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Formulation and *in vitro* Evaluation of Lacosamide Microspheres

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Abstract

The present study was aimed at the formulation and in-vitro evaluation of Lacosamide-loaded microspheres for sustained drug delivery. Lacosamide, an antiepileptic drug with a relatively short half-life, was incorporated into microspheres using suitable polymers to achieve prolonged drug release and improve patient compliance. Microspheres were prepared by using Solvent evaporation method and evaluated for particle size, percentage yield, drug entrapment efficiency, surface morphology, in-vitro drug release, release kinetics, and stability. FTIR studies confirmed the compatibility of Lacosamide with the selected excipients, indicating the absence of significant drug–polymer interactions. The prepared microspheres exhibited particle sizes ranging from 253 to 367 µm, percentage yield from 72.63% to 87.10%, and drug entrapment efficiency from 71.29% to 89.53%. Scanning Electron Microscopy (SEM) studies revealed that the microspheres were spherical with a smooth surface morphology. In-vitro drug release studies performed in phosphate buffer pH 7.4 demonstrated sustained drug release over 12 hours. Among all formulations, F7 was found to be the optimized formulation, exhibiting the highest drug entrapment efficiency (89.53%), percentage yield (87.10%), and cumulative drug release (99.43% at 12 hours). Stability studies conducted for 90 days at different storage conditions showed no significant changes in physical appearance or drug release profile, confirming the stability of the optimized formulation. The results suggest that Lacosamide-loaded microspheres are a promising sustained-release drug delivery system capable of improving therapeutic efficacy, reducing dosing frequency, and enhancing patient compliance in the management of epilepsy.

Keywords: Lacosamide, Microspheres, Sustained Release, Drug Entrapment Efficiency, FTIR, SEM, In-vitro Drug Release, Drug Release Kinetics, Stability Studies

Introduction

Epilepsy is a chronic neurological disorder characterized by recurrent, unprovoked seizures resulting from abnormal and excessive neuronal activity in the brain. Lacosamide is a functionalized amino acid derivative used as an antiepileptic drug for the treatment of partial-onset seizures.[1] Microspheres are multiparticulate drug delivery systems consisting of small spherical particles in which the drug is dispersed, entrapped, or encapsulated within a polymeric matrix. [2] They generally range from a few micrometers to several hundred micrometers in size and offer several advantages over conventional single-unit dosage forms. [3] Microspheres can provide controlled drug release, improve drug stability, reduce dosing frequency, and minimize fluctuations in plasma drug concentrations. Furthermore, their relatively large surface area and multiparticulate nature may facilitate more uniform distribution within the gastrointestinal tract and reduce the risk of dose dumping associated with some single-unit sustained-release systems. [4] The incorporation of lacosamide into a polymeric microsphere system therefore

represents a promising strategy for developing a controlled-release oral dosage form. Such a formulation may prolong drug release, potentially decrease dosing frequency, and provide improved control of drug exposure compared with conventional immediate-release formulations. [5] Accordingly, the present research was undertaken with the objective of formulating and in-vitro evaluating lacosamide-loaded microspheres, with particular emphasis on optimizing the formulation variables and assessing their physicochemical characteristics, drug entrapment, and in-vitro drug-release behavior. The optimized microsphere formulation may provide a useful platform for achieving sustained delivery of lacosamide and improving the overall performance of antiepileptic therapy. [6]

Materials

Lacosamide was procured from Hetero Labs, HYD, Eudragit RS and Ethyl cellulose was obtained from Synpharma Research Labs, Hyderabad. Other chemicals and the reagents used were of analytical grade.

Methodology

Formulation Table

Table 1: Formulation development of microspheres

F. no	Drug	Ethyl cellulose(mg)	Eudragit RS 100(mg)	Polyvinyl alcohol (ml)	Dichloromethane: Ethanol (1:1)	Water
F1	100	100	-	100	10	Q.s
F2	100	200	-	100	10	Q.s
F3	100	300	-	100	10	Q.s
F4	100	400	-	100	10	Q.s
F5	100	-	100	100	10	Q.s
F6	100	-	200	100	10	Q.s
F7	100	-	300	100	10	Q.s
F8	100	-	400	100	10	Q.s

Solvent Evaporation Technique[7]

1. Preparation of Internal Phase

- Accurately weigh the required quantity of Lacosamide and Polymer.
- Dissolve polymer in a mixture of dichloromethane and ethanol (1:1).
- Add Lacosamide to the polymer solution and stir until a homogeneous solution is obtained.

