The Pharma Innovation Journal 2022; 11(1): 1009-1012

www.ThePharmaJournal.com

The Pharma Innovation

**ISSN (E): 2277- 7695**
**ISSN (P): 2349-8242**
**NAAS Rating: 5.23**
TPI 2022; 11(1): 1009-1012

www.thepharmajournal.com
Received: 12-10-2021
Accepted: 21-12-2021

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# Gastroretentive effervescent floating tablets of diclofenac sodium and effect of different polymers on drug release

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**Abstract**
Floating dosage forms are formulated with a lower density than gastric contents in order to achieve a longer residence time in the stomach, which results in the system floating on the gastric contents of the stomach for a longer period of time without affecting the gastric emptying rate. The objective of this study was to manufacture and evaluate an *in-vitro* floating tablets using diclofenac sodium. The solid dosage forms, tablets were made using a direct compression method using effervescent technology & matrix forming Polymers. sodium bicarbonate, citric acid, HPMC and microcrystalline cellulose (MCC) used as excipients, Carbapol was used to decrease drug release, and sodium bicarbonate and citric acid were used to achieve effervescence. Buoyancy, Floating time & dissolution rate of five formulations was made with different concentrations of HPMC, Carbapol, and MCC was determined. The optimized F4 formulation released 231.0 percent of the drug in 6 hours with a floating lag time of 56 seconds, while the unoptimized F1 formulation released 492.2 percent of the drug in 6 hours with a floating lag time of 31 seconds. it can be maintained by increasing the polymer concentration according to an *in vitro* dissolution study.

**Keywords:** Gastroretentive tablets, floating tablets, diclofenac sodium, effervescent tablets, carbopol

## Introduction
To increase the bioavailability of the active ingredient, a floating drug delivery system (FDDS) has been developed to extend gastric retention time of dosage forms [1, 2]. Due to its relatively low density compared to the density of gastric juice, this system is characterized by longer buoyancy (Floating) of the dosage form in gastric contents. The drug is administered carefully at the desired controlled rate while floating on the stomach contents, resulting in increased gastric residence time, slow prolong drug release, increased therapeutic efficacy, and reduced drug intervals, all of which improve patient compliance [3, 4]. Low-density systems that have sufficient buoyancy to swim on the stomach contents and remain in the stomach for long periods of time are known as floating systems or hydrodynamically controlled systems. The effervescent technology utilized sodium bicarbonate and organic acids such as citric and tartaric acid in formulations to create carbon dioxide gas bubbling which generate upward force and makes the system float in gastric juices [5, 6]. Gas generation systems and volatile liquid/vacuum systems are two different types of effervescent systems.
Non-Effervescent system is based on the mechanism of swelling or bioadhesion of the polymer to the lining of the digestive tract. Cellulosic hydrocolloids, polysaccharides, and highly expandable gelling or matrix-forming materials, including polycarbonate, polyacrylate, polymethacrylate, polystyrene, and bioadhesive polymers such as chitosan and carbopolare used to manufacture Single-layer floating tablets, double-layer floating tablets [7, 8]. Alginate spheres and hollow microspheres used are examples of non-foaming active ingredient delivery systems
When the dosage form is administered, it comes into contact with gastric juices, creating bubbling $CO_2$ gas. The low density polymer HPMC of varying degrees provides a low density system that allows the liquid in the tablet to penetrate and float. The device is designed to float and exhibit delayed release for better patient compliance as well as reducing drug dosing frequency and side effects [9, 10].
The aim of this study was to increase the bioavailability of drugs that have a low rate of absorption from the gastrointestinal tract. The non-steroidal anti-inflammatory drug diclofenac sodium is used to treat pain and inflammation. Because Diclofenac sodium has a short half-

life, it generally has to be administered several times a day to maintain its therapeutic benefits. Diclofenac sodium is a mildly acidic drug with a moderate pH (pKa 4.0). Its solubility in acidic pH is very low. After oral administration, the gastrointestinal tract is rapidly but not completely absorbed. The floating tablet form has a longer duration of gastric retention, which increases the bioavailability of the drug The goal is to increase the bioavailability of drugs with a low rate of absorption in the gastrointestinal Tract. Diclofenac sodium is a nonsteroidal anti-inflammatory drug that is given orally; the gastrointestinal system absorbs the drug quickly, but with no effect. The floating tablet form has a longer gastrointestinal resistance and increases the bioavailability of the drug. It can be used to compress most drugs directly. The purpose of this study was to determine the effect of synthetic polymers on drug release by examining the formulation, physicochemical properties and *in vitro* evaluation of diclofenac sodium floating tablets containing synthetic polymers.

## Materials and Methods

Diclofenac sodium was purchased from CDH New Delhi, HPMC K100LV, Carbopol 934P, Microcrystalline cellulose, PVP, Citric acid, Sodium bicarbonate, Magnesium stearate, talcum were of SD Fine Chem Limited New Delhi. All the chemicals were used as received

## Preformulation Studies

Diclofenac sodium, HPMC, MCC, PVP, citric acid and sodium bicarbonate were mixed evenly with isopropyl alcohol used as granulating agent, sieved through a 16 mesh sieve and dried for 1 h at 30 °C in a tray dryer. After the granules are completely dry, magnesium stearate was added, