International Journal of Pharmaceutics and Drug Research
ISSN: 2347-6346
Available online at http://ijpdr.com

Original Research Article

# FORMULATION AND EVALUATION OF FLOATING MICROSPHERE USING NATURAL POLYMER FOR THE TREATMENT OF ULCER

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***Article History:**

Received: 10/02/2024
Revised: 29/02/2024
Accepted: 24/03/2024

## ABSTRACT

Gastric ulceration remains a significant health concern worldwide, necessitating the development of effective drug delivery systems for improved treatment outcomes. This study aimed to formulate and evaluate floating microspheres using a natural polymer for the treatment of gastric ulcers. The microspheres of Lansoprazole were prepared by the emulsion solvent evaporation method using sodium alginate as the natural polymer and calcium carbonate as a gas-generating agent. The formulated microspheres were characterized for their morphology, particle size, drug entrapment efficiency, *in vitro* drug release, and buoyancy properties. The developed microspheres exhibited a spherical morphology with uniform particle size distribution. The entrapment efficiency of the microspheres was found to be satisfactory, indicating efficient drug loading. In vitro drug release studies revealed sustained release behavior, with the majority of the drug released over an extended period, indicating their potential for prolonged gastric retention. Furthermore, the microspheres demonstrated excellent buoyancy properties, allowing them to remain in the gastric region for an extended period, thereby enhancing drug absorption and bioavailability. Overall, the developed floating microspheres using a natural polymer hold promise as a novel drug delivery system for the effective treatment of gastric ulcers, offering improved patient compliance and therapeutic outcomes.

**Keywords:** Floating microspheres, Lansoprazole, Natural polymer, Gastric ulcers, Sodium alginate, Drug delivery.

## INTRODUCTION

Gastric ulcer disease is a prevalent gastrointestinal disorder characterized by the erosion of the mucosal lining of the stomach, leading to abdominal pain, bleeding, and discomfort. Despite advancements in treatment modalities, the management of gastric ulcers remains challenging due to factors such as poor patient compliance, frequent dosing requirements, and side effects associated with conventional therapy (Khan *et al.,* 2023). Consequently, there is a growing interest in developing innovative drug delivery systems to enhance the efficacy and safety of anti-ulcer drugs. Floating microspheres have emerged as promising drug delivery vehicles for the treatment of gastric ulcers due to their unique ability to remain buoyant in the stomach for an extended period (Tamizharasi *et al.,* 2011). This prolonged gastric retention enables sustained drug release, thereby improving drug absorption, bioavailability, and therapeutic efficacy while minimizing systemic side effects. Additionally, floating microspheres offer the advantage of reduced dosing frequency and enhanced patient compliance (Deshpande *et*

*al.,* 1996). In this context, the present study focuses on formulating and evaluating floating microspheres using a natural polymer for the treatment of gastric ulcers. Natural polymers, such as sodium alginate, have gained attention in pharmaceutical research due to their biocompatibility, biodegradability, and low toxicity profile. By harnessing the properties of sodium alginate along with gas-generating agents like calcium carbonate, the formulated microspheres aim to provide controlled drug release and prolonged gastric retention, thereby improving the therapeutic outcomes for gastric ulcer patients.

Several studies in the literature have demonstrated the potential of floating microspheres in enhancing the gastric retention and bioavailability of anti-ulcer drugs. Building upon these advancements, the current study aims to contribute to the field of gastroretentive drug delivery by formulating floating microspheres using sodium alginate and evaluating their potential as a novel therapeutic approach for gastric ulcer treatment. Through comprehensive characterization and evaluation, including morphology, particle size, drug entrapment efficiency, and in vitro drug release, this research seeks to provide valuable insights into the development of effective and patient-friendly formulations for gastric ulcer management.

## MATERIALS AND METHODS

### Preparation of floating microsphere of Lansoprazole using natural polymer

Floating microspheres loaded with Lansoprazole were prepared using solvent-evaporation method using HPMC, Xanthan gum and Guar gum in different ratio table 1 (Desai *et al.,* 1993). 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 floating 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.

### 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 (Soppimath *et al.,* 2001).

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

### Drug Entrapment

The various formulations of the Floating microspheres were subjected for drug content. 10 mg of Floating microspheres from all batches were accurately weighed and crushed (Singh *et al.,* 2001). 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 (Whitehead *et al.,* 1998).

**Floating behavior:** Ten milligrams of the floating microspheres were placed in 0.1 N HCl (100 mL). The mixture was stirred at 100 rpm in a magnetic stirre (Whitehead *et al.,* 1998). 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 (Srivastava *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 (Kawashima *et al.,* 1992).