2. Preparation of External Phase

- Prepare 100 mL of 1% w/v Polyvinyl Alcohol (PVA) solution in distilled water.
- Stir continuously to obtain a clear solution.

3. Emulsification

- Add the drug-polymer solution slowly into the PVA solution under mechanical stirring at 1000–1200 rpm.
- Continue stirring for 2–3 hours at room temperature to form an oil-in-water (O/W) emulsion.

4. Solvent Evaporation

- Continuous stirring facilitates evaporation of the organic solvent.
- As the solvent evaporates, polymer precipitates around the drug forming microspheres.

5. Collection of Microspheres

- Separate the formed microspheres by filtration.
- Wash repeatedly with distilled water to remove residual PVA and unentrapped drug.

6. Drying

- Dry the microspheres at room temperature for 24 hours or in a hot-air oven at 40°C until constant weight is achieved.

7. Storage

- Store the dried microspheres in a desiccator until further evaluation

Evaluation of Microspheres

Percentage Yield

The percentage yield of the prepared microspheres was determined to evaluate the efficiency of the production process. After preparation, the microspheres were collected, washed thoroughly to remove any unentrapped drug or residual solvent, and dried to a constant weight. The dried microspheres were then accurately weighed. The practical yield obtained was compared with the total weight of the drug and polymer initially used in the formulation. The percentage yield indicates the effectiveness of the preparation method and the extent of material loss during the manufacturing process. All measurements were performed in triplicate, and the average value was reported. [8]

$$\% \ Yield = \frac{\text{Actual Weight of Product}}{\text{Total Weight of Excipient and Drug}} \times 100$$

Drug Entrapment Efficiency

The drug entrapment efficiency of the prepared microspheres was determined by estimating the amount of drug encapsulated within the polymeric matrix. An accurately weighed quantity of microspheres equivalent to about 10 mg of drug was crushed and transferred into a suitable volumetric flask containing an appropriate solvent capable of dissolving both the drug and polymer. The mixture was sonicated for 15–30 minutes to ensure complete extraction of the entrapped drug and then filtered through a 0.45 µm membrane filter. The filtrate was suitably diluted and analyzed using a UV-Visible spectrophotometer at the predetermined wavelength (λmax) of the drug. The actual amount of drug present in the microspheres was calculated from the calibration curve. The drug entrapment efficiency was determined by comparing the experimentally measured drug content with the theoretical drug content of the formulation. [9]

% Drug Entrapment = Amount of Drug Actually Present / Theoretical Drug Loaded Expected × 100

Particle Size Analysis

The particle size of the prepared microspheres was determined using a laser diffraction particle size analyzer. A known quantity of microspheres was dispersed in distilled water containing a small amount of surfactant (0.1% Tween 80) to prevent particle aggregation. The dispersion was sonicated for a few minutes to obtain a uniform suspension. The sample was then introduced into the particle size analyzer, and the mean particle size along with the particle size distribution was recorded. [10]

Morphological Characterization Using SEM

The surface morphology and shape of the microspheres were examined using scanning electron microscopy (SEM). A small amount of dried microspheres was mounted on an aluminum stub using double-sided adhesive tape and coated with a thin layer of gold under vacuum using a sputter coater to enhance conductivity. The coated samples were observed under the SEM at suitable accelerating voltage and different magnifications. Photomicrographs were captured to evaluate the surface characteristics, shape, porosity, and structural integrity of the microspheres. [11]

