*Research Article*

# Fabrication and characterization of floating microspheres of Dexrabeprazole Sodium to improve bioavailability

**Krishna Kumar Kashyap*, Anjana Bharadwaj**

*RKDF College of Pharmacy, SRK University, Hoshangabad road, Misrod, Bhopal - 462026 (MP) India*

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**Abstract**

**Objective:** Aim of present study was to develop floating drug delivery system (FDDS) to prolong the residence time of the dosage form within the GI tract. **Material and methods**: Floating microspheres containing dexrabeprazole were prepared by emulsion solvent diffusion technique using various proportions of drug and polymer, such as Ethyl cellulose and Hydroxypropylmethylcellulose (HPMC). The drug to polymer ratio used to prepare the different formulations was 1:7. The prepared floating microspheres were characterized for shape and surface morphology, size, percent drug loading and *in vitro* drug release. **Results and conclusion**: Formulation F1 showed good results with respect to the various evaluation parameters among various batches (F1-F8). The particle size increased with increase in polymer concentration. The drug entrapment efficiency was increased with increase in concentration of polymers. *In-vitro* buoyancy and the in vitro drug release decreased with respect to increase in concentration of polymers. The developed system has the dual advantages of being gastro-retentive, to increase oral bioavailability and releasing drug in a controlled manner.

***Keywords*:** Floating drug delivery systems, gastric residence time, microsphere, dexrabeprazole, formulation

## Introduction

The oral route is predominant and most preferred route for drug delivery but drug absorption is unsatisfactory and highly variable in the individuals despite excellent in-vitro release pattern. The major problem is in the physiological variability such as GI transit in addition to gastric retention time (GRT), the later plays a dominating role in overall transit of the dosage forms. The GRT of ever oral controlled release system is less than 12 h. These aspects lead to developing a drug delivery system which will remain in the stomach for prolonged and predictable time (Shiv et al. 2004; Bharat et al. 2017).

For the development of oral drug delivery system, it is necessary to optimize both the release rate of drug from the system and the residence time of the system within the gastrointestinal tract. Various attempts have been made to prolong the residence time of dosage forms within the stomach.

***Address for Corresponding Author:***
Krishna Kumar Kashyap
RKDF College of Pharmacy, SRK University, Hoshangabad road, Misrod, Bhopal - 462026 (MP) India
Email: krishnakashyap500@gmail.com

The prolongation of gastric residence time (GRT) of delivery devices could be achieved by adhesion to the mucous membranes by maintaining them in buoyant fashion in gastric juice or by preventing there passage through pylorus, using high density systems, delayed gastric emptying devices (Uma et al. 2003).

Floating drug delivery system (FDDS) is designed to prolong the residence time of the dosage form within the GI tract. It is the formulation of drug and gel forming hydrocolloids meant to remain buoyant on stomach contents. This not only prolong GI residence time but also does so in an area of GI tract that would maximize drug reaching its absorption site in solution form being ready for absorption. Drug dissolution and release from the tablet floating in gastrointestinal fluids occur at the stomach under fairly controlled condition. The retentive characteristics of the dosage forms in gastric content are most significant for drugs (Shah et al., 2017).

## Materials and methods

Dexrabeprazole sodium was generously supplied as a gift samples by Bioplus Life Science, Bangalore. Ethyl

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Cellulose and H.P.M.C. K4 were the gift samples obtained from Mapromax, Life sciences Pvt. Ltd., Dehradun (India). All other chemicals and reagents were used of analytical grade.

**Preparation of floating microspheres**

Floating microsphere containing dexrabeprazole was prepared using emulsion solvent diffusion technique. The drug to polymer ratio used to prepare the different formulations was 1:7. The polymer content was a mixture of Ethyl cellulose Hydroxypropylmethylcellulose (HPMC) as shown in Table 1. The drug polymer mixture is dissolved in a mixture of ethanol (8 ml) and dichloromethane (8 ml) was dropped in to 0.75% polyvinyl alcohol solution (200 ml). The solution was stirred with a propeller-type agitator at 40C temperatures for 1 hour at 300 rpm. The formed floating microspheres were passed through sieve no.12 and washed with water and dried at room temperature in a dessicator. The various batches of floating microsphere were prepared as shown in table 1 (Kawashima et al. 1992).

**Characterization of prepared floating microspheres**

The prepared floating microspheres were characterized for shape and surface morphology, size, percent drug loading and in vitro drug release in different pH of GIT.

***Particle size determination***

The particle size of formulation was determined by optical microscopy using a calibrated ocular micrometer (Jain et al. 2005).

