ORIGINAL ARTICLE

Formulation Development and Characterization of Baclofen Floating Drug Delivery System

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Abstract

Background: Gastro retentive systems are retained in the stomach for a prolonged period. The objective of the present study was to formulate gastro floating tablet of Baclofen respectively. **Methods:** The physicochemical parameters such as hardness, weight variation, variability, *in-vitro* dissolution studies, and floating lag time (FLT) were performed to optimize the formulations. **Results:** Post compression parameters were in pharmacopieal limits. The FLT of optimized formulation was found <5 min and floated on the test media (0.1N HCL) for up to 24 h. Among Nine formulations, F4 formulation provides 99.62% drug was released at 24 h. **Conclusions:** The formulated floating tablets showed good buoyancy properties, thus could be a promising formulation for improving bioavailability and decreasing drug toxicity.

Key words: Buoyancy, floating lag time, gastric emptying time, gastro floating, skeletal relaxant

INTRODUCTION

Floating Drug Delivery System are staying in the stomach for a prolonged period of time due to irregular gastric residence time of dosage forms leading to variations of plasma drug concentration.[1,2] For this reason, gastro floating dosage forms are preferably used to reduce the variations of gastric residence time. Simultaneously, the floating behavior of gastro floating dosage forms help to prolong the gastric residence time. Among the gastroretentive dosage forms, the gastro-floating delivery method is one of the most promising dosage forms since it has a lower impact on gastrointestinal tract (GIT) motility.[3]

Baclofen is not a direct painkiller. It is a muscle relaxant commonly used where certain muscles are in constant contraction. It is used in the treatment of long-term pain conditions. It works by relaxing the muscles and relieving the spasm. Therefore, floating drug delivery system will prolong the release of Baclofen at stomach site which could be helpful for improving the drug bioavailability.[4] As a result, the goal of this study was to develop floating tablets and improve them based on floating lag time (FLT), buoyancy qualities and *in-vitro* drug release.

MATERIALS AND METHODS

Materials

Baclofen was purchased from Yarrow Chemicals, Mumbai, India. Cetyl Alcohol, Sodium Bicarbonate, Carbopol, Magnesium Stearate, and Talc were procured from S.D. Fine Chemicals, Mumbai. All other ingredients used in the study were analytical grade.

Calibration curve of baclofen

An equivalent weight of 100 mg of Baclofen was dissolved in small quantity of ethanol in 100 ml standard flask and make up the volume upto 100 ml with pH 1.2 medium. A series of Baclofen concentrations from 1 to 25 µg/ml of Baclofen were prepared, absorbance was measured at 230 nm respectively, and calibration curve was shown in Figure 1 respectively.

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Methods

Preparation of Baclofen floating tablet

The granules of the Baclofen were prepared using wet granulation method. Tragacanth mucilage was prepared and to this added hydroxypropyl methylcellulose (HPMC) K4M, cetyl alcohol and sodium bicarbonate. All the ingredients were mixed thoroughly to form wet dump mass and pass through sieve No [#16]. Wet granules were obtained and placed the wet granules in hot air oven at 50°C for 20–30 min.[5] After completion of drying and dry granules were passed through sieve No [#22]. Uniformly, sized Baclofen granules were subjected for physic-chemical estimation and then added sufficient quantity of magnesium stearate and talc for good tablet production. Finally, physico-chemical evaluated granules were subjected for tablet compression using tablet machine.[6] The formulation table is depicted in Table 1.

Pre compression parameters

The following pre compression parameters[7] are as follows:

- Angle of repose
- Bulk density
- Tapped density
- Carr's index
- Hausner's ratio.

