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Review Paper

Formulation and Characterization of Sustained-Release Microspheres of Oxazepam

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ABSTRACT

The aim of this study was to formulate and characterize oxazepam-loaded microspheres for sustained drug release to enhance its therapeutic efficacy in the treatment of anxiety and insomnia. Various formulations of microspheres were prepared using HPMC, ethyl cellulose (EC), and guar gum as polymers, and their physical properties, such as yield, drug entrapment efficiency, buoyancy, and floating lag time, were evaluated. The optimized formulation (F4) exhibited a high percentage yield (73.32±0.22%) and drug entrapment efficiency (72.23±0.32%). Furthermore, F4 showed the shortest floating lag time (55±3 sec.) and the highest percentage buoyancy (76±2%), indicating its ability to remain buoyant in the gastric medium for prolonged periods. In-vitro drug release studies demonstrated that formulation F4 provided a sustained release of oxazepam over 12 hours, with 98.78% drug release, significantly improving upon the rapid release observed with marketed formulations. The release kinetics followed a zero-order release model (R^2 = 0.9748), ensuring a constant drug release rate. These results suggest that oxazepam-loaded microspheres could serve as an effective sustained-release formulation for long-term management of anxiety disorders, reducing dosing frequency and improving patient compliance.

INTRODUCTION

Oxazepam is a commonly prescribed anxiolytic drug belonging to the benzodiazepine class, primarily used for the treatment of anxiety disorders, alcohol withdrawal symptoms, and insomnia. However, its clinical application is often limited by its short half-life and the requirement

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for frequent dosing, which may lead to poor patient compliance (Ali et al., 2017). To overcome these limitations, sustained-release formulations have emerged as a potential strategy for improving therapeutic outcomes by providing controlled and prolonged drug release, thus minimizing the frequency of administration and reducing side effects associated with peak plasma concentrations. Microencapsulation, the process of encapsulating drugs in microspheres, is a widely used technique in the development of sustained-release formulations. Microspheres are spherical particles ranging from 1 to 1000 microns in size and are designed to release the drug gradually over an extended period. The use of polymeric materials in the preparation of microspheres allows for better control of drug release, biocompatibility, and stability (Kumari et al., 2018). Among the various polymers employed in the formulation of microspheres, biodegradable polymers like poly (lactic-co-glycolic acid) (PLGA) have gained significant attention due to their controlled release properties and safe degradation into non-toxic metabolites (Zhao et al., 2020). The objective of this study was to formulate and characterize sustained-release microspheres of oxazepam using biodegradable polymers, specifically PLGA, to enhance the pharmacokinetic profile and improve the therapeutic efficacy of oxazepam. The microspheres were prepared using a solvent evaporation method, a common technique for the preparation of microspheres, which involves dissolving the drug and polymer in a volatile solvent and allowing the solvent to evaporate, forming solid microspheres. The physicochemical properties, drug encapsulation efficiency, in vitro drug release, and stability of the formulated microspheres were evaluated. This research aims to develop a controlled-release system for oxazepam that minimizes the need for frequent administration, enhances patient compliance, and ensures sustained therapeutic levels of the drug over time.

MATERIAL AND METHODS

MATERIAL

For the formulation development of oxazepam-loaded microspheres, various chemicals and materials were utilized. Oxazepam, the active pharmaceutical ingredient, was sourced from Pharmaceutical Company. The polymeric materials used for encapsulation included Hydroxypropyl Methylcellulose (HPMC), Ethylcellulose (EC), and Guar gum, all of which were obtained from HiMedia Laboratories Private Limited, Mumbai. These polymers play a crucial role in controlling the drug release profile of the microspheres. The solvents required for the formulation process, including methanol, ethanol, and chloroform, were sourced from Qualigens Fine Chemicals, Mumbai. Additionally, Di potassium hydrogen orthophosphate from S. D. Fine Chem. Ltd., Mumbai, was used in the formulation for pH adjustment during the preparation process. These materials were carefully selected to ensure the optimal formation of oxazepam-loaded microspheres with desirable characteristics for sustained drug release.