***Floating behavior of floating microsphere***

100 mg of the floating microsphere were placed in 0.1 N HCI. The mixture was stirred with paddle at 100 rpm. The layer of buoyant microspheres was pipetted and separated by filtration at 1, 2, 4 and 6 hours. The collected microspheres were dried in a desiccator over night. The percentage of microspheres was calculated by the following equation:

$$\%\ \text{floating microsphere} = \frac{\text{Weight of floating microsphere}}{\text{Initial weight of floating microsphere}} \times 100$$

***Drug entrapment***

The various formulations of the floating microspheres were subjected for drug content. 50 mg of floating microspheres from all batches were accurately weighed and crushed. The powdered of microspheres were dissolved with 10ml ethanol in 100ml volumetric flask and makeup the volume with 0.1 N HCl. This resulting solution is than filtered through whatmann filter paper No. 44. After filtration, from this solution 10 ml was taken out and diluted up to 100 ml with 0.1 N HCl. The absorbance was measured at 260.0 nm against blank. The percentage drug entrapment was calculated as follows:

$$\%\ \text{Drug entrapment} = \frac{\text{Calculated drug concentration}}{\text{Theoretical drug concentration}} \times 100$$

***Percentage yield***

The prepared microspheres with a size range of 609-874 µm 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.

***Shape and surface morphology***

In order to examine the surface morphology, the formulations were viewed under scanning electron microscopy. The samples for SEM were prepared by lightly sprinkling the floating microspheres powder on a double adhesive tape, which stuck to an aluminum stub. The stubs were then coated with gold to a thickness of about 300Å using a sputter water. The samples were then randomly scanned for studying surface morphology but show the images of coating to prove internal surface (Jagdale et al. 2009; Garg et al. 2019; Gattani et al. 2009).

***In-vitro release studies***

The drug release rate from floating microspheres was

**Table 1.** Formulation of the floating microspheres prepared

| Sr. No | Formulation Code | Dexrabeprazole (gm) | EC (gm) | HPMC (gm) |
|---|---|---|---|---|
| 1 | **$F_1$** | 0.1 | 0.8 | 0.1 |
| 2 | $F_2$ | 0.1 | 0.7 | 0.2 |
| 3 | $F_3$ | 0.1 | 0.6 | 0.3 |
| 4 | $F_4$ | 0.1 | 0.5 | 0.4 |
| 5 | $F_5$ | 0.1 | 0.4 | 0.5 |
| 6 | $F_6$ | 0.1 | 0.3 | 0.6 |
| 7 | $F_7$ | 0.1 | 0.2 | 0.7 |
| 8 | $F_8$ | 0.1 | 0.1 | 0.8 |

carried out using the USP type II (Electro Lab.) dissolution paddle assembly. 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 100 rpm. 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 were treated with methyl orange and analyzed spectrophotometrically at 260 nm to determine the concentration of drug present in the dissolution medium (Garg et al. 2019; Kim et al. 2002). Percentage cumulative drug release was calculated.

**Results and discussion**

Floating microsphere containing dexrabeprazole was prepared by emulsion solvent diffusion technique using various proportions of drug and polymer, such as HPMC (batch F1-F7) and EC. The drug to polymer ratio used to prepare the different formulations was 1:7. The polymer content was a mixture of Ethyl cellulose and Hydroxypropylmethyl cellulose (HPMC).

***Particle size analysis***

Particle size was determined by optical microscopy method. It plays important role in floating ability and release of drug from microsphere. If size of microspheres is less than 500 m release rate of drug will be high and floating ability will reduce, white microspheres ranging between 200m - 500m, the floating ability will be more and release rate will be in sustained manner. The mean particle size of dexrabeprazole sodiummicrosphere was in range 210 - 264 m (Table 2).

***Floating behavior of microsphere***

Dexrabeprazole sodium Microsphere was dispersed in 0.1 HCl as simulate gastric fluid. Floating ability of different formulation was found to be differed according to EC and HPMC ratio. $F_1$-$F_4$ formulations showed best floating ability (91.47-72.97%) in 6 hours. $F_5$-$F_7$ formulation showed less floating ability (66.12-45.09%) as showed in Table 3. The floating ability of microsphere is decreased by increasing the HPMC ratio.

***Drug Entrapment***

The drug entrapment efficacies of different formulations were in range of 48.47 - 74.19 % w/w as shown in Table No-7.8. Drug entrapment efficacy slightly decrease with increase HPMC content and decreased EC ratio in Microspheres. This is due to the permeation characteristics of HPMC that could facilitate the diffusion of part of entrapped drug to surrounding medium during preparation of Dexrabeprazole sodium microspheres.

***Percentage Yield***

Percentage yield of different formulation was determined by weighing the Microspheres after drying. The percentage yield of different formulation was in range of 56.84 - 82.87% as shown in table 4.

***Scanning Electronic Microscopy***

Shape and surface characteristic of Dexrabeprazole sodium microspheres examine by Scanning Electronic Microscopy analysis (Figure 1). Surface morphology of formulation examines at different magnification, which illustrate the smooth surface of floating Microspheres.