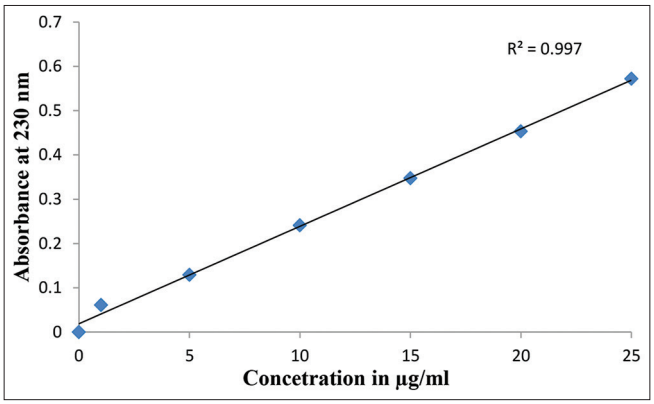

Figure 1: Calibration curve of baclofen in 0.1 HCl

Post compression parameters

Post compression parameters such as weight variation, hardness, friability, thickness, *in-vitro* buoyancy, and dissolution studies were evaluated using standard procedure.[8]

In-vitro buoyancy study

The tablets were placed in the USP type II Apparatus filled with 900 mL of 0.1N HCl at 37.5°C and spun at 50 rpm for the *in-vitro* floating study. Each tablet formulation's FLT and floating time (FT) were measured.[9,10]

In vitro dissolution study

The *in-vitro* dissolution study was performed using the USP type II apparatus filled with 900 ml of pH 1.2 HCl at 50 RPM and 37 ± 0.5°C temperature. 5 mL of sample was withdrawn from the dissolution apparatus and replaced with 5 mL of fresh dissolution medium. After filtration through a Whatman filter paper, the samples were quantified using a ultraviolet (UV) spectrophotometer at 230 nm for Baclofen.[11,12]

In vitro release kinetics

The release kinetics was examined according to different models such as zero-order kinetics, first-order kinetics, Higuchi kinetics, and Korsmeyer-Peppas models. The correlation coefficient was utilized to establish the best fitting model for the drug release.[13,14]

RESULTS AND DISCUSSION

The gastro-floating Baclofen tablets were successfully prepared using wet granulation technique. The tablets with a density lower than the gastric fluids were produced by integrating a CO_2-generating agent (sodium bicarbonate) and lower density substance to lengthen the drug's residence period in the stomach. Regression coefficient R^2 value 0.997 was observed in Figure 1.

Table 1: Formulation of baclofen floating tablets

Ingredients	Formulation code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Baclofen	30	30	30	30	30	30	30	30	30
HPMC K4M	75	100	125	75	100	125	75	100	125
Carbopol	25	25	25	50	50	50	75	75	75
Cetyl alcohol	50	50	50	75	75	75	100	100	100
Sodium bi carbonate	30	30	30	30	30	30	30	30	30
Magnesium Stearate	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Talc	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Total Weight	215	240	265	265	290	315	315	340	365

*Quantities per each tablet expressed in mg, HPMC: Hydroxypropylmethyl cellulose

Table 2: Post compression parameters

FC	Weight variation (mg)	Hardness (kg/cm²)	Thickness (mm)	Friability (%)	Drug content (%)
F1	211±1.064	4.7±0.081	2.82±0.14	0.16±0.02	88.21±1.05
F2	232±1.042	4.6±0.432	2.91±0.17	0.32±0.09	89.64±1.52
F3	261±1.042	4.2±0.651	3.12±0.43	0.36±0.32	87.74±1.74
F4	259±1.103	4.9±0.815	3.04±0.34	0.25±0.65	89.28±1.62
F5	283±1.072	4.3±0.381	2.95±0.35	0.29±0.21	88.86±1.43
F6	312±1.074	5.2±0.861	3.54±0.56	0.33±0.18	87.44±1.38
F7	311±1.064	4.8±0.227	3.21±0.65	0.19±0.15	86.31±1.43
F8	332±1.042	5.4±0.328	3.65±0.12	0.37±0.42	85.41±1.69
F9	361±1.042	5.1±0.749	4.12±0.64	0.16±0.51	89.57±1.32

*All the resultant data's were expressed as Mean±S.D (*n*=3)

Table 3: FLT of formulations (F1-F9)

RPM	Formulation Codes								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
50	33	14	12	12	47	15	23	10	18
100	27	09	07	06	27	10	11	06	09

FLT: Floating lag time

Floating behavior and *in-vitro* drug release were taken into account when formulating the tablets. Table 1 shows the specifics of the formulas. All post compression parameters of prepared floating tablets was reported in Table 2. The % weight variation of each tablet formulation was found within the pharmacopeia limits. Hardness of all the tablets was determined using a Monsanto hardness tester. The hardness was the range from 4.2 kg/cm² to 5.4 kg/cm². The result indicates that increasing the concentration of HPMC K4M and hardness also increased, which may be due to increase the cohesiveness between the molecules.