In-Vitro Drug Release Study

The in-vitro drug release study was carried out using USP dissolution apparatus II (paddle method). Microspheres equivalent to a predetermined quantity of drug were placed in 900 mL of dissolution medium maintained at 37 ± 0.5°C and stirred at 50 rpm. The dissolution medium generally consisted of 7.4 phosphate buffer. At specified time intervals, 5 mL samples were withdrawn and replaced with an equal volume of fresh dissolution medium maintained at the same temperature. The samples were filtered through a membrane filter and analyzed spectrophotometrically at the drug's λmax. The cumulative percentage drug release was calculated and plotted against time. [12]

Kinetics of Drug Release Studies

To understand the mechanism of drug release from the microspheres, the dissolution data obtained from the in-vitro release studies were fitted into various kinetic models including Zero-order, First-order, Higuchi, Korsmeyer-Peppas, and Hixson-Crowell models. The cumulative percentage drug release data were plotted according to the mathematical equations of each model, and the correlation coefficient (R^2) values were determined. The model exhibiting the highest R^2 value was considered the best-fit model and was used to explain the release mechanism, whether diffusion-controlled, erosion-controlled, or a combination of both. [13]

Stability Studies

The stability studies of the optimized microsphere formulation were conducted according to ICH Q1A(R2) guidelines. The formulation was packed in suitable airtight containers and stored under accelerated stability conditions at 40 ± 2°C and 75 ± 5% relative humidity for a period of three months. Samples were withdrawn at predetermined intervals of 0, 1, 2, and 3 months and evaluated for physical appearance, particle size, drug content, entrapment efficiency, and in-vitro drug release characteristics. The results obtained after storage were compared with the initial values to assess any significant changes. The absence of noticeable variations in the evaluated parameters indicated good stability of the microsphere formulation during the storage period. [14]

Results and Discussion

Characterization of Microspheres

Particle Size Analysis

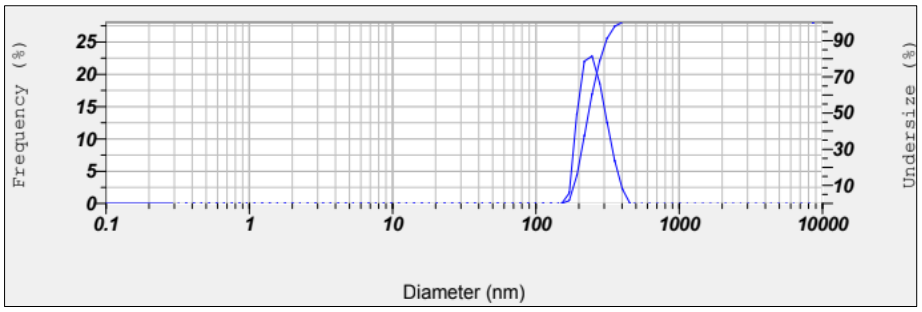


Fig 1: Particle size analysis of Optimized formulation

Table 2: Particle size of Different formulations of Microspheres

Formulation code	Mean particle size* (µm)
F1	293
F2	348
F3	367
F4	358
F5	268
F6	290
F7	253
F8	318

Discussion

Among all formulations, F7 exhibited the smallest particle size (253 µm), indicating efficient emulsification and solvent evaporation during preparation. Smaller particle size generally provides a larger surface area which facilitates uniform drug release and enhanced entrapment. The variation in particle size among formulations may be attributed to differences in polymer concentration and viscosity of the dispersed phase.

Percentage Yield

Table 3: Percentage yield for different formulation

Formulation	Percent Yield*(%)
F1	72.63
F2	78.85
F3	80.26
F4	83.38
F5	84.6
F6	86.33
F7	87.10
F8	80.16

Discussion

The highest yield was observed for F7 (87.10%), indicating minimal material loss during preparation and effective microsphere formation. Increased polymer concentration may have improved the solidification process and reduced drug diffusion into the external phase, resulting in higher production yield.

