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Original Research Article

FORMULATION AND CHARACTERIZATION SUSTAINED RELEASE FLOATING MICROSPHERES OF PROPAFENONE

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ABSTRACT

The present study was aimed at the formulation and evaluation of sustained release floating microspheres of Propafenone hydrochloride to improve its gastric residence time and oral bioavailability. Microspheres were prepared using different polymers such as HPMC, ethyl cellulose, and guar gum by solvent evaporation technique. The prepared microspheres were characterized for percentage yield, drug entrapment efficiency, buoyancy, floating lag time, particle size, zeta potential, and surface morphology. Among the formulations, batch F5 exhibited the highest percentage yield (82.25 ± 0.65%), drug entrapment efficiency (79.15 ± 0.44%), and excellent buoyancy (80.36 ± 0.33%) with a short floating lag time (53 ± 9 s). SEM analysis confirmed spherical shape with smooth surface, while particle size and zeta potential values indicated good stability. The *in-vitro* drug release profile of optimized formulation F5 demonstrated sustained release of 98.85% over 12 h compared to rapid release from marketed tablets. Kinetic modeling revealed that the drug release followed the Korsmeyer–Peppas model (R^2 = 0.9915), suggesting a non-Fickian diffusion-controlled mechanism. Thus, Propafenone hydrochloride floating microspheres represent a promising gastroretentive delivery system for sustained therapeutic effect and enhanced bioavailability.

Keywords: Propafenone hydrochloride, Floating microspheres, Sustained release, Solvent evaporation, Gastroretentive drug delivery, Drug release kinetics, Bioavailability.

INTRODUCTION

Oral drug delivery is the most prevalent and patient-friendly method due to its convenience, safety, and non-invasiveness. However, conventional dosage forms often suffer from issues such as variable gastric emptying rates, limited gastric residence time (GRT), and poor bioavailability for drugs with narrow absorption windows in the upper gastrointestinal tract (GIT) (Deshpande *et al.*, 1997; Singh and Kim, 2000)

To overcome these limitations, gastro-retentive drug delivery systems (GRDDS), particularly floating microspheres (also known as microballoons), have attracted considerable attention. Floating microspheres are low-density, multiparticulate systems designed to remain buoyant on gastric contents for prolonged periods, enabling sustained and localized drug release in the stomach and upper GIT (Singh and Kim, 2000; Babita *et al.*, 2025). Unlike single-unit floating tablets, microspheres provide uniform distribution throughout the stomach and reduce the risk of dose dumping, leading to more reliable drug absorption (Jogi *et al.*, 2016).

Propafenone Hydrochloride is a Class IC antiarrhythmic agent widely used in the management of atrial and ventricular arrhythmias due to its potent sodium channel-blocking activity and membrane-stabilizing effects (Martin and Sundaram, 2025). However, Propafenone has a short elimination half-life (2–10 hours), low oral bioavailability (approximately 10%), and a narrow absorption window, necessitating frequent dosing and limiting therapeutic efficacy (Jogi *et al.,* 2016; Martin and Sundaram, 2025) Considering these pharmacokinetic challenges, a sustained-release floating microsphere formulation of Propafenone HCl holds considerable potential. By extending gastric retention and enabling controlled release, this gastro-retentive approach can improve the drug's bioavailability, reduce dosing frequency, and maintain therapeutic plasma levels over extended periods (Jogi *et al.,* 2016; Babita *et al.,* 2025)

This study aims to develop and characterize sustained release floating microspheres of Propafenone HCl using suitable polymers and techniques to achieve prolonged gastric residence and controlled drug release. Microspheres will be formulated to exhibit sufficient buoyancy, optimized entrapment efficiency, and a sustained release profile, thereby enhancing therapeutic effectiveness and patient compliance.