METHODS

Preparation of sustain release microsphere of Oxazepam

Sustain release microspheres loaded with Oxazepam were prepared using solvent-evaporation method using HPMC, EC and Guar gum in different ratio table 7.1 as reported by Gunjal and Gaikwad, (2013) with slight modification. Drug and polymer in proportion of drug and polymers were dissolved in 1:2 mixture of solvent system of ethanol and dichloromethane. This clear solution was poured slowly in a thin stream into the aqueous solution of 1% polyvinyl

alcohol. The emulsion was continuously stirred for 3 h at a speed of 500 rpm at 27±2°C. The sustain release microspheres were collected by decantation, while the non-floating microspheres were discarded. The microspheres were dried overnight at 40±2°C and stored in desicator.

Table 1: Formulations of sustain release microspheres of Oxazepam

S. No.	Formulation Code	Oxazepam (mg)	HPMC (mg)	EC (mg)	Guar gum (mg)
1.	F1	15	100	25	-
2.	F2	15	100	50	-
3.	F3	15	100	75	-
4.	F4	15	150	25	10
5.	F5	15	150	50	20
6.	F6	15	150	75	30

Evaluation of microspheres

Percentage yield

The prepared microspheres with a size range of 1μm to 1000μm were collected and weighed from different formulations. The measured weight was divided by the total amount of all non-volatile components which were used for the preparation of the microspheres (Kawashima *et al.*, 1992).

$$\% \text{ Yield } = \frac{\text{Actual weight of product}}{\text{Total weight of drug and polymer}} x\ 100$$

Drug entrapment

The various formulations of the sustain release were subjected for drug content. 10 mg of sustain release from all batches were accurately weighed and crushed (Sushma and Sriram, 2013). The powder of microspheres were dissolved in 10 ml 0.1 N HCl and centrifuge at 1000 rpm. This supernatant solution is than filtered through whatmann filter paper No. 44. After filtration, from this solution 0.1 ml was taken out and diluted up to 10 ml with 0.1 N HCl. The percentage drug entrapment was calculated using calibration curve method.

Floating behavior: Ten milligrams of the sustain release were placed in 0.1 N HCl (100 mL). The mixture was stirred at 100 rpm in a magnetic stirrer (Sharma *et al.*, 2015). After 10 h, the layer of buoyant microsphere was pipetted and separated by filtration. Particles in the sinking particulate layer were separated by filtration. Particles of both types were dried in desiccators until a constant weight was obtained. Both the fractions of microspheres were weighed and buoyancy was determined by the weight ratio of floating particles to the sum of floating and sinking particles.

$$\text{Percent buoyancy} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} x\ 100$$

Measurement of mean particle size

The mean size of the microspheres was determined by Photo Correlation Spectroscopy (PCS) on a submicron particle size analyzer (Malvern Instruments) at a scattering angle of 90°. A sample (0.5mg) of the microspheres suspended in 5 ml of

distilled water was used for the measurement (Jain *et al.*, 2005).

Determination of zeta potential

The zeta potential of the drug-loaded microspheres was measured on a zeta sizer (Malvern Instruments) by determining the electrophoretic mobility in a micro electrophoresis flow cell. All the samples were measured in water at 25°C in triplicate (Yadav and Patel, 2013).

Shape and surface characterization of microspheres by scanning electron microscopy (SEM)

From the formulated batches of microspheres, formulations (F3) which showed an appropriate balance between the percentage releases were examined for surface morphology and shape using scanning electron microscope Jeol Japan 6000 (Gadad *et al.*, 2016; Sammour *et al.*, 2012). Sample was fixed on carbon tape and fine gold sputtering was applied in a high vacuum evaporator. The acceleration voltage was set at 10KV during scanning. Microphotographs were taken on different magnification and higher magnification (200X) was used for surface morphology.