Scanning Electronic Microscopy

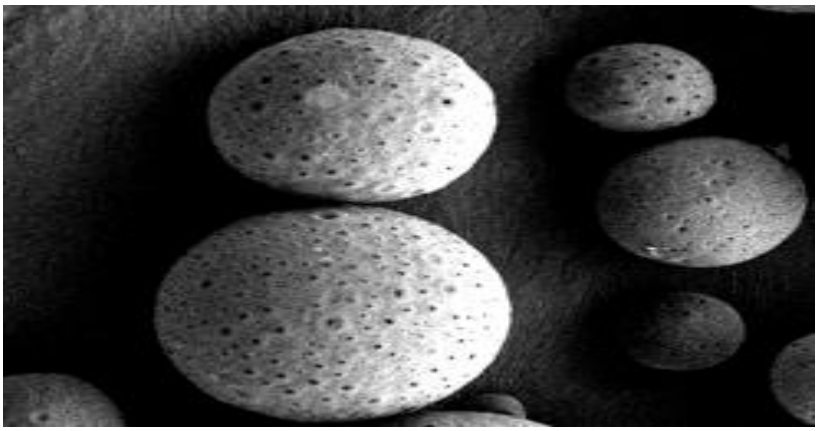


Fig 2: SEM Analysis of Optimized formulation

Discussion

No visible cracks or surface imperfections were observed. The spherical morphology confirms successful formation of microspheres by the solvent evaporation technique and contributes to sustained drug release behavior.

Drug Entrapment Efficiency

Table 4: Drug entrapment for different formulation

Formulation	Drug Entrapment Efficiency
F1	71.29
F2	82.25
F3	78.63
F4	77.81
F5	83.56
F6	85.90
F7	89.53
F8	80.25

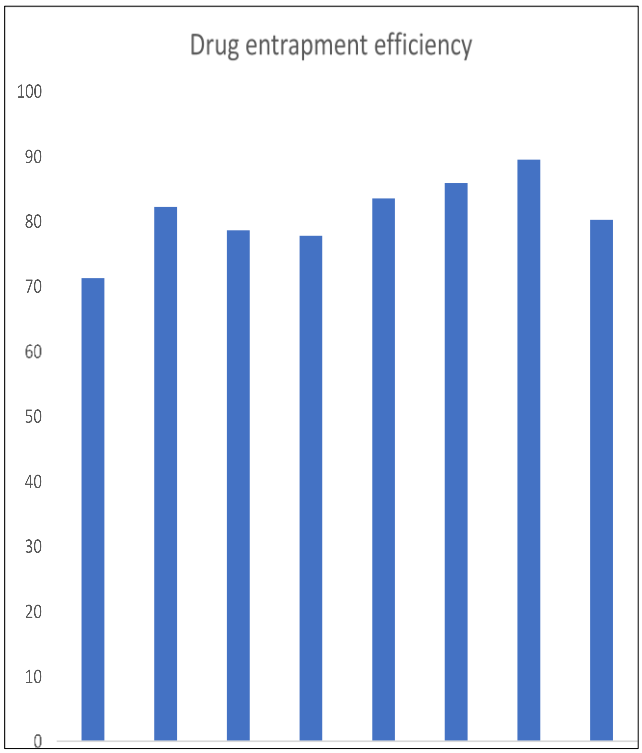


Fig 3: Drug entrapment efficiency for different formulation

Discussion

The optimized formulation F7 showed the highest entrapment efficiency (89.53%). This may be attributed to the optimum polymer-to-drug ratio, which reduced drug diffusion during preparation and enhanced encapsulation. Higher entrapment efficiency is advantageous because it ensures uniform drug loading and minimizes drug wastage.

***In-Vitro* Drug Release Study**

Table 5: Comparative *In-Vitro* Drug Release Profile for Formulation in 7.4 phosphate buffer

Time (hrs.)	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
1	17.53	18.43	19.37	20.13	18.43	20.13	22.36	24.59
2	25.83	26.97	28.73	30.12	34.59	27.81	31.26	32.47
3	32.29	33.53	35.81	41.56	43.15	44.29	45.79	46.81
4	49.51	43.69	45.37	53.25	55.97	58.42	59.43	57.43
6	61.28	59.86	63.25	65.89	66.37	68.91	69.79	67.12
8	75.32	74.23	76.58	77.81	78.49	79.80	78.12	77.82
10	84.97	81.28	83.35	86.93	87.91	88.98	89.16	83.16
12	92.35	93.20	94.81	96.87	97.83	98.58	99.43	96.31