MATERIALS AND METHODS

Materials

For the formulation and development of sustained release floating microspheres of Propafenone hydrochloride, various polymers and excipients were utilized. Propafenone hydrochloride was obtained as a gift sample from a pharmaceutical company. Hydroxypropyl methylcellulose (HPMC), ethyl cellulose (EC), and guar gum were procured from HiMedia Laboratories Pvt. Ltd., Mumbai, and served as the primary polymers for sustained drug release and buoyancy. Potassium dihydrogen phosphate was supplied by Loba Chemie Pvt. Ltd., Mumbai, while methanol, ethanol, and chloroform were purchased from Qualigens Fine Chemicals, Mumbai, and used as solvents during microsphere preparation. Hydrochloric acid (HCl) and sodium hydroxide, obtained from S. D. Fine Chem. Ltd., Mumbai, were used for pH adjustment in dissolution and formulation studies.

Methods

Preparation of floating microsphere of Propafenone hydrochloride

Floating microspheres containing Propafenone hydrochloride were successfully prepared by the solvent evaporation method, employing various proportions of hydroxypropyl methylcellulose (HPMC), ethyl cellulose (EC), and guar gum as polymeric carriers. The formulations (F1–F6) are outlined in Table 1, wherein the drug-to-polymer ratio was systematically varied to study its impact on microsphere characteristics.

For each formulation, Propafenone HCl (150 mg) along with respective amounts of HPMC, EC, and Guar gum were accurately weighed and dissolved in a solvent system composed of ethanol and dichloromethane in a 1:2 ratio. This resulted in a homogenous polymer-drug solution.

The resulting solution was slowly poured in a thin stream into an aqueous solution of 1% polyvinyl alcohol (PVA) under continuous stirring. The emulsification process was

maintained at a stirring speed of 500 rpm and temperature of 27 ± 2℃ for duration of 3 hours, allowing for complete evaporation of the organic solvents (Gunjal *et al.*, 2013).

During the stirring process, floating microspheres were formed and gradually separated by decantation. Non-floating microspheres settled at the bottom and were discarded. The floating microspheres were collected, washed with distilled water, and then dried in a hot air oven at 40 ± 2℃ overnight. The final product was stored in a desiccator for further evaluation.

Table 1: Formulations of floating microspheres of Propafenone hydrochloride

S. No.	F. Code	Propafenone HCl (mg)	HPMC (mg)	EC (mg)	Guar gum (mg)
1.	F1	150	50	100	-
2.	F2	150	50	150	-
3.	F3	150	50	200	-
4.	F4	150	100	50	10
5.	F5	150	150	50	20
6.	F6	150	200	50	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 Floating microspheres were subjected for drug content. 10 mg of Floating microspheres 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 floating microspheres 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; Wasnik *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 Floating microspheres was carried out using the USP type II (Electro Lab.) dissolution paddle assembly (Korsemeyer *et al.,* 1983). 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 282nm to determine the concentration of drug present in the dissolution medium.

RESULTS AND DISCUSSION

The sustained release floating microspheres of Propafenone hydrochloride were successfully prepared and evaluated for their percentage yield, drug entrapment efficiency, buoyancy, particle size, surface morphology, zeta potential, and *in-vitro* drug release characteristics.

The percentage yield of the formulations (Table 2) ranged between 73.32 ± 0.63% (F3) and 82.25 ± 0.65% (F5), indicating good reproducibility of the solvent evaporation method. The optimized formulation F5 exhibited the highest yield, which may be attributed to the appropriate polymer ratio and process parameters ensuring minimal drug and polymer loss during formulation.

The drug entrapment efficiency (Table 3) varied between 72.23 ± 0.15% (F3) and 79.15 ± 0.44% (F5). A higher entrapment in F5 suggested that the polymeric blend used in this batch was optimal for retaining drug molecules within the microsphere matrix, thereby ensuring better controlled release properties.

The floating ability (Table 4) of microspheres is a critical factor for ensuring gastric retention. The floating lag time (FLT) ranged between 53 ± 9 sec (F5) and 83 ± 6 sec (F1), while buoyancy varied from 72.25 ± 0.22% (F3) to 80.36 ± 0.33% (F5). The short FLT and high buoyancy of F5 confirmed its superior floating behavior, which can prolong gastric residence time and enhance drug absorption in the upper GIT.