***In-vitro* release studies**

The *in vitro* drug release rate from sustain release was carried out using the USP type II (Electro Lab.) dissolution paddle assembly (Wasnik *et al.*, 2012). A weighed amount of sustain release equivalent to 100 mg drug were dispersed in 900 ml of 0.1 N HCI (pH=1.2) maintained at 37 ± 0.5°C and stirred at 55rpm. One ml sample was withdrawn at predetermined intervals and filtered and equal volume of dissolution medium was replaced in the vessel after each withdrawal to maintain sink condition. The collected samples analyzed spectrophotometrically at 282nm to determine the concentration of drug present in the dissolution medium.

Drug release kinetic data analysis

Several kinetic models have been proposed to describe the release characteristics of a drug from matrix. The following three equations are commonly used, because of their simplicity and applicability. Equation 1, the zero-order model equation (Plotted as cumulative percentage of drug released vs time); Equation 2, Higuchi's square-root equation (Plotted as cumulative percentage of drug released vs square root of time); and Equation 3, the Korsemeyer-Peppas equation (Plotted as Log cumulative percentage of drug released vs Log time).

RESULTS AND DISCUSSION

The formulation and characterization of oxazepam-loaded microspheres were evaluated for various attributes, including yield, drug entrapment, buoyancy, floating lag time, and in-vitro drug release profile. The formulation of microspheres with the different combinations of polymers such as HPMC, EC, and Guar gum provided insights into the efficiency of the drug release mechanism and its control. Table 2 shows the percentage yield for different formulations, with formulation F4 exhibiting the highest yield (73.32±0.22%), followed by formulations F2 (69.98±0.32%) and F6 (69.98±0.25%). These results suggest that F4 was the most stable formulation in terms of production yield, likely due to the polymeric combination chosen, which provides better stability during the formulation process. Drug entrapment efficiency (Table 3) was also highest in F4 (72.23±0.32%), indicating that this formulation could retain the highest amount of oxazepam within the microspheres, ensuring controlled release over time. The ability of the microspheres to float in the gastrointestinal tract is

crucial for ensuring prolonged drug release. As shown in Table 4, formulation F4 exhibited the shortest floating lag time (55±3 sec.) and the highest percentage buoyancy (76±2%), which is ideal for sustained drug release. These results indicate that the microspheres have excellent buoyancy properties, which would ensure that the formulation stays afloat in the gastric medium for an extended period, thus enhancing drug absorption. In-vitro release studies (Table 5) showed that formulation F4 exhibited a controlled release profile with 98.78% drug release at 12 hours, while the marketed oxazepam tablet (15mg) showed a rapid release, with 68.85% release at 1 hour and almost complete release within 2 hours. This demonstrates that formulation F4 can sustain the release of oxazepam over a period of 12 hours, offering a longer therapeutic action. This prolonged release profile is advantageous in treating conditions like anxiety and insomnia, where maintaining a stable drug concentration over time is essential. The release kinetics data (Table 6) for the optimized formulation F4 indicate a close fit to the zero-order release model with an R^2 value of 0.9748. This suggests that the drug release from the microspheres is independent of the concentration of the drug and is controlled by the diffusion of the drug through the matrix. The Korsmeyer-Peppas model (R^2 = 0.7788) also provided a good fit, suggesting a combined mechanism of drug release, including diffusion and erosion. The regression analysis for formulation F4 (Table 7) reveals that the zero-order model is the best fit for the drug release profile, which is ideal for controlled-release formulations. This indicates that the microspheres release oxazepam at a constant rate, ensuring a steady plasma drug concentration and minimizing fluctuations in drug levels.