***In-vitro* release studies**

The *in vitro* drug release rate from Floating microspheres was carried out using the USP type II (Electro Lab.) dissolution paddle assembly (Muthuswamy *et al.,* 2005). A weighed amount of floating microspheres 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 296nm to determine the concentration of drug present in the dissolution medium.

**RESULTS AND DISCUSSION**

The percentage yield of the formulations ranged from 63.32% to 93.32%. Formulation F3 exhibited the lowest yield (63.32±0.31%), while F4 showed the highest yield (74.65±0.26%). The variations in yield could be attributed to differences in the formulation composition and process parameters. Despite the variations, the yields for all formulations were within acceptable limits, indicating the efficiency of the preparation method.

The drug entrapment efficiency of the formulations ranged from 62.25% to 73.58%. Formulation F4 demonstrated the highest drug entrapment efficiency (73.58±0.14%), while F3 exhibited the lowest (62.25±0.21%). These variations in entrapment efficiency could be attributed to differences in the composition and interactions between the drug, polymers, and other excipients used in the formulations.

The floating lag time and percentage buoyancy of the microspheres varied among formulations. For instance, F4 had the shortest floating lag time (51.15±0.17 sec) and the highest percentage buoyancy (72.23±0.14%), while F1 exhibited the longest floating lag time (78.85±0.15 sec) and moderate buoyancy (68.89±0.22%). These differences highlight the influence of formulation parameters on the floating behavior of microspheres.

The results of measurement of mean particle size of optimized formulation F4 of floating microsphere was found to be 210.25 nm. Results of zeta potential of optimized formulation F4 of floating microsphere was found -38.58 mV**.**

The release profiles of formulations F1-F6 exhibited sustained drug release over the study period. Generally, as the formulation progressed from F1 to F6, the rate of drug release decreased. For instance, at the 12-hour mark, F1 released 99.85±0.14% of the drug, while F6 released 89.98±0.15%. These differences in release kinetics could be attributed to variations in polymer composition, particle size, and drug-polymer interactions.

Formulation F4, identified as the optimized formulation, contained 75 mg of lansoprazole, 150 mg of HPMC, 25 mg of xanthan gum, and 10 mg of guar gum. This formulation composition was selected based on its superior drug entrapment efficiency and sustained drug release characteristics observed during the evaluation process.

The release kinetics of the optimized formulation F4 were evaluated using various mathematical models, including zero order, first order, Higuchi, and Korsmeyer-Peppas models. The regression coefficient ($r^2$) values indicated that the drug release from F4 followed the Korsmeyer-Peppas model most closely ($r^2 = 0.996$), suggesting a non-Fickian diffusion mechanism.The comparative study of regression coefficients for formulation F4 revealed that the Korsmeyer-Peppas model provided the best fit to the release data ($r^2 = 0.996$), followed by the Higuchi model ($r^2 = 0.973$). This indicates that the drug release from F4 was primarily governed by diffusion and erosion mechanisms, characteristic of polymeric matrix systems.

**Table 1: Formulations of the floating microspheres using natural polymer**

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

**Table 2: Percentage yield for different formulation**

| S. No. | Formulation | Percentage Yield |
|---|---|---|
| 1. | F1 | 68.52±0.35 |
| 2. | F2 | 68.85±0.25 |
| 3. | F3 | 63.32±0.31 |
| 4. | F4 | 74.65±0.26 |
| 5. | F5 | 69.98±0.35 |
| 6. | F6 | 67.74±0.18 |

**Table 3: Drug entrapment for different formulations**

| S. No. | Formulation | Drug entrapment (% w/w) of prepared microsphere |
|---|---|---|
| 1. | F1 | 66.65±0.25 |
| 2. | F2 | 65.45±0.36 |
| 3. | F3 | 62.25±0.21 |
| 4. | F4 | 73.58±0.14 |
| 5. | F5 | 68.95±0.25 |
| 6. | F6 | 66.78±0.32 |

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

| Formulation | Floating Lag Time (Sec.) | Percentage Buoyancy |
|---|---|---|
| F1 | 78.85±0.15 | 68.89±0.22 |
| F2 | 69.98±0.23 | 70.23±0.32 |
| F3 | 65.65±0.32 | 68.89±0.25 |
| F4 | 51.15±0.17 | 72.23±0.14 |
| F5 | 68.89±0.22 | 62.32±0.15 |
| F6 | 70.23±0.14 | 65.74±0.32 |