The particle size analysis of optimized F5 (Figure 1) revealed a uniform distribution in the microsphere size range, which plays a

significant role in both drug release and floating capacity. The zeta potential data (Figure 2) indicated adequate stability of the microspheres due to sufficient surface charge, preventing aggregation. Furthermore, scanning electron microscopy (SEM) showed that the microspheres were spherical with smooth surfaces, further supporting uniform drug entrapment and sustained release characteristics.

The *in-vitro* release study (Table 5) demonstrated that formulations F1–F4 and F6 exhibited comparatively faster drug release, while F5 showed a controlled and sustained drug release pattern (17.75% at 0.5 h to 98.85% at 12 h). The marketed immediate release formulation released almost 98.45% of drug within 2 h, confirming the need for a sustained release dosage form. The release of F5 followed a biphasic pattern with an initial lag phase followed by sustained drug release up to 12 h, which is desirable for reducing dosing frequency and maintaining therapeutic levels for a prolonged period.

The release kinetics study (Table 6) indicated that the optimized batch F5 best fitted the Korsmeyer–Peppas model (R^2 = 0.9915), followed by the Zero-order model (R^2 = 0.9882). This suggests that the drug release mechanism was predominantly controlled diffusion, possibly coupled with polymer matrix relaxation (anomalous transport).

Formulation F5 emerged as the optimized formulation due to its high yield, better entrapment efficiency, desirable floating properties, and sustained drug release profile compared to other batches. These findings highlight the potential of floating microspheres as an effective gastroretentive drug delivery system for Propafenone hydrochloride, which can improve therapeutic efficacy and patient compliance.

Table 2: Percentage yield for different formulation

S. No.	Formulation	Percentage Yield
1.	F1	76.65±0.32
2.	F2	79.98±0.15
3.	F3	73.32±0.63
4.	F4	76.65±0.74
5.	F5	82.25±0.65
6.	F6	79.12±0.36

Table 3: Drug entrapment for different formulations

S. No.	Formulation	Drug entrapment (% w/w) of prepared microsphere
1.	F1	74.65±0.32
2.	F2	74.88±0.25
3.	F3	72.23±0.15
4.	F4	75.65±0.36
5.	F5	79.15±0.44
6.	F6	74.95±0.43

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

Formulation	Floating Lag Time (Sec.)	Percentage Buoyancy
F1	83±6	78.85±0.25
F2	76±4	76.65±0.36
F3	72±6	72.25±0.22
F4	74±8	74.65±0.41
F5	53±9	80.36±0.33
F6	69±6	74.45±0.22