Table 2: Percentage yield for different formulation

S. No.	Formulation	Percentage Yield
1.	F1	64.45±0.25
2.	F2	69.98±0.32
3.	F3	68.85±0.15
4.	F4	73.32±0.22
5.	F5	68.74±0.32
6.	F6	69.98±0.25

Table 3: Drug entrapment for different formulations

S. No.	Formulation	Drug entrapment (% w/w) of prepared microsphere
1.	F1	65.56±0.45
2.	F2	68.85±0.23
3.	F3	65.45±0.15
4.	F4	72.23±0.32
5.	F5	67.85±0.18
6.	F6	68.98±0.19

Table 4: Percentage Buoyancy and floating lag time of floating microsphere

Formulation	Floating Lag Time (Sec.)	Percentage Buoyancy
F1	68±4	68±7
F2	65±6	72±6
F3	60±4	69±3
F4	55±3	76±2

F5	63±5	69±7
F6	69±3	71±5

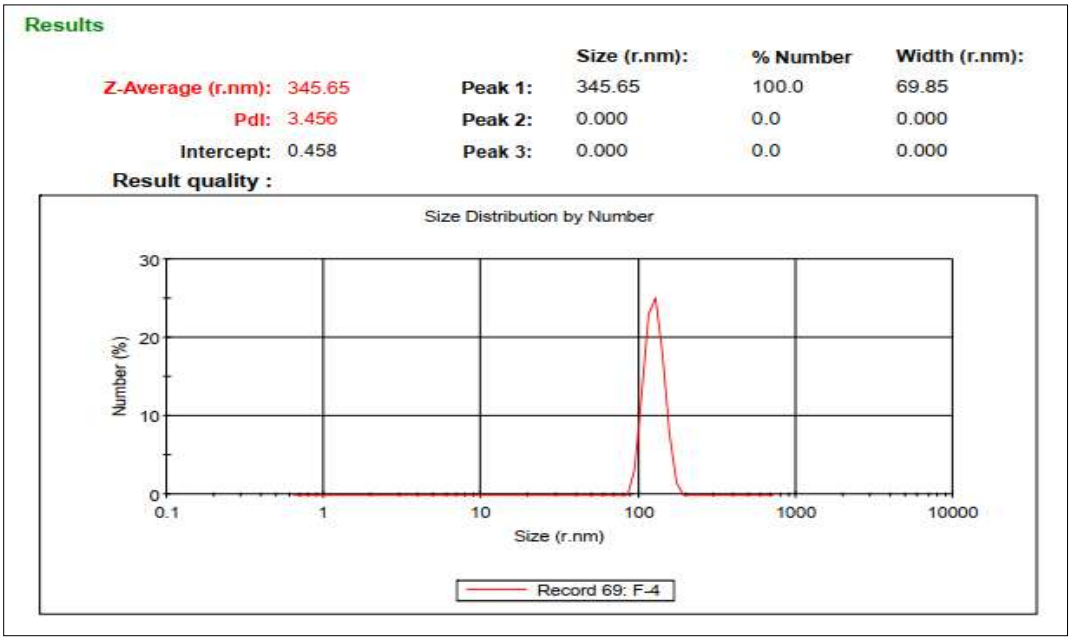

Figure 1: Particle size data of optimized microsphere formulation F4