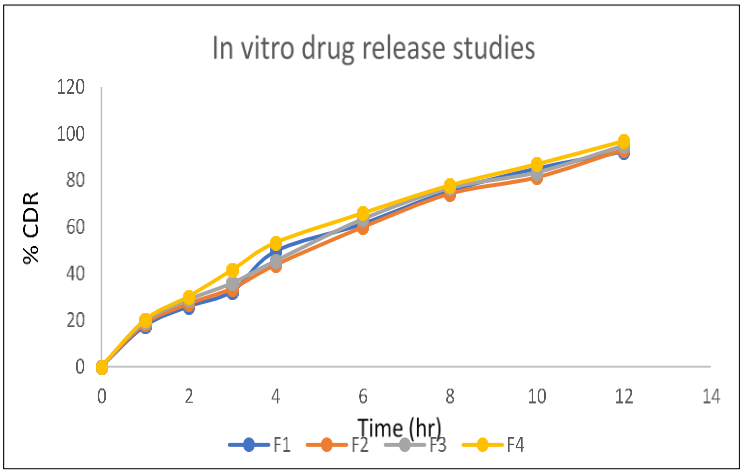


Fig 4: Comparative In-Vitro Drug Release Profile Of (F1-F4) formulation

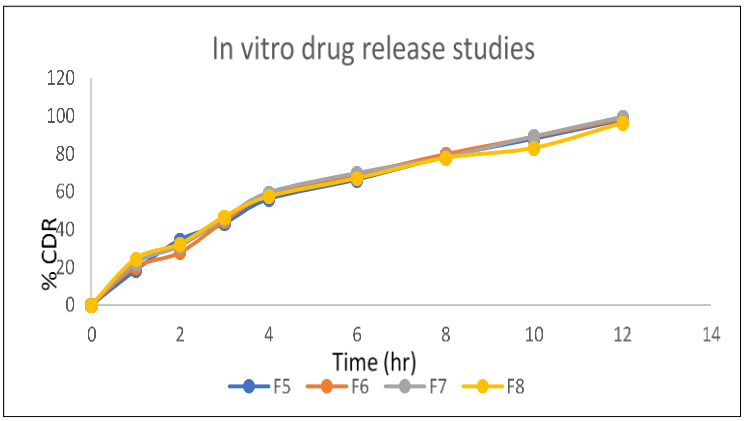


Fig 5: Comparative In-Vitro Drug Release Profile Of (F5-F8) formulation

Discussion

The optimized formulation f7 exhibited the highest drug release (99.43%) at 12 hours. Initially, a moderate release was observed due to the release of surface-associated drug, followed by a controlled release phase resulting from diffusion through the polymer matrix. The sustained release profile suggests that the microspheres are capable of maintaining prolonged drug availability and reducing dosing frequency.