**Table 2.** Mean particle size of different formulations

| S. No | Formulation code | Mean particle size (μm) |
|---|---|---|
| 1. | $F_1$ | 212±12 |
| 2. | $F_2$ | 225±21 |
| 3. | $F_3$ | 264±23 |
| 4. | $F_4$ | 236±25 |
| 5. | $F_5$ | 242± 24 |
| 6. | $F_6$ | 244±40 |
| 7. | $F_7$ | 210±23 |

**Table 3.** Percentage buoyancy for different formulation

| Formulation | 1 hour | 2 hours | 4 hours | 6 hours |
|---|---|---|---|---|
| $F_1$ | 98.41 | 97.08 | 93.23 | 91.47 |
| $F_2$ | 98.11 | 95.58 | 92.17 | 87.34 |
| $F_3$ | 98.54 | 95.64 | 85.34 | 78.45 |
| $F_4$ | 99.54 | 92.49 | 80.57 | 72.97 |
| $F_5$ | 98.72 | 91.95 | 73.49 | 66.12 |
| $F_6$ | 98.45 | 86.62 | 65.14 | 57.76 |
| $F_7$ | 88.34 | 75.41 | 56.04 | 45.09 |

**Table 4.** Drug entrapment for different formulation

| Formulation | Drug entrapment (% w/w) | Percent Yield (%) |
|---|---|---|
| $F_1$ | 76.19 | 82.87 |
| $F_2$ | 70.59 | 78.53 |
| $F_3$ | 66.23 | 76.47 |
| $F_4$ | 64.76 | 71.56 |
| $F_5$ | 61.01 | 69.31 |
| $F_6$ | 57.38 | 66.03 |
| $F_7$ | 48.47 | 56.84 |

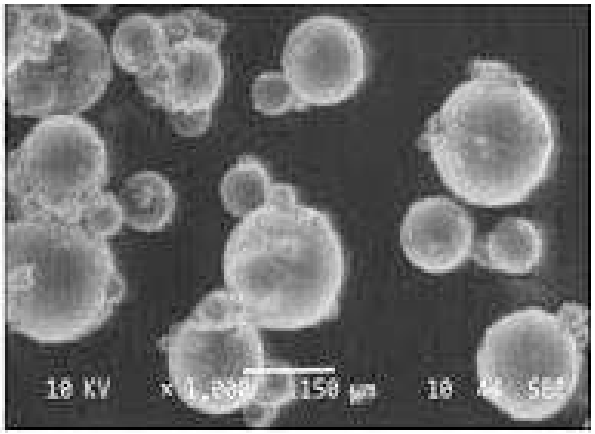


**Figure 1.** Scanning Electronic Microscopy Image of Optimized Formulation F-1

**Table 5.** Release study of Formulation F1- F7

| Time | F1 | F2 | F3 | F4 | F5 | F6 | F7 |
|---|---|---|---|---|---|---|---|
| 0.5 | 16.429 | 15.000 | 13.571 | 14.286 | 17.857 | 16.429 | 14.286 |
| 1 | 25.714 | 17.857 | 17.143 | 17.857 | 27.143 | 25.000 | 22.143 |
| 1.5 | 28.571 | 25.714 | 22.857 | 25.714 | 32.143 | 29.286 | 32.143 |
| 2 | 53.571 | 30.000 | 28.571 | 30.000 | 40.000 | 40.000 | 35.714 |
| 3 | 65.000 | 55.714 | 41.429 | 36.429 | 55.714 | 49.286 | 53.571 |
| 4 | 72.143 | 70.000 | 46.429 | 46.429 | 62.857 | 70.000 | 48.571 |
| 6 | 82.143 | 75.000 | 70.000 | 63.571 | 66.429 | 82.143 | 55.714 |
| 8 | 82.857 | 75.714 | 74.286 | 75.000 | 80.000 | 84.286 | 80.143 |

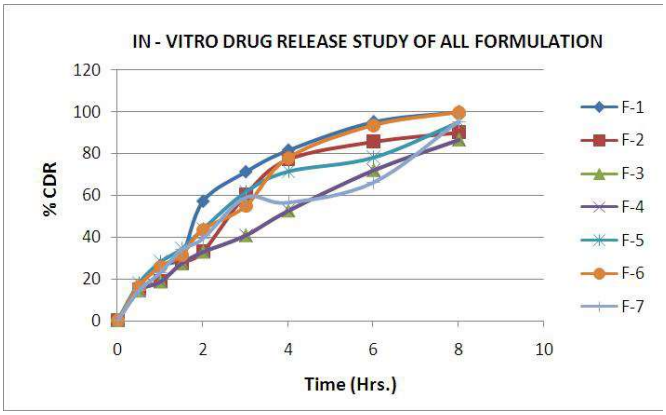


**Figure 2.** Graph of release study of formulation F1-F7

## Conclusion

The result obtained from all the experiments perform as a part of project work suggested that it is possible to prepare an intragastric floating and sustained release floating microspheres preparation using ethyl cellulose, HPMC and emulsion solvent diffusion technique. Floating microspheres drug delivery system provides the possibility of enhancing the bioavailability and control the release of formulation exhibiting absorption window by prolonging the gastric emptying time of the dosage form ensuring availability of drug at the absorption site for the desired period of time. As the floating microspheres showed a good buoyancy and drug release properties so that it has a great potential for its use both in powder form for dry suspension and granular form for table ting.

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## Conflict of interests

No conflict

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