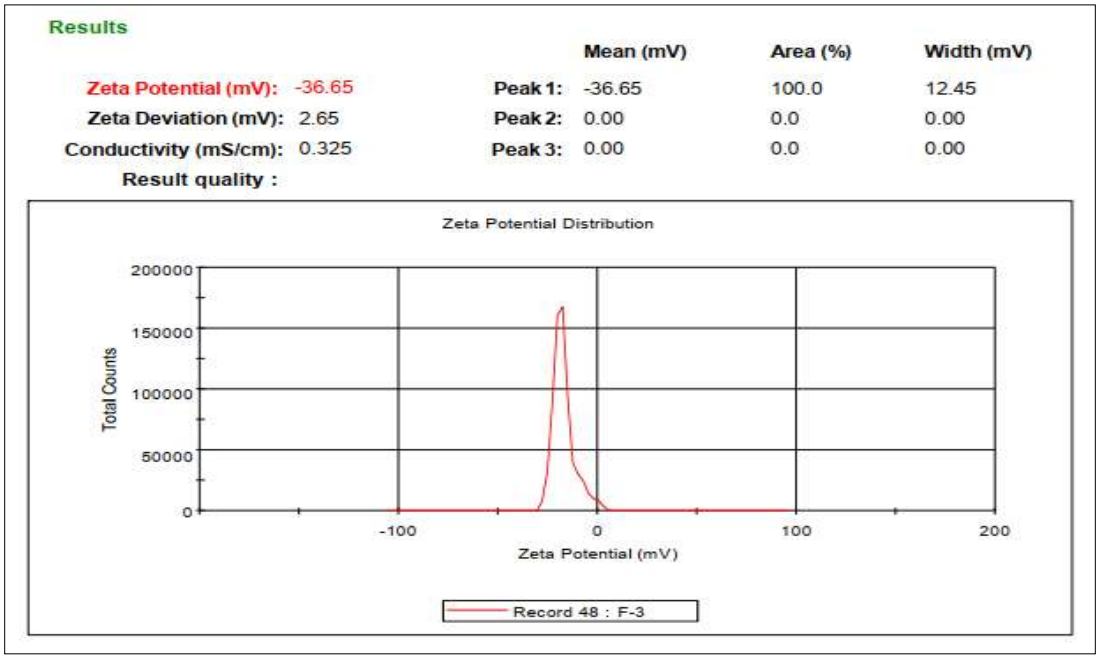

Figure 2: Zeta potential data of floating microsphere F4

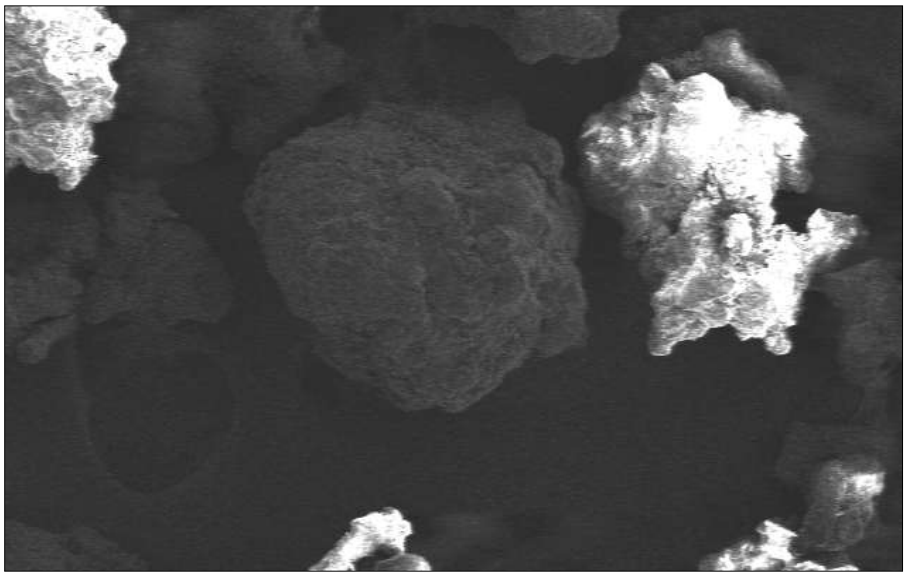

Figure 3: Graph of scanning electron microscopy (SEM) of optimized formulation F4

Table 5: Release Study data of formulation F1-F6

Time (Hrs)	% of Drug Release						
	F1	F2	F3	F4	F5	F6	Marketed Formulation (Oxazepam 15mg Tablet)
0.5	36.65	33.25	29.98	25.45	20.23	16.65	36.65
1	55.58	50.32	45.65	41.12	33.36	26.65	68.85
2	69.95	64.47	63.32	59.98	45.52	38.87	88.85
4	78.85	75.52	74.45	68.87	53.32	46.65	93.32
6	95.65	93.32	90.56	83.32	68.87	55.58	-
8	98.85	98.85	96.65	91.14	76.66	63.32	-
10	-	-	99.12	96.65	83.32	79.98	-
12	-	-	-	98.78	97.74	86.65	-