The % drug content of all tablets was found in between 85.41% and 89.64% of Baclofen, which was within acceptable limits and showed in Table 3. *In-vitro* floating behavior, a short FLT and buoyancy let the tablet stay in the upper GIT longer, allowing for better drug absorption. As a result, research into the *in-vitro* floating behavior of a floating dosage form was observed in Figure 2. All of the Baclofen tablet formulations with varied composition displayed buoyancy and floated for up to 12 h on the surface of 0.1 NHCl medium. By varying the amount of sodium bicarbonate in tablet formulations, it is possible to reduce the density of the tablets and release CO_2 as a result of the reaction between sodium bicarbonate and gastric acid to achieve tablet flotation. Because of this, various ratios of Sodium carbonate and cetyl alcohol in the sustained release mixture assisted to FLT was reduced from 33 to 6 min [Figure 3]. Due to the presence of hydrophilic polymer, Baclofen and sodium bicarbonate in the formulations, the inconsistency in the polymer viscosity may have enhanced medium uptake. Cetyl alcohol is a lipophilic excipient and

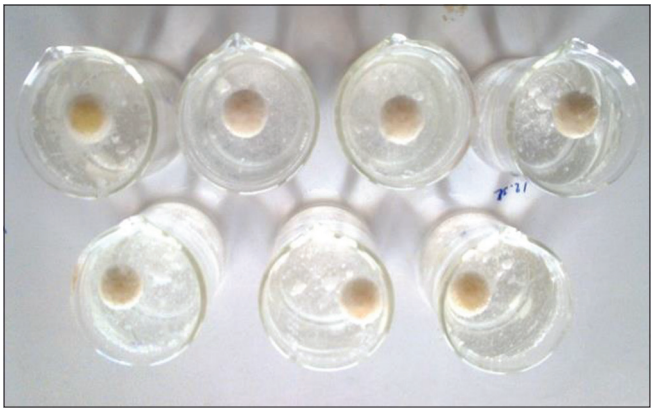

Figure 2: *In-vitro* buoyancy studies

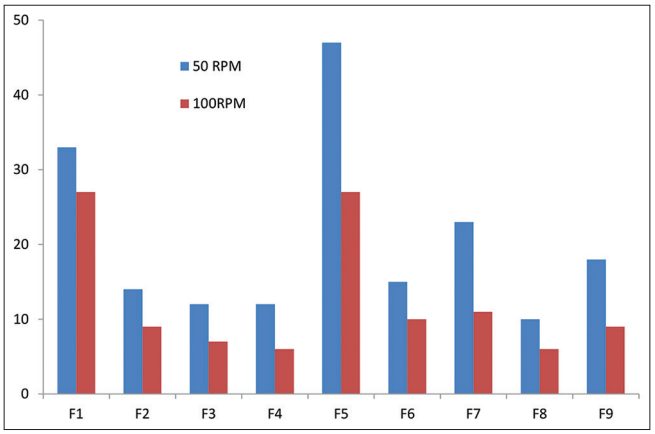

Figure 3: Floating lag time of tablets

added to the formulations to improve the floating qualities. As a result, optimizing the amount of cetyl alcohol in the formulation may result in improved floating behavior. The hardness of the tablet had a significant impact on the floating behavior, hence its impact on FLT was assessed. The FLTs for the tablets with a 4.2 kg/cm² to 5.4 kg/cm² were 6–33 min, indicating that the FLT increased as hardness increased. The density of the tablets was increased by increasing the hardness of the tablets. A hydrophilic matrix made up of polymers such as carbopol and HPMC K4M can produce

a gel network around its matrix, allowing the drug to be released in a diffuse or matrix erosion manner and used as a sustained-release substance. The viscosity of carbopol, on the other hand, had only a little effect on Baclofen release. The carbopol matrix, in which the percentage of polymer in the formulation was increased from 15% to 34%, had no effect on Baclofen release. However, the introduction of HPMC K4M in a sustained the release system, the release of Baclofen from tablet was significantly changed.