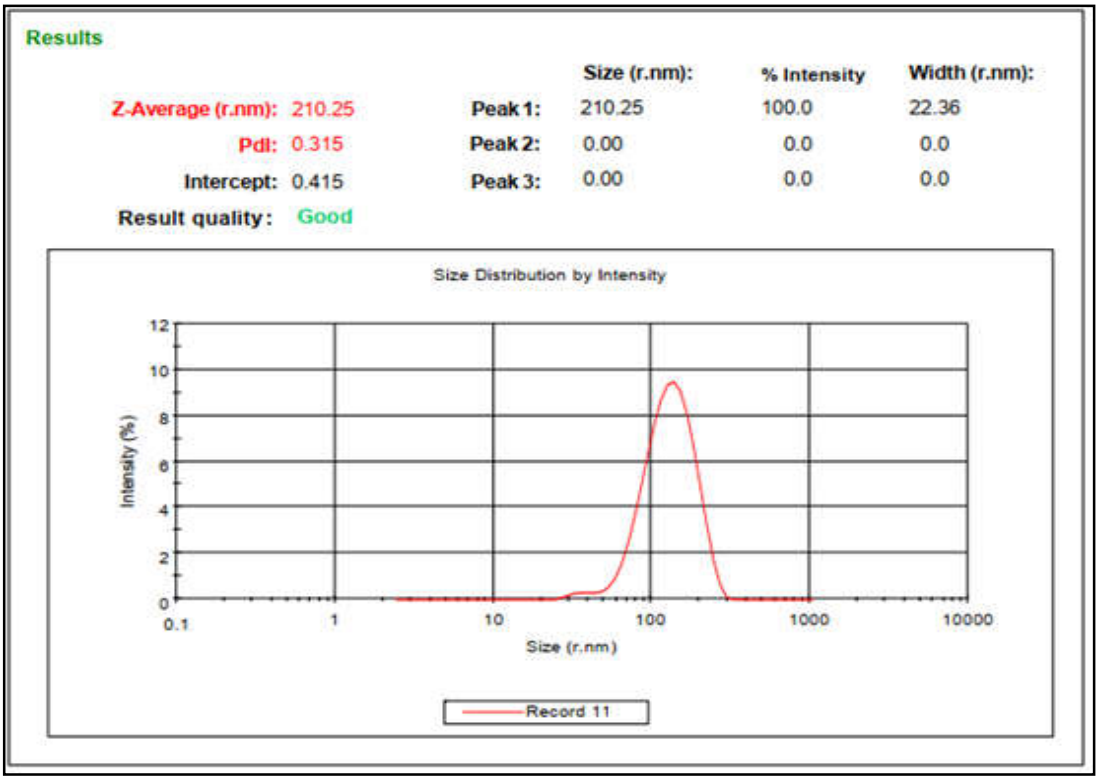


**Figure 1: Particle size data of optimized microsphere formulation F4**

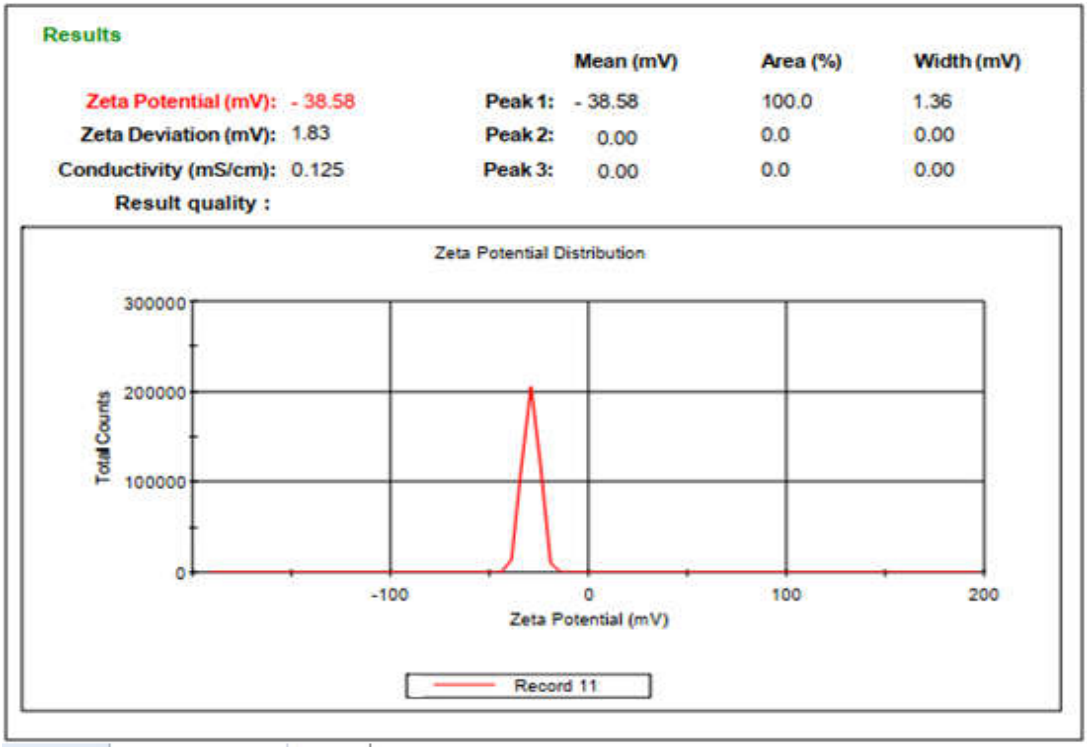


**Figure 2: Zeta potential data of floating microsphere F4**

**Table 5: Release Study data of formulation F1-F6**

| Time (Hrs) | Percentage drug release | | | | | |
|---|---|---|---|---|---|---|
| | F1 | F2 | F3 | F4 | F5 | F6 |
| 0.5 | 38.85±0.15 | 35.65±0.22 | 30.25±0.33 | 25.65±0.32 | 20.23±0.39 | 18.85±0.15 |
| 1 | 55.65±0.22 | 50.12±0.45 | 45.52±0.25 | 36.65±0.14 | 30.14±0.25 | 26.65±0.32 |
| 2 | 68.89±0.32 | 63.32±0.15 | 60.23±0.14 | 45.65±0.25 | 36.65±0.15 | 30.36±0.14 |
| 4 | 73.32±0.14 | 70.23±0.32 | 68.85±0.56 | 66.36±0.36 | 45.58±0.25 | 41.12±0.54 |
| 6 | 98.85±0.15 | 89.95±0.28 | 73.36±0.47 | 74.65±0.45 | 56.65±0.25 | 52.23±0.65 |
| 8 | 99.12±0.65 | 96.96±0.65 | 92.23±0.58 | 85.56±0.74 | 69.98±0.32 | 58.89±0.36 |
| 10 | 99.36±0.32 | 99.45±0.47 | 99.12±0.65 | 91.15±0.32 | 88.85±0.58 | 71.12±0.28 |
| 12 | 99.85±0.14 | 99.85±0.21 | 99.65±0.36 | 98.85±0.36 | 93.32±0.44 | 89.98±0.15 |

**Table 6: Formulations detail of Optimized formulation F4**

| S. No. | Formulation Code | Lansoprazole (mg) | HPMC (mg) | Xanthan gum (mg) | Guar gum (mg) |
|---|---|---|---|---|---|
| 1. | F4 | 75 | 150 | 25 | 10 |

**Table 7: 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 | 25.65 | 1.409 | 74.350 | 1.409 |
| 1 | 1 | 0 | 36.65 | 1.564 | 63.350 | 1.564 |
| 2 | 1.414 | 0.301 | 45.65 | 1.659 | 54.350 | 1.659 |
| 4 | 2 | 0.602 | 66.36 | 1.822 | 33.640 | 1.822 |
| 6 | 2.449 | 0.778 | 74.65 | 1.873 | 25.350 | 1.873 |
| 8 | 2.828 | 0.903 | 85.56 | 1.932 | 14.440 | 1.932 |
| 10 | 3.162 | 1 | 91.15 | 1.960 | 8.850 | 1.960 |