Drug Release Kinetics

Zero Order Kinetics

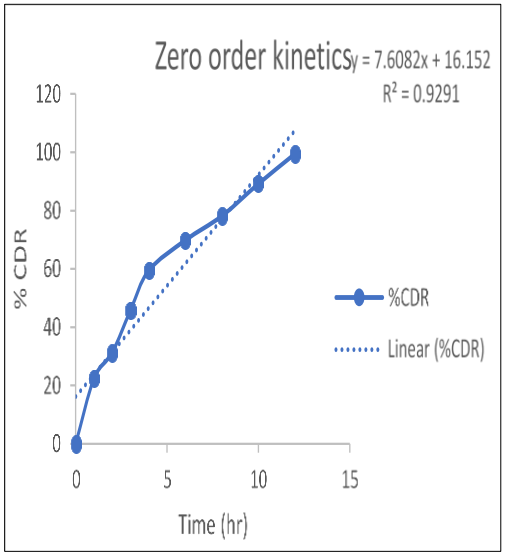


Fig 6: Zero order kinetics of optimized formulation

First Order Kinetics

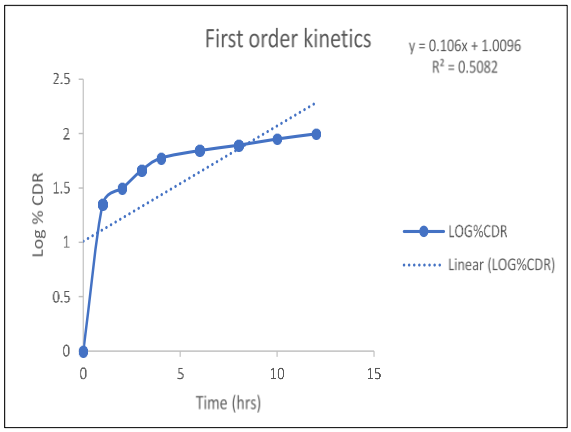


Fig 7: First order kinetics optimized formulation

Higuchi Model

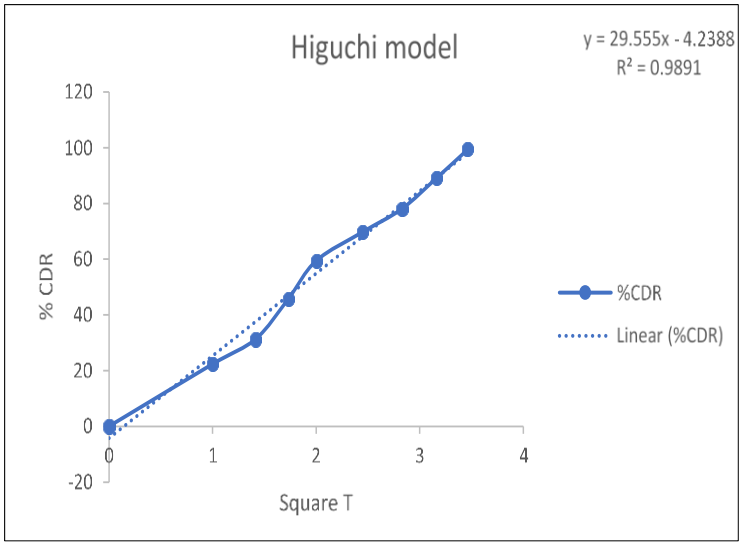


Fig 8: Higuchi model optimized formation

Korsmeyer Peppas

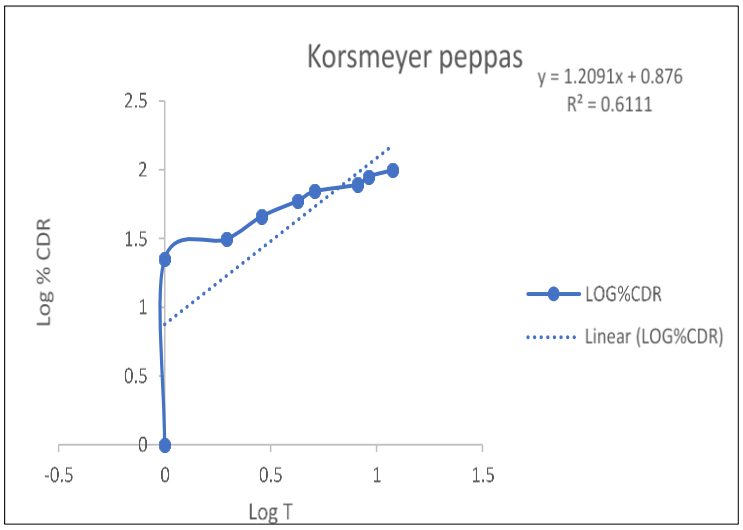


Fig 9: Korsmeyer peppas optimized formulation

Discussion

Based on the overall kinetic analysis, the optimized formulation F7 predominantly followed the Higuchi diffusion model with contribution from anomalous diffusion mechanisms.

Stability Study

Stability study was carried out for the F7 formulation by exposing it to different temperature 25°C, 30°C and 40°C for 90 days. The sample was analyzed for drug content at the regular intervals. It was found that no remarkable change in the drug release of F7 formulation. This indicates that F7 was stable for following temperature.

Table 6: Results of stability studies of optimized formulation F-7

S.NO	Time in days	Physical changes	Mean % drug release		
			Lacosamide		
			25^0C/60%	30^0C/75%	40^0C/75%
1.	01	No Change	99.43	99.43	99.43
2.	30	No Change	98.42	98.15	98.34
3.	60	No Change	97.58	97.25	97.42
4.	90	No Change	96.31	96.20	96.31

Conclusion

Lacosamide-loaded microspheres were successfully formulated and evaluated for sustained drug delivery. FTIR studies confirmed compatibility between Lacosamide and the selected excipients, while SEM analysis demonstrated the formation of spherical and uniform microspheres. Among all formulations, F7 was identified as the optimized formulation based on its smallest particle size (253 µm), highest percentage yield (87.10%), highest drug entrapment efficiency (89.53%), and maximum cumulative drug release (99.43% at 12 hours). The optimized microspheres provided a controlled and sustained release of Lacosamide over 12 hours, which may help in maintaining therapeutic drug levels for an extended period and reducing dosing frequency. Drug release kinetics suggested a diffusion-controlled mechanism, and stability studies confirmed that the formulation remained stable under various storage conditions for 90 days. Therefore, the developed Lacosamide microsphere formulation (F7) can be considered a promising sustained-release drug delivery system for improving the therapeutic effectiveness and patient compliance in the management of epilepsy. Further in-vivo studies are recommended to establish its clinical potential.

References

1. Cawello W. Clinical pharmacokinetic and pharmacodynamic profile of lacosamide. Clinical Pharmacokinetics. 2015;54(9):901–914.
2. Cawello W, Stockis A, *et al*. Pharmacokinetics of lacosamide in healthy subjects and patients with epilepsy. Epilepsy Research. 2010;91(2–3):203–210.
3. Chung S, Sperling MR, Biton V, *et al*. Lacosamide as adjunctive therapy for partial-onset seizures: a randomized, double-blind, placebo-controlled trial. Epilepsia. 2010;51(6):958–967.
4. Varde NK, Pack DW. Microspheres for controlled release drug delivery. Expert Opinion on Biological Therapy. 2004;4(1):35–51.
5. McGinity JW, O'Donnell PB. Preparation of microspheres by the solvent evaporation technique. Advanced Drug Delivery Reviews. 1997;28(1):25–42. doi:10.1016/S0169-409X(97)00049-5.
6. Freitas S, Merkle HP, Gander B. Microencapsulation by solvent extraction/evaporation: reviewing the state of the art of microsphere preparation process technology. Journal of Controlled Release. 2005;102(2):313–332.
7. Sah H. Microencapsulation by solvent evaporation: state of the art for process engineering approaches. Journal of Controlled Release. 2008;128(1):10–18.
8. Sato T, Kanke M, Schroeder HG, DeLuca PP. Porous biodegradable microspheres for controlled drug delivery. I. Assessment of processing conditions and solvent removal techniques. Pharmaceutical Research. 1988;5(1):21–30. doi:10.1023/A:1015855210319.
9. Jain RA. The manufacturing techniques of various drug loaded biodegradable poly(lactide-co-glycolide) (PLGA) devices. Biomaterials. 2000;21(23):2475–2490.
10. Lee YJ, Kim MS. Advances in drug-loaded microspheres for targeted, controlled, and sustained drug delivery: potential, applications, and future directions. Biomedicine & Pharmacotherapy. 2025;186:118244. doi:10.1016/j.biopha.2025.118244.
11. U.S. Food and Drug Administration. Lacosamide Tablets: Prescribing Information. The prescribing information reports approximately 100% oral bioavailability and an elimination half-life of approximately 13 hours.
12. Ben-Menachem E. Lacosamide: an investigational drug for the treatment of partial-onset seizures. Expert Review of Neurotherapeutics. 2008;8(12):1855–1864.
13. Cawello W, Bökens H, Nickel B, Andreas JO, Halberstadt G. Lacosamide: pharmacokinetic profile and metabolism. Epilepsia. 2012;53(Suppl 5):1–8.
14. Kadir E, Aydin RS, Akin M, *et al*. Lacosamide Loaded Polymeric Microneedle Patches for Enhanced Brain Delivery and Epilepsy Treatment. Pharmaceutics. 2021;13(10):1652.

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