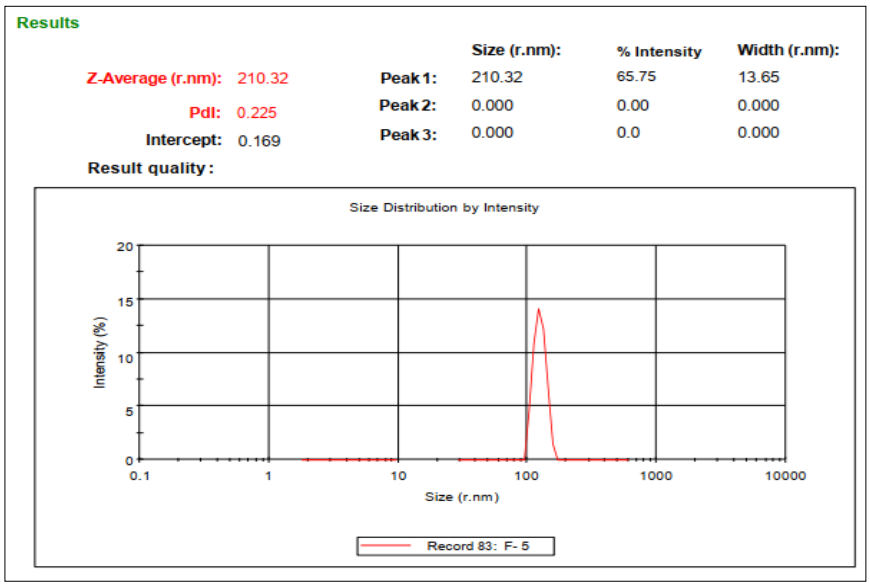

Figure 1: Particle size data of optimized microsphere formulation F5

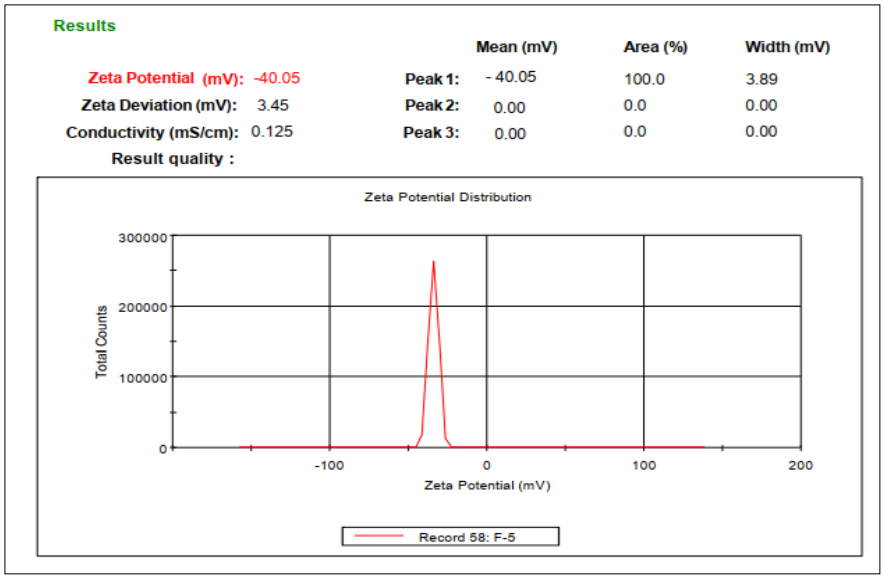

Figure 2: Zeta potential data of floating microsphere F5

Table 5: *In-vitro* release study data of formulation F1-F6

Time (Hrs)	% of Drug Release						
	F1	F2	F3	F4	F5	F6	Marketed Formulation (Propafenone hydrochloride 60mg Tablet)
0.5	42.25	45.85	43.36	22.32	17.75	13.25	69.98
1	56.98	55.69	52.25	36.65	23.36	20.36	86.65
2	63.32	69.98	65.45	46.65	36.45	31.14	98.45
4	75.45	79.98	73.32	59.98	45.85	42.25	-
6	86.65	88.85	83.32	73.32	63.32	55.65	-
8	93.32	96.65	90.36	89.98	74.65	69.98	-
10	98.85	99.45	98.87	98.85	83.32	78.85	-
12	99.12	99.85	99.05	99.02	98.85	83.32	-

Table 6: Comparative study of regression coefficient for selection of optimized Formulation F5

Release Kinetics	Zero order	First order	Higuchi	Korsmeyer peppas
R^2	0.9882	0.7681	0.9870	0.9915

CONCLUSION

The present study successfully demonstrated the formulation and evaluation of Propafenone hydrochloride-loaded sustained release floating microspheres using polymers such as HPMC, ethyl cellulose, and guar gum. The prepared microspheres showed good percentage yield, high drug entrapment efficiency, excellent buoyancy, and prolonged floating ability, indicating their suitability as a gastroretentive system. The optimized formulation (F5) exhibited sustained drug release for up to 12 h, with release kinetics best fitting the Korsmeyer–Peppas model, suggesting a non-Fickian diffusion mechanism. These findings confirm that floating microspheres can effectively improve the gastric residence time and provide controlled drug release, which may enhance the oral bioavailability and therapeutic efficacy of Propafenone hydrochloride. Thus, this delivery approach offers a promising alternative to conventional dosage forms for the management of cardiac arrhythmias.

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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