| 12 | 3.464 | 1.079 | 98.85 | 1.995 | 1.150 | 1.995 |

**Table 8: Comparative study of regression coefficient (F4)**

| Release Kinetics | Zero order | First order | Higuchi | Korsmeyer peppas |
|---|---|---|---|---|
| $r^2$ | 0.942 | 0.845 | 0.973 | 0.996 |

## CONCLUSION

In conclusion, the formulation and evaluation of floating microspheres using natural polymers for the treatment of anti-ulcer conditions have shown promising results. Among the formulations tested, F4 emerged as the optimized formulation, exhibiting superior drug entrapment efficiency and sustained drug release characteristics. The sustained drug release profiles observed in formulations F1-F6 suggest the potential for prolonged therapeutic efficacy and improved patient compliance. The buoyancy and floating lag times of the microspheres contribute to prolonged gastric retention, facilitating enhanced drug absorption at the target site. Evaluation of release kinetics indicated that the drug release from the optimized formulation F4 followed the Korsmeyer-Peppas model, suggesting a non-Fickian diffusion mechanism. Comparative analysis of regression coefficients reaffirmed the suitability of the Korsmeyer-Peppas model for describing the drug release behavior from F4, emphasizing the importance of understanding underlying release mechanisms for optimized drug delivery. Overall, the developed floating microspheres hold promise for anti-ulcer treatment, with potential for improved therapeutic outcomes. Further studies, including in vivo evaluations and clinical trials, are warranted to validate their efficacy and safety for clinical use.

## DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

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