Table 6: Release Kinetics of optimized formulation of microsphere F4

Time (h)	Square Root of Time(h)$^{1/2}$	Log Time	Cumulative% Drug Release	Log Cumulative % Drug Released	Cumulative %Drug Remaining	Log Cumulative % Drug Remaining
0.5	0.707	-0.301	25.45	1.406	74.55	1.872
1	1	0	41.12	1.614	58.88	1.770
2	1.414	0.301	59.98	1.778	40.02	1.602
4	2	0.602	68.87	1.838	31.13	1.493
6	2.449	0.778	83.32	1.921	16.68	1.222
8	2.828	0.903	91.14	1.960	8.86	0.947
10	3.162	1	96.65	1.985	3.35	0.525
12	3.464	1.079	98.78	1.995	1.22	0.086

Table 7: Comparative study of regression coefficient for selection of optimized Formulation F4

Release Kinetics	Zero order	First order	Higuchi	Korsmeyer peppas
R^2	0.9748	0.9733	0.9604	0.7788

CONCLUSION

The development of oxazepam-loaded microspheres using HPMC, EC, and Guar gum as

matrix-forming agents has resulted in an optimized formulation (F4) that exhibits high drug entrapment efficiency, excellent buoyancy, and a controlled, sustained drug release profile. The formulation offers several advantages, including prolonged drug action and a steady release of oxazepam, which can improve patient compliance and therapeutic efficacy, especially for the treatment of anxiety and related disorders. Further in-vivo studies are recommended to confirm the clinical benefits of these microspheres in providing sustained therapeutic effects.

REFERENCES

1. Ali, H.S., Waqas, M. & Khan, Z. (2017) Recent advances in the formulation of controlled release drug delivery systems. Journal of Drug Delivery Science and Technology, 40, 136–147.
2. Jain, Awasthi, S.K. AM, Jain, N.K., Agrawal, G.P. (2005) Calcium silicate-based microspheres of repaglinide for gastroretentive floating drug delivery: Preparation and in vitro characterization. Journal of Controlled Release, 107, 300–309.
3. Yadav, H. & Patel, H. (2013) Formulation and evaluation of floating microspheres of etodolac. American Journal of Pharmacy and Health Research, 1, 45–54.
4. Gadad (2016) Formulation and evaluation of gastroretentive floating microspheres of lafutidine A.P., naik, S.S., Dandagi, P.M. & Bolmal, U.B. Indian Journal of Pharmaceutical Education and Research, 50, S76–S81.
5. Sammour, El-Ghamry, H.A., El-Nahas, H.M. & Barakat, W. (2012) Development and characterization of controlled release ketoprofen microspheres O.A. Journal of Applied Pharmaceutical Sciences, 2, 60–67.
6. Sharma, Kohli, M., S. & Dinda, A. (2015) In vitro and in vivo evaluation of repaglinide loaded floating microspheres prepared from different viscosity grades of HPMC polymer. Saudi Pharmaceutical Journal, 23, 675–682.
7. Kumari, S., Kumar, S. & Yadav, M. (2018) Microencapsulation techniques for controlled drug delivery systems. Journal of Pharmaceutics and Nanotechnology, 6, 25–40.
8. Kawashima, Niwa, Y., T., Takeuchi, H., Hino, T. & Itoh, Y. (1992) Hollow Microsphe res for use as a floating controlled drug delivery system in the stomach. Journal of Pharmaceutical Sciences, 81, 135–140.
9. Sushma, R. & Sriram, N. (2013) Preparation and evaluation of floating microspheres of repaglinide. International Journal of Advanced Pharmaceutics, 3, 30–36.
10. Wasnik, Parmar, S., P., Singh, D. & Ram, A. (2012) Preparation and characterization of floating drug delivery system of azithromycin. Acta Poloniae Pharmaceutica, 69, 515–522.
11. Zhao, X., Liu, Y. & Zhang, M. (2020) PLGA-based microspheres for controlled drug delivery: Applications and progress. Drug Delivery and Translational Research, 10, 527–540.
12. Gunjal (2013), 1(9) A review on floating microspheres as gastroretentive drug delivery system. American Journal of Pharmacy and Health Research. M. & Gaikwad, A., 2321, 3647.

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