SOLID LIPID NANOPARTICLES OF GABAPENTIN FOR PARTIAL SEIZURES

Shital Kamathe[a], Nagesh C.[a]*, Suma N.[a], Pankaj Patil[a] and Chaitali Muchandi[a]

(Received 12 June 2021) (Accepted 11 April 2023)

ABSTRACT

The goal of this research was to create a stable formulation of gabapentin solid lipid nanoparticles which would allow it to pass across the blood-brain barrier more easily. They were prepared by solvent evaporation method. In the present investigation, beeswax and carnauba wax were used as solid lipids, egg lecithin was used as a surfactant and Tween 80 was used as a co-surfactant. Nine formulations were formulated using different concentrations of solid lipid and surfactant. The prepared formulations were evaluated for various tests. The results shown that F_6 formulation, containing higher concentration of egg lecithin, was a better formulation as percentage drug content was 97.57±0.62%, entrapment efficiency was 95.95±0.07% and *in vitro* release of gabapentin was 97.18±1.02% at the end of 12 h. After *in vivo* testing, it was observed that animals treated with gabapentin loaded solid lipid nanoparticles had seizures that appeared later than animals treated with traditional gabapentin formulations. Hence it was concluded that solid lipid nanoparticles is a promising drug delivery system to achieve increased permeability through blood brain barrier.

Keywords: Solid lipid nanoparticle, gabapentin, Blood brain barrier, permeability

INTRODUCTION

Pharmacotherapy for CNS illnesses is challenging since the adequate amount of active pharmaceutical ingredient (API) may not enter the brain because of presence of the blood brain barrier (BBB). One such CNS disorder is partial seizures. Seizures are widespread and prevalent disorder that affects a huge number of people. Inconsistency with medicine is a major issue with seizures, owing to the negative side effects of long-term therapy[1].

Researchers have attempted a variety of medication delivery techniques to treat seizures, including emulsions, suspensions and liposomes. However, because most of these formulations fail to attain the necessary drug concentration in the brain, researchers have taken advantage of the needs for drug molecules to cross the BBB, and they have proposed that pharmaceuticals can be administered by shrinking their size using a nanotechnology technique. Nanoparticles, solid lipid nanoparticles (SLNs), nanosuspensions, nanoemulsions, and nanocrystals are all examples of colloidal drug carriers[2]. Polymeric nanoparticles offer a better pharmacological efficacy than conventional pharmaceutical formulations due to their increased permeability, however they are extremely toxic[3]. Hence SLNs were created to lower the toxicity of polymeric nanoparticles. SLNs have the potential to carry hydrophilic or lipophilic drugs[4]. SLNs can increase drug permeability across the BBB, making them an attractive drug targeting approach for CNS diseases. Because SLNs are lipoidal in nature, highly water soluble drugs can be encapsulated within the solid core, which can easily cross the BBB and deliver the medication to the intended site of action, resulting in increased bioavailability and lower toxicities associated with nanoparticles[5].

The model drug in this study was gabapentin. It is an Antiepileptic Drug (AED) that is a cyclic GABA analogue with low side effects and is well tolerated. It is an anticonvulsant drug that can be used to treat almost any type of seizure. Gabapentin's water solubility prevents it from passing through the BBB, resulting in a decreased bioavailability (60%) and a half-life of 5-7 hours[6]. Gabapentin is a BCS class III medication with a low permeability and high solubility. As a result, the current work attempted to produce gabapentin SLNs with enhanced permeability and bioavailability.

[a] Department of Pharmaceutics, Maratha Mandal's College of Pharmacy, Belgaum-590 016, Karnataka, India
*For Correspondence: Email: nagesh_73@rediffmail.com

https://doi.org/10.53879/id.60.05.13037

MATERIALS AND METHODS

Gabapentin was received as a gift sample from Glenmark Pharma, Goa. Beeswax and carnauba wax were purchased from Flora Chemicals, India. Egg lecithin was purchased from Milton Chemicals, Mumbai. Tween 80 was purchased from Bombay Research Laboratory. Ninhydrine was purchased from Chemika-Biochemika Reagents, Ottokemi. Standard conventional gabapentin tablets of 300mg were purchased from local market. All of the other chemicals and solvents used were of analytical quality.

Preformulation studies

Preformulation investigations were conducted prior to formulation, since they are used to identify components and indicate purity.

