivery system using sonication approach

Felbamate solid lipid nanoparticles were prepared using micro-emulsion method. During preparation, addition of organic phase containing polymer in to the aqueous phase results in rapid miscibility of organic solvent in to aqueous phase leading to increase in the polarity of organic solvent, which in turn decreases the solubility of polymer and initiate nucleation of polymer. However, sonication process inhibits the nucleation of polymer at the initial stage. The cationic nature of polymer provides higher zeta potential to the formed nanoparticles and develops an electrostatic force and keeps the nanoparticles in Brownian motion which inhibits the further growth of polymeric nanoparticles resulting in the formation colloidal nanoformulation. Brownian motion of nanoparticles overcomes the Van der Waals force of attraction and gravitational force resulting in the prevention of aggregation and sedimentation of nanoparticles. Prepared nanoparticles were characterized for distribution width, mean particle size, surface area, span, and uniformity using laser particle size analyser. However, these characterization parameters depend on process parameters such as organic solvent, polymer concentration, percentage of organic solvent, volume of aqueous phase, concentration, temperature generated during sonication process, sonication duration and drug concentration. Hence, a step-by-step optimization was carried out to evaluate the effect of these process parameters on prepared polymeric nanoparticles and the particle size spectrum of optimization batch (FSN01 to FSN12). The experiments were performed in triplicate and characterization results were expressed in table 2 and student t test (Graph Pad Prism software; version 6.0) was used to evaluate the significance of difference. The differences were considered significant if P value <0.05 and non-significant if P value >0.05.

Table 2
Characterization of prepared SLN's

Run	Average Particle size (nm)	Span	Surface Area (m2g-1)	Polydispersity index
FSN01	723	1.924	17.1	1.619
FSN02	186	1.021	47.6	0.199
FSN03	177	0.843	50.8	0.252
FSN04	225	1.13	34.6	0.419
FSN05	1175	2.974	14.8	1.947
FSN06	192	1.342	30.1	0.428
FSN07	856	1.852	14.5	1.54
FSN08	388	1.352	32.5	0.487
FSN09	1025	2.825	15.6	1.91
FSN10	556	1.652	21.5	0.849
FSN11	165	0.82	51.9	0.299
FSN12	196	0.995	46.1	0.25

Drug Content, Encapsulation Efficiency & Drug Loading Estimation

The amount of Felbamate encapsulated in nanoparticles determines the effectiveness of prepared Nano formulations. Hence, drug content, encapsulation efficiency and drug loading estimation were performed as per procedure mentioned. Drug content was estimated by performing an assay whereas encapsulation efficiency and drug loading were calculated by measuring the free Felbamate in the Nano formulation. The results were summarised in table 3

Table 3
Drug Content, Encapsulation Efficiency & Drug Loading Estimation of Optimized Formulation (FSN 11)

Evaluation parameter	Nano formulation
Process yield (%)	86.73
Mean particle size (nm)	140-195
Polydispersity Index (Pdi)	0.299
Zeta potential (mV)	- 29.5 ± 1.16
Drug loading (%)	93.93%
Encapsulation efficiency (%)	93.93 ± 0.72
Drug content (%)	99.86 0.59

Drug content in formulations was between the range of 99 and100 which shows that there was no post-formulation degradation or drug loss. In stirring approach, encapsulation efficiency and drug loading was found to be 93.93%. Hence, prepared Felbamate solid lipid nanoparticles are expected to display superior pharmacological activities.

Particle Surface Morphology Analysis

Particle surface morphology decides the basic function of particle degradation, release of drug from polymer matrix, transport of particles in the body, internalization of drug. The surface morphology analysis for the prepared plain and Felbamate solid lipid nanoparticles were performed by field emission scanning electron microscopy (FESEM) and transmission electron microscopy (TEM) and the TEM images were displayed in figure 1 as well as the FESEM images were displayed in figure 2.