With the increased thickness of the gel layer, increasing the amount of carbopol in the weight of total compositions reduced drug release as expected. Carbopol has significant impact on the release and floating properties of the system. Because of the resistance of medium imbibition generated by the lipophilic substance, the addition of cetyl alcohol further slowed Baclofen release. The rotational speed of 50 RPM had less impact on Baclofen release in the 0.1N HCl medium. Thus, the motility of the GIT had no effect on Baclofen release from tablet. In a dissolution study, the gastro-floating matrix tablets of optimized formulations are illustrated in Figure 2. The tablets were still floating on the medium's surface after 24 h, retaining their shape and integration. Baclofen release profiles were sustained for 24 h in a 0.1 N HCl medium. The effect of medium, pH and rotation speed on the release of Baclofen was shown in Figure 4. Since the release mechanism is relied on diffusion, the kinetic profile of all prepared formulations was shown in Figures 5 and 6.

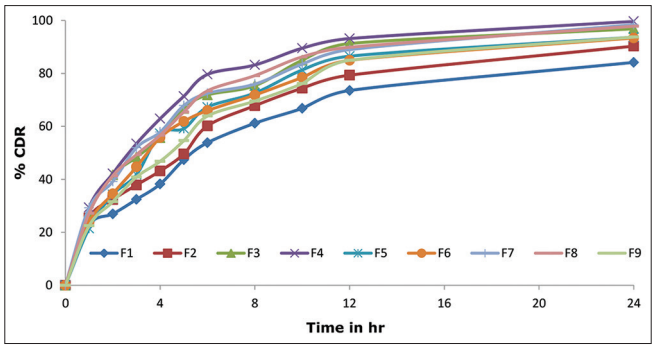

Figure 4: *In-vitro* release profiles of baclofen floating tablets (F1-F9)

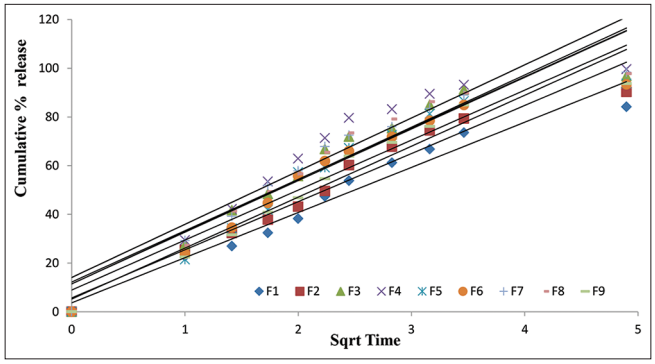

Figure 5: Higuchi plot of baclofen floating tablets (F1-F9)

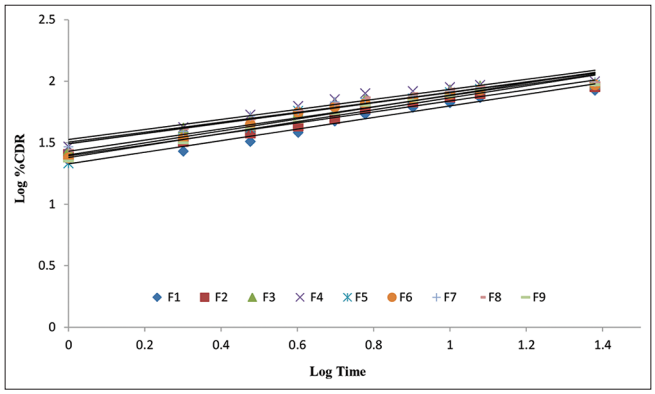

Figure 6: Peppas Plot of baclofen floating tablets (F1-F9)

CONCLUSIONS

The wet granulation process was employed to develop Baclofen gastro-floating tablets. Baclofen release was sustained through a diffusion-dependent manner. Totally nine baclofen floating tablets were fabricated with suitable excipients. The tablets floated on the test medium for up to 24 h with in a 6 min floating lag period. In conclusion, the use of a gastro-floating tablet resulted in sustained Baclofen release with enhanced absorption, which would be an effective therapy for skeletal relaxant stimulant. Formulation F4 showed maximum drug release profile than other formulations respectively.

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