Identification and purity tests

Melting point of gabapentin was determined by using capillary method in which drug is placed inside the capillary tube, it is attached to a thermometer and placed inside the Thiele's tube. Further with the help of Bunsen burner, Thiele's tube is heated to obtain melting point range of gabapentin. The purity of gabapentin was checked by FTIR and absorption maxima obtained. Pure drug spectrum was obtained by infrared absorption spectral analysis using FT-IR spectrophotometer (FT-IR 200 by Shimadzu Corporation, Japan). The sample solution was scanned between 400-800nm in UV-Spectrophotometer 1800, to check the maximum absorption.

Compatibility studies: The Fourier Transform Infrared Spectroscopic studies by KBr pellet technique was used to find the interaction between pure drug, lipids, surfactants and its physical mixtures. To determine compatibility of drug and excipients, the IR spectrum of the solid dispersion was compared to the spectrum of pure gabapentin.

Analytical method development: 100 mg gabapentin was accurately weighed and transferred to a volumetric flask containing 100 mL of distilled water, where it was dissolved and diluted to 50 mL. 10 mL 0.2 % ninhydrine in methanol was added to the forsaid solution. The flask was heated for 10 minutes on a water bath at 85 °C before cooling to room temperature. With distilled water, the volume was made to 100 mL. Aliquots of 0.5, 1.0, 1.5, 2.0 and 2.5mL were taken from this solution and placed in 10 mL volumetric flasks with distilled water to achieve concentrations of 50, 100, 150, 200, and 250 µg mL^{-1} respectively. A UV-visible spectrophotometer – Shimadzu 1800 was used to measure the absorbance of the solutions at 570nm[7].

FORMULATION DEVELOPMENT

Preparation of solid lipid nanoparticles of gabapentin

By using the solvent evaporation approach, solid lipid nanoparticles were produced. Table I shows the various formulations of drug-loaded SLNs made with different quantities of carnauba wax, beeswax and egg lecithin. Required quantities of gabapentin, carnauba wax, beeswax and egg lecithin were taken in a beaker of 250 mL capacity and were dissolved in chloroform. The lipid phase was homogenized roughly for 5 minutes at 6000rpm using a high-speed stirrer. Aqueous media was created simultaneously by dispersing Tween 80 in distilled water in another beaker and it was poured into

Table I: Composition of solid lipid nanoparticles of gabapentin

Sl. No.	Ingredient	Formulation code								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1.	Gabapentin (mg)	250	250	250	250	250	250	250	250	250
2.	Beeswax(mg)	250	250	250	500	500	500	750	750	750
3.	Carnauba wax (mg)	250	250	250	500	500	500	750	750	750
4.	Egg lecithin (mg)	250	500	750	250	500	750	250	500	750
5.	Tween 80 (mL)	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75
6.	Water (mL)	50	50	50	50	50	50	50	50	50
7.	Chloroform (mL)	10	10	10	10	10	10	10	10	10

Note: The quantities given were to produce 50 mL of dispersion

the lipid phase with continuous stirring at 3000 rpm. Oil in water (O/W) type of coarse emulsion was obtained. The beaker containing this O/W emulsion was placed under high speed stirrer and the machine was operated at 1000 rpm for 2 h to get nanoparticles with complete evaporation of the organic solvent[8].

CHARACTERIZATION OF SLNS

Drug content

To determine the drug content of the formulation, 5 mL dispersion of SLNs containing gabapentin was taken in 100 mL of volumetric flask, to that 10 mL of 0.2% w/V Ninhydrin in methanol solution was added. The flask was heated on water bath for 10 min at 85±5 ^{0}C. Pale purple color was developed. Solution was allowed to cool at room temperature and with distilled water; a volume of up to 100 mL was produced. The absorbance of the solution was measured after its filtration using UV-Visible spectrophotometer at 570 nm. Solution treated similarly without formulation was used as blank. The amount of gabapentin in each formulation was determined[7].

Entrapment efficiency

A fixed quantity of drug loaded SLNs (5mL) was taken in a centrifuge tube and centrifuged for 20 min at 3000 rpm at room temperature. The lipid portion was separated and the drug in the supernatant was determined. For that purpose, in a 100 mL volumetric flask, supernatant liquid was taken and to that 10 mL of 0.2 % ninhydrin in methanol solution was added, the flask was heated at 85±5^{0}C for 10 min. solution was allowed to cool at room temperature. The volume was raised to 100 mL with distilled water, and the solution's absorbance was measured at 570nm[9].

The amount of drug entrapped in SLNs was calculated by using following equation

$$\% \text{ Entrapment efficiency} = \frac{\text{Total Drug} - \text{Unentrapped drug}}{\text{Total Drug}} \times 100$$

Release studies for solid lipid nanoparticles

The Franz diffusion cell has been used to study the drug release of SLN dispersions. To study diffusion, cellophane membrane was first pre-soaked in water 24 h. The donor compartment was then attached to the membrane, and 5 mL of dispersion was added to the donor compartment, which was then placed over the receptor compartment, containing 20 mL of distilled water. The diffusion cell assembly was mounted on magnetic stirrer with hot plate and was maintained at 37 ^{0}C and stirrer was adjusted to a speed of 50 rpm. From the receptor compartment, 1 mL of sample was withdrawn manually at definite time intervals replacing with fresh distilled water to maintain sink condition and samples withdrawn were analyzed for *in vitro* drug release of gabapentin using a UV visible spectrophotometer at 570nm[10].

Drug release kinetics and data analysis

The data from release studies was fitted into zero order, first order, Higuchi matrix, and Korsemeyer-Peppas models to analyse the mechanism for the dosage form's drug release pattern and release rate kinetics. The best fit model was chosen by comparing the acquired r^2 – values. The rate of drug release is independent of its concentration in a zero order system, but the rate of drug release is dependent on the concentration of the substances used in a first order system. The Higuchi model describes drug release from matrix systems, while the Korsemeyer-Peppas model is utilized to determine drug release from polymeric systems.

Zeta potential analysis

The colloidal characteristics of the prepared SLNs formulation were determined using zeta potential analysis. The zeta potential analyzer was used to examine the suitable diluted preparations employing electrophoretic light scattering and Laser Doppler Velocimetry methods. Charge on nanoparticles and their mean zeta potential values with a variation of 5 measurements were obtained directly from measurements at a temperature of 25^{0}C[11].

Surface morphology study

The shape, surface properties, and size of the SLNs were analyzed using a scanning electron microscope (JEOL-JSM-6360, Japan) fitted with a digital camera and operated at an acceleration voltage of 18kV, followed by photographs[12].

Stability studies

The optimized formulation was stored in airtight sealed glass vials to check the stability of the preparations. At definite time intervals (0, 1, 2, 3 months) the SLNs dispersion was analyzed for drug content, entrapment efficiency and *in vitro* release profile by UV-visible spectrophotometer at 570 nm. According to ICH recommendations, stability tests for the dispersion should be conducted at 40°C and 75% relative humidity in accordance with international climatic zones and conditions[13,14].

IN VIVO EVALUATION

The *in vivo* experimental study was planned to compare the effect of drug between conventional and targeted drug delivery system using two animal models of Swiss albino mice. A prior permission for animal experimentation has been obtained from the Institutional Animal Ethical Committee (IAEC).

Animals: Swiss albino mice, male or female, weighing 25-30 g and three to four months old, were procured from Institutional animal house. Good laboratory practice has been followed to handle the animals. Standard polypropylene cages were used to house them with controlled room temperature. Animals were kept in a 12 h light dark circle. They were provided with standard laboratory food and water *ad libitum.* Before 12 h of the experiment food was withdrawn.

Drugs: Conventional tablets of gabapentin containing 300mg of drug were used as standard, the prepared formulation of solid lipid nanoparticles containing gabapentin was used as test and water was used as vehicle. The dose of drug required for animals was calculated by using the formula:

Human dose (mg kg^{-1}) X conventional factor (12.33 for mice)

300/70X12.33 = 52.84 mg kg^{-1}

Study design

The antiepileptic activity of gabapentin test and standard formulations in mice was evaluated on Maximal Electroshock induced Seizures (MES) and Pentylenetetrazol induced Seizures (PTZ) models following chronic treatment for 14 days. On the 14th day, both experiments were started 60 minutes after oral dosing with test formulation and vehicle[15].

In MES-induced seizures, shock was delivered using an electro convulsiometer using ear electrodes. The stimulus intensity was 34-36 mA for 0.2 seconds. The duration of tonic flexion, tonic extension and chronic convulsions were all considered as evaluation measures. The time was calculated using a stopwatch.

In PTZ induced seizures, after treatment with test drug, PTZ was administered intraperitoneally in a dose of 40mg kg^{-1} to induce seizures, and the animals were examined for 30 minutes. Stopwatch was used to compute evaluation parameters such as the beginning of the first myoclonic jerk, tonic clonic convulsion and animal mortality.

Procedure

All experimental animals were categorized into 3 groups (6 mice in each group for each model). Group-1 was considered as control and received vehicle. Group-2 was considered standard and received standard gabapentin tablets; group-3 was considered as test group and received prepared nanoparticulate formulation of gabapentin. All animals under investigation were treated with respective formulation for time period of 14 days. On the last day 60 min after dosing seizures were induced in animals and evaluation parameters were studied.

RESULTS AND DISCUSSION

Preformulation studies

Preformulation testing includes determining the physical and chemical properties of pharmacological compounds, as well as the medication's interaction with excipients. These studies are necessary for the development of a stable, acceptable, safe, and effective formulation.

Identification and purity tests: Melting point of gabapentin was found to be 162 ^{0}C, which was equal to the reported melting point of standard drug. By comparing sample and standard drug spectra obtained by FT-IR studies, it was observed that all the peaks of the sample drug are present in the same frequencies as observed in standard gabapentin spectrum. (Fig. 1)**.** The absorption maxima was observed at 570 nm, the observed peak of drug was similar to that of lambda max of standard gabapentin. These tests confirmed that drug under investigation was gabapentin and it is pure.

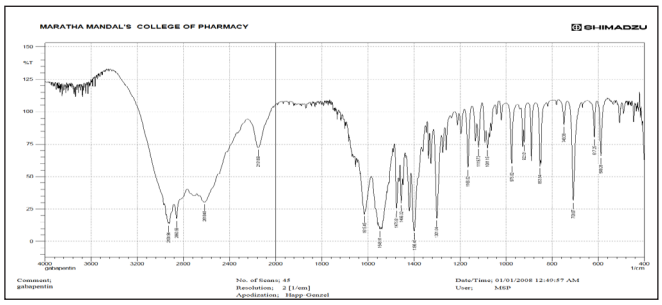

Fig. 1: The IR spectrum of gabapentin

Compatibility studies: Some characteristic peaks for gabapentin were identified and observed at specific wavelength like OH stretch at 2930.96 cm^{-1}, C=O stretch at 1615 cm^{-1}, cycloalkanes at 1081 cm^{-1}, carboxylic acid at 1166.02 cm^{-1} and C-N-C at 708.87. These peaks were nearer to standard peaks and similar peaks were observed even after physical mixture of drug with excipients. As

a result, it confirms that the peaks of pure drug (Fig. 1) did not alter much after mixing with lipid matrix (Fig. 2). The physical mixture had the gabapentin and lipid peaks, showing that there were no significant interactions between the gabapentin and the excipients included, confirming drug stability.

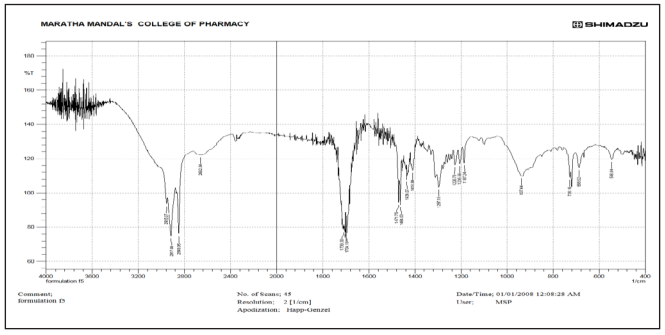

Fig. 2: The IR spectrum of formulation F6

Calibration curve: Standard calibration curve for gabapentin in distilled water was obtained with Beer-Lambart range from 50-300 µg mL^{-1} with correlation coefficient of 0.999.

Formulation development

A total of nine formulations were designed; composition is shown in Table I. In each formulation, different concentrations of solid lipid and surfactants were used. Selection of solid lipid was based on solubility of drug in molten lipid, which increases entrapment efficiency of SLNs. Solubility studies of drug in different lipids (stearic acid, beeswax and carnauba wax) were carried out to identify suitable lipid for the development of gabapentin loaded SLNs. The results obtained were 5 mg g^{-1}, 18 mg g^{-1} and 16 mg g^{-1} for stearic acid, bees wax and carnauba wax, respectively. Highest solubility of gabapentin was observed in bees wax compared to other lipids, hence bees wax and carnauba wax were selected as solid lipids. In each formulation the drug concentration was kept constant (250 mg). Bees wax and carnauba wax were used in the range of 250 mg to 750 mg. Egg lecithin was used as surfactant in the range of 250 mg to 750 mg. Tween 80 was used as co-surfactant and concentration of which is kept constant in all formulations i.e. 0.75 mL. Chloroform was used as organic phase whereas 50 mL of aqueous phase(water) was used to disperse the solid lipid. SLNs were prepared by using solvent evaporation method, which produces particles slowly due to evaporation of organic solvent[7]. The lipid was dissolved in a water immiscible organic solvent, which was subsequently emulsified in an aqueous phase. As the organic solvent evaporates, the particles slowly grow.

Characterization of SLNs

Drug content: Efficacy of drug formulation depends on its drug content. Lesser drug content shows no pharmacological response. Hence amount of drug in formulations must be desirable to show pharmacological activity without toxicity. The drug content of SLNs loaded with gabapentin was found to be within the range of 77.81±1.24% to 97.57±0.62 % in distilled water. The results shown that the drug content of all the batches were uniform; this confirms that mixing of contents was proper. The results are shown in the Table II.

Entrapment efficiency: Entrapment efficiency (EE) is often used to calculate the percent of drug successfully entrapped in nanoparticles. Only entrapped drugs can diffuse over the BBB, making it a significant physicochemical property of a formulation. After separating unentrapped drug from entrapped drug, the EE of SLNs was calculated. Percentage entrapment efficiencies of all the formulations were found to be satisfactorily high, from 89.62±0.22 % to 95.95±0.07%. The formulation F6 had shown maximum entrapment of gabapentin (95.95±0.07%). It was observed that maximum concentration of surfactant shows higher entrapment efficiency. The results of entrapment efficiency are shown in Table II.

***In vitro* drug release study**: *In vitro* drug release study was performed for SLNs using Franz diffusion cell.

Table II: Percentage drug content and percentage entrapment efficiency and percentage cumulative drug release for all formulations

Formulation Code	% Drug content	% Entrapment	% Cumulative drug release at the end of 12 h
F1	82.28±0.62	90.36±0.10	90.10±1.32
F2	86.47±0.81	92.42±0.15	92.33±0.48
F3	91.62±0.46	91.72±0.00	92.33±0.48
F4	80.52±1.02	89.62±0.22	92.58±1.37
F5	85.93±0.62	91.74±0.19	94.09±2.07
F6	97.57±0.62	95.95±0.07	97.95±0.79
F7	77.81±1.24	91.09±0.14	92.62±0.99
F8	86.34±0.46	93.44±0.15	93.29±0.43
F9	91.48±1.02	94.37±0.23	95.16±0.24

Note: The values presented are arithmetic mean ± SD's of three determinations.

The conditions were maintained at 50 rpm, media used was 20 mL of distilled water at temperature 37±0.5^{0}C. *In vitro* drug release profiles for F1-F9 formulations are tabulated in the Table II. The amount of surfactant used had a great influence on the release pattern of SLNs. Increasing the concentration of egg lecithin from 0.5, 1 to 1.5% w/V led to corresponding increase in the percentage of gabapentin released. The effect of lipid concentration on SLNs release profile was also observed, up to certain increase in lipid concentration it showed increased drug release but further increase in the concentration of lipid resulted in decreased percentage of gabapentin release. The results indicated that formulation F6 was better in terms of drug release (Fig. 4).

Release kinetic data: The results of the *in vitro* drug release investigations were interpreted in a variety of data analysis kinetic models, including zero order kinetics, first order kinetics, Higuchi's classical diffusion equation, and Korsemeyer-Peppas release kinetics. Release kinetic data of solid lipid nanoparticles was tabulated in Table III. From the data, it was observed that release of gabapentin from F1-F9 formulation follows zero order kinetics (Fig. 3, Fig. 4 and Fig. 5), since R^2 value of zero order kinetics was in the range of 0.986-0.998. The data was fitted into Higuchi mode, which is shown in Fig. 6, the results were found in the range of 0.879-0.934 indicating that the drug release takes place by diffusion mechanism. The slope value of Korsemeyer-Peppas plot is a key indicator to know type of release mechanism. Slope value of all formulations were in the range of 0.763-0.864, indicating that drug release takes place by non-Fickian diffusion mechanism[16]. The correlation coefficient for all the formulations and 'n' values of Korsmeyer-Peppas model for all the formulations are Tabulated in Table III.

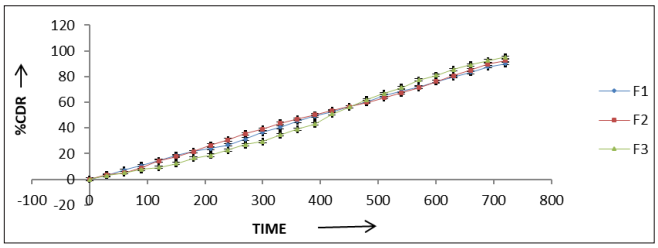

Fig. 3: Zero order release profile for formulations F1-F3

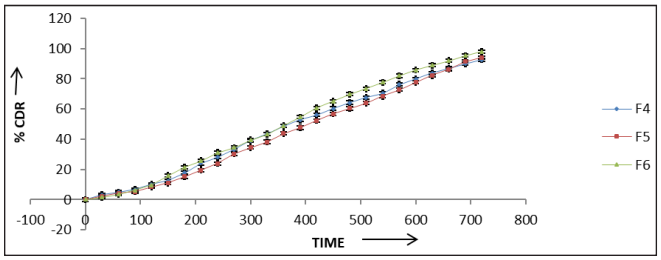

Fig. 4: Zero order release profile for formulations F4-F6

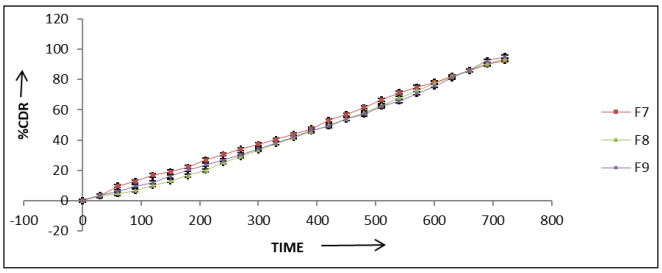

Fig. 5: Zero order release profile for formulations F7-F9

Table III: Release kinetics data of F1-F9 formulations

Formulation code	Mathematical models (kinetics)				
	Zero order (R^2)	First order (R^2)	Higuchi (R^2)	Korsemeyer-Peppas	
				N	(R^2)
F1	0.998	0.916	0.928	0.774	0.934
F2	0.994	0.889	0.934	0.784	0.926
F3	0.986	0.851	0.879	0.806	0.889
F4	0.995	0.915	0.923	0.812	0.896
F5	0.994	0.861	0.901	0.830	0.868
F6	0.995	0.845	0.924	0.864	0.865
F7	0.997	0.890	0.926	0.763	0.946
F8	0.994	0.865	0.899	0.802	0.894
F9	0.994	0.815	0.904	0.774	0.929

Note: The values presented are arithmetic mean ± SD's of three determination

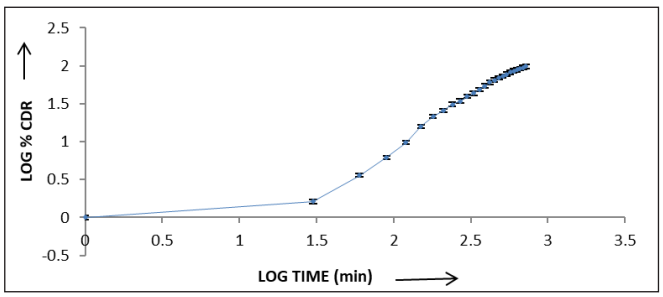

Fig. 6: Korsemeyer-Peppas profile for formulation F6

Zeta potential and polydispersity index: Zeta potential is used to measure the charge on the particles. It allows predictions about storage stability of colloidal dispersion[17,18]. The surface charge of F6 formulation was found to be - 4.71mV, indicating initiation of agglomeration upon storage. The polydispersity index is a measure of the width of the dispersion of the particles[19]. Polydispersity index of the F6 formulation was found to be 0.734 indicating very broad distribution of droplet size. Data related to this is tabulated in Table IV.

Table IV: Particle size, polydispersity index and zeta potential by zeta sizer

Formulation Code	Particle size by zeta sizer (nm)	Polydis-persity index	Zeta potential
F1	1055	0.065	-0.0482
F2	2345	1	-0.585
F3	1476	1	0.332
F4	1550	0.641	-0.529
F5	1163	1	0.132
F6	2823	0.734	-4.71
F7	1097	0.086	-0.174
F8	2432	0.405	-1.06
F9	1942	0.924	-0.0533

SLNs Surface morphology study: Morphology in terms of surface of the particles for best formulation (F6) was observed using scanning electron microscope in 18kv with magnification of 100X. The image obtained is shown in Fig. 7. It was observed that the particles were grossly spherical in shape and its size was about 200-300 nm.

Stability study: The accelerated stability studies were carried out according to ICH guidelines. Best formulation F6 was packed in airtight sealed glass vials and was stored in ICH certified stability chambers maintained at 40 ^{0}C and 75% RH for 3 months. The formulation was evaluated at definite time intervals (0, 1, 2, 3 months)

Fig. 7: Image of scanning electron microscopy of F6 formulation

for change in appearance, the drug content, entrapment efficiency and *in vitro* drug release profile.

It was noted that the F6 formulation was without any microbial or fungal growth or bad odour and showed slight decrease in drug content, drug entrapment and drug release. The results of drug content and drug release data are shown in Table V.

Table V: Stability studies data for F6 formulation

Time (days)	Physical appear-ance	Drug content (%)	% Entrapment efficiency	% CDR at the end of 9 h
30	No change	94.46±0.84	93.79±0.20	95.15±0.46
60	No change	92.57±0.70	92.89±0.02	93.23±1.77
90	No change	90.26±0.62	92.12±0.11	90.74±0.98

Note: The values presented are arithmetic mean ± SD's of three determination

***In vivo* evaluation**: After *in vivo* evaluation, it was observed that the animals treated with SLNs formulations had shown late appearance of seizures as compared to the animals treated with conventional gabapentin formulation. Evaluation parameters related to these studies are shown in Table VI and Table VII for MES and PTZ induced seizures respectively. It indicates the increased permeability and bioavailability of gabapentin.

Table VI: Effect of gabapentin on MES induced seizures

Treatment groups	Dose (mg kg^{-1}) orally	Tonic flexon (sec)	Tonic extension (Sec)	Clonic phase (Sec)
Vehicle control	10.5 mL kg^{-1}	1.25±0.20	13.12±0.12	8.15±0.34
Standard	52.84 mg kg^{-1}	7.03±0.13	20.18±0.19	prevented
Test	26.42 mg kg^{-1}	8.11±0.07	24.16±0.23	prevented

Note: The values presented are arithmetic mean ± SD's of three determination

Table VII: Effect of gabapentin on PTZ induced seizures

Treatment groups	Dose (mg kg^{-1}) orally	Onset of first jerky movement (min)	Latency of onset of seizure (min)	Duration of seizure (min)
Vehicle control	10.5 mL kg^{-1}	1.21±0.19	3.12±0.24	1.15±0.34
Standard	52.84 mg kg^{-1}	4.16±0.11	12.11±0.19	0.43±0.12
Test	26.42 mg kg^{-1}	9.21±0.14	18.13±0.12	0.19±0.11

Note: The values presented are arithmetic mean ± SD's of three determination

CONCLUSION

A satisfactory attempt has been made to formulate and evaluate SLNs of gabapentin by using solvent evaporation technique. From the study, it was concluded that drug and excipients were compatible with each other. Amount of drug content for all formulations was observed in the range of 80.52-97.57%. Entrapment of gabapentin in SLNs was found in the range of 89.62-95.95%. It was also observed that all formulations follow zero order release kinetics and type of diffusion was non-Fickian diffusion model. By analyzing the results of drug release, efficiency of drug entrapment and drug release studies, formulation F6 was stated as best formulation. Surface topography studies for best formulation showed that particles were glossy and spherical in shape, also the zeta potential studies reveled that there was no aggregation between the particles and SLNs dispersion will remain stable for longer duration of time. *In vivo* evaluation showed that animals with conventional gabapentin formulation got early occurrence of seizures when compared with animals treated with SLNs of gabapentin and shown better results as compared with conventional dosage form. Hence, it was concluded that hydrophilic drugs like gabapentin can be successfully incorporated into solid lipid nanoparticles to enhance permeability.

REFERENCES

1. Basavraj P., Shivkumar B., Shivkumar H. and Manjunath V. J.: Evaluation of anticonvulsant activity of *Tabernaemontana divaticata* (Linn) R. BR. Flower extract. **Int. J. Pharm. Pharm. Sci.,** 2011,03(03), 310-315.
2. Eidi H., Joubert O., Nemos C., Grandemange S., Mograbi B., Foliguet B., Tournebize J., Maincent P., Le Faou A., Aboukhamis I. and Rihn B. H.: Drug delivery by polymeric nanoparticles induces autophagy in macrophages. **Int. J. Pharm.,** 2012, 422, 495-503.
3. Yadav N., Khatak S. and Singh S.U.: Solid lipid nanoparticles–A review. **Int. J. App. Pharm.** 2015,05(02), 08-18.
4. Ramteke K. H., Joshi S.A. and Dhole S.N.: Solid lipid nanoparticles. **IOSR J. Pharm.,** 2012, 02(06), 34-44.
5. Muthadi R. and Sairam N.: Novel approaches in solid lipid nanoparticles and drug targeting. **IJPAR,** 2016, 05(01), 19-40.
6. Gilman A. G.: 'The Pharmacological Basis of Therapeutics'-Drugs acting on the central nervous system. 10th Ed. ISBN 9780071354691: McGraw Hill, New York.2001.pp.538.
7. Galande V.R., Baheti K.G. and Dehghan M.H.: UV-Vis spectrophotometric method for estimation of gabapentin and methylcobalamin in bulk and tablet. **Int. J. Chemtech. Res.,** 2010, 02(01), 695-699.
8. Pooja D., Tunki L., Kulhari H., Reddy B.B. and Sistla R.: Optimization of solid lipid nanoparticles prepared by a single emulsification solvent evaporation method. **Data Br**., 2016, 6, 15-19.
9. Yasir M. and Sara U.V.S.: Preparation and optimization of haloperidol loaded solid lipid nanoparticles by Box-Behnken design. **J. Pharm. Res.,** 2013, 7, 551-558.
10. Nair R., Vishnu P. and Arunkumar K. S.: Formulation and evaluation of solid lipid nanoparticles of water soluble drug : Isoniazide. **J. Pharm. Sci. Res.,** 2011, 3(05), 1256-1264.
11. Sriharitha, Preethi J. and Hemanth S.: A Review on nanoparticles in targeted drug delivery system. **J. Mater. Sci.,** 2016, 4(4), 1-6.
12. Manjunath K., Reddy S. J. and Venkateswarlu V.: Solid lipid nanoparticles as drug delivery systems. **Methods Find Exp. Clin. Pharmacol.,** 2005, 27(2), 1-20.
13. Stability testing: Photostability testing of new drug substances and products Q1B. International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human use.1-16.
14. Verma V.K. and Ram A.: Preparation, characterization and *In vitro* release of piroxicam loaded solid lipid nanoparticles. **IJPSN**, 2010, 3(3), 1136-1146.
15. Anovadiya A. P., Sanmukhani J. J., Vadgama V. K. and Tripathi C. B.: Evaluation of antiepileptic and memory retention activity of curcumin per SE and in combination with antiepileptic drugs. **Asian J. Pharm. Clin. Res.,** 2013, 6(2), 145-148.
16. Silpa N., Chakravarthi N., Chandramouli Y. and Pavankumar K.H.: Moxifloxacin loaded solid lipid nanoparticles (SLNs): preparation and characterization. **Asian J. Pharm. Res.,** 2012, 2(2), 105-112.
17. Surrender V. and Deepika M.: Solid lipid nanoparticles : a comprehensive review. **J. Chem. Pharm. Res.,** 2016, 8(8), 102-114.
18. Khalil R. M., El-Bary A.A., Kassem M.A., Ghorab M.M. and Ahmed M.B.: Solid lipid nanoparticles for topical delivery of Meloxicam: Development and *in vitro* characterization. 1st Annual International Interdisciplinary Conference. 2013,779-798.
19. Yassin A. E. B., Md. Anwer K., Mowafy H. A., El-Bagory I. M., Bayomi M. A. and Alsarra I. A.: Optimization of 5-fluorouracil solid lipid nanoparticles: a preliminary study to treat colon cancer. **Int. J. Med. Sci.,** 2010, 7(6), 398-408.