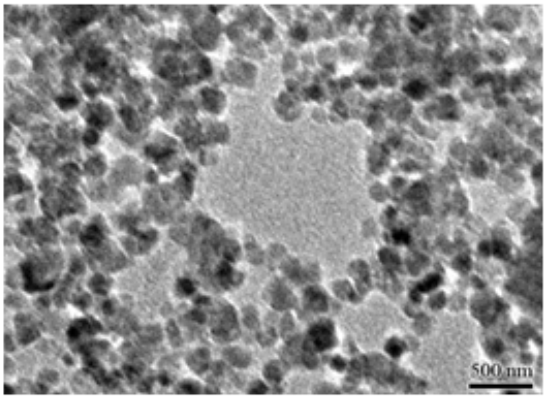

Figure 1a
TEM image of plain nanoparticles prepared using stirring approach

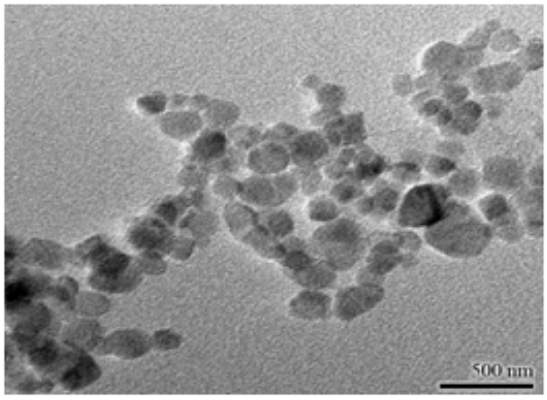

Figure 1b
TEM image of Felbamate solid lipid nano nanoparticles (FSN 11)

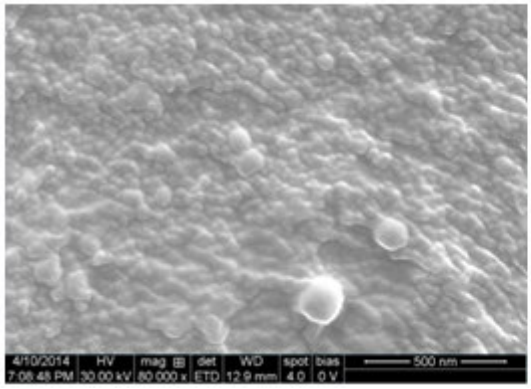

Figure 2a
FESEM image of plain nanoparticles prepared using stirring approach

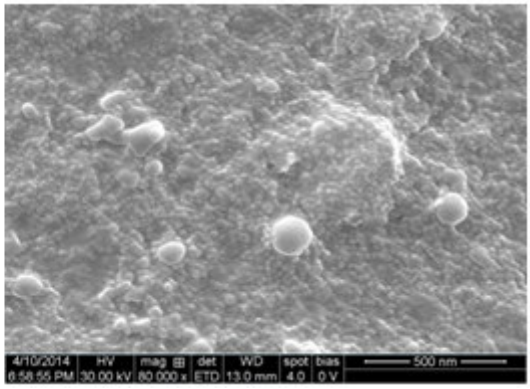

Figure 2b
FESEM image of Felbamate solid lipid nanoparticles (FSN 11)

***In vitro* drug release study**

In vitro drug release from the drug loaded nanoparticles prepared by both sonication approach and stirring approach was assessed in simulated gastrointestinal conditions. The pH condition used was pH 1.2 for a period of 2 hrs (Stomach), pH 4.5 for 2 hrs (Duodenum) followed by pH 7.4 (Distal ileum and colon) for the remaining period of the study using a USP dissolution test apparatus type 2 and *in vitro* drug release of both the approaches were shown in table 4. The drug release was found to be less than 5% upto 4 hrs and the drug release increased when the pH of the medium was adjusted to 7.4.

Table 4
***In vitro* release profile of Felbamate solid lipid nanoparticles**

Time	Drug release
0 hrs	0.00 ± 0.00
1 hrs	0.00 ± 0.00
2 hrs	0.00 ± 0.00
4 hrs	1.58 ± 0.40
6 hrs	29.14 ± 1.12
8 hrs	60.55± 1.09
10 hrs	74.25 ± 1.26
12 hrs	86.14 ± 2.14
24 hrs	98.79 ± 1.71

Release kinetics

To know the mechanism of drug release, the results of *in vitro* release profile obtained from the optimized formulation (FSN 11) were treated according to Zero Order Release, First Order Release, Higuchi Model, Korsmeyer-Peppas Model and Hixson Crowell Cube Root Law. The release rate kinetics data of the formulation is shown in table 5.

Table 5
Determination coefficients (r^2) and release exponent (n) of kinetic data analysis ofFelbamate release from nanoparticles

Zero order r^2	First Order r^2	Higuchi model r^2	Korsmeyer-Peppas model		Hixson-Crowell cube root law r^2
			r^2	n	
0.7714	0.7714	0.5034	0.7576	0.3393	0.9452

It is concluded that the Felbamate solid lipid nanoparticles prepared by both sonication approach and stirring approach gave a good fit to the Hixson Crowell cube root law. The diffusion exponent (n) value were greater than 0.89, this result indicated that the release of drug from the polymer matrix formulations was found to be super case-II transport, i.e., drug release by both diffusion and relaxation of polymer chain.

***In vivo* Acute Toxicity Study**

The animals in various treatment groups as well as the control group did not demonstrate any mortality. Throughout the observation period, the animals in any of the groups did not display any treatment related abnormal behaviour.

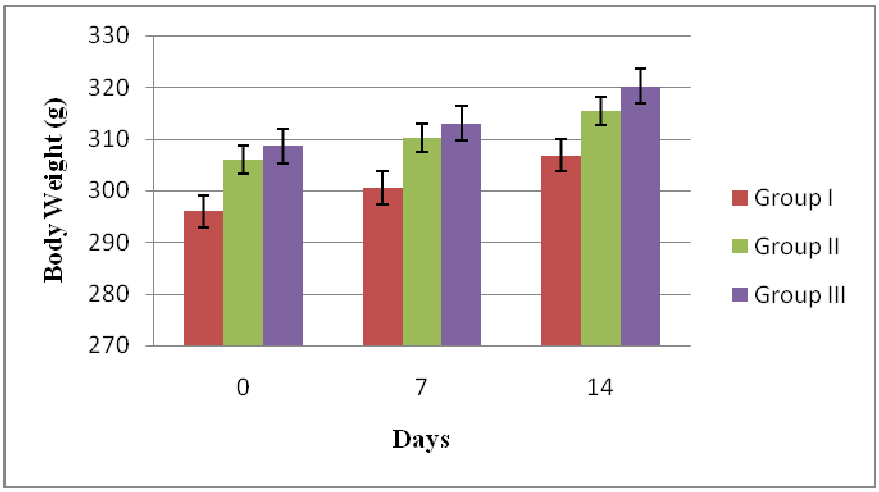

Figure 3
Body weight (g) of animals in various treatment groups

No significant differences were observed in body weights of the animals of the treatment groups when compared with that of the control group. Results confirmed that prepared plain and Felbamate solid lipid nanoparticles do not produce any sign of toxicity at given single oral dose and found to be safe. The results are shown in figure 3.

***In vivo* Bioavailability Studies**

The plasma drug concentration-time profile of Felbamate was constructed following the oral administration of pure Felbamate suspension and Felbamate solid lipid nano formulation as per the procedure mentioned and the results were summarized in table 6.

Table 6
Pharmacokinetic parameters of Felbamate after oral administration of free drug and Nano formulation (5 mg/kg) in rats

Parameter	Pure Felbamate Suspension	Felbamate Nanoformulation
T_{max} (Hrs)	0.6 ± 0.08	11 ± 0.33 ***
C_{max}(ng/mL)	133.15 ± 11.55	198.42 ± 16.87 ***
AUC (ng.hrs/mL)	178.80 ± 60.61	1916.52 ± 79.14 ***
AUMC (ng.hrs/mL)	287.55 ± 23.26	2197.30 ± 85.12 ***
$t_{1/2}$ (Hrs)	0.81 ± 0.02	3.19 ± 0.22 ***
Ke (Hrs^{-1})	0.92 ± 0.02	0.09 ± 0.01***
MRT (Hrs)	1.49 ± 0.30	19.07 ± 1.36 ***
Cl (mL/hrs.kg)	0.02 ± 0.03	0.001 ± 0.02 ***
Relative Bioavailability (%)	-	969

The values are represented as Mean ± SD; (n = 6); P < 0.001
AUC: Area under the curve; AUMC: Area under mean curve; t1/2: half life; Ke: Elimination rate constant; MRT: Mean residence time; Cl: Clearance; Cmax: Maximum plasma concentration; Tmax: Time to reach maximum plasma concentration

It was observed that, after oral administration of the pure felbamate suspension, the drug was detected rapidly in the plasma in the initial hours, indicates the high permeability coefficient of drug in upper part of GIT. Thereafter, the drug-plasma concentration decreased quickly to undetectable levels after 8 hrs. The results showed a significant difference between the pharmacokinetic profiles of Felbamate encapsulated nanoformulation and free Felbamate suspension.. The area under the curve (AUC) of Felbamate in rats treated with nanoparticles was 1916.52 ± 79.14 ng.hrs/mL, which was significantly improved (*** $p < 0.001$) compared with that of free Felbamate suspension (178.80 ± 60.61 ng.hrs/mL). The improved AUC of Felbamate nanoparticles is due to more uptake of Felbamate in the intestine from the nanoformulation. In the case of Felbamate encapsulated nanoformulation, the Cmax was reached at 12 hrs and then gradually decreased over the next 12 hrs, which indicated the prolonged residence time of the released drug in the colon with slow leaching of the drug to systemic circulation. This might be due to low permeability and compromised surface area. In summary, the present study indicates that administration of Felbamate encapsulated nanoformulation leads a prolonged plasma half-life and enhanced distribution when compared to Felbamate alone.

Stability studies

Prepared Felbamate loaded polymeric nanoformulation was subjected for stability studies as per the procedure mentioned. At the regular intervals the stored samples were evaluated for average particle size, particle size uniformity, surface area, zeta potential, drug content and drug release. The results were summarized in table 7 and figure 4.

Table 7
Average particle size, polydispersity index, zeta potential and drug content estimation of prepared polymeric nanoparticles subjected to accelerated stability study as per ICH guidelines (40°C ± 2°C/75% RH ± 5% RH)

Trials	Period (Months)	Average particle size (nm)	Polydispersity index (Pdi)	Zeta Potential (mV)	Drug Content (%)
Nano	0	108 ± 0.45	0.299 ± 0.04	- 29.4 ± 1.36	97.86 ± 1.67
	3rd	108 ± 0.35	0.299 ± 0.41	- 29.1 ± 1.20	97.35 ± 1.42
	6th	108 ± 0.64	0.299 ± 0.24	- 29.2 ± 0.98	96.80 ± 1.26

The values are expressed as Mean ± SD; n=3;

Prepared Felbamate loaded nanoparticles showed insignificant change in average particle size, polydispersity index, zeta potential, drug content and drug release after stability storage at both long term and accelerated conditions.

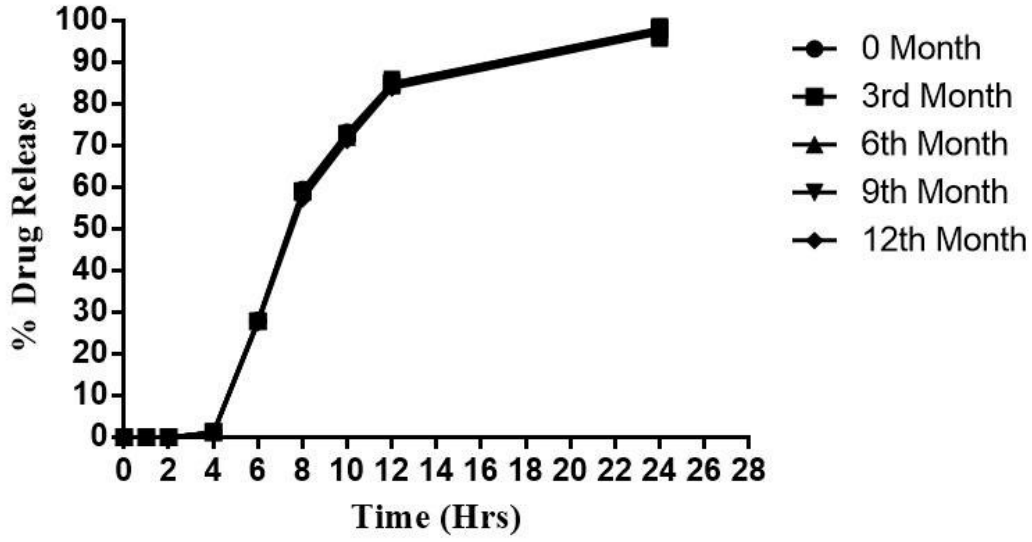

Figure 4
In vitro release profile of Felbamate from the prepared nanoparticles subjected to long term stability study as per ICH guidelines (25°C ± 2°C/60% RH ± 5% RH).

CONCLUSION

Felbamate loaded solid lipid nanoparticles were prepared by micro emulsion method using stirring and sonication approach and from the results, it can be concluded that the drug release from the optimized formulation is prolonged for 12 hours and from in vivo studies it can be concluded that the plasma half life is prolonged and distribution is enhanced when compared to felbamte alone.

AUTHORS CONTRIBUTION STATEMENT

Dr.Pratap Kumar Sahu conceived the idea and guided me in conducting this research study and also reviewed the manuscript. Mr.Ramanuj Prasad Samal carried out the research study, evaluated the results and drafted the manuscript.

CONFLICT OF INTEREST

Conflict of interest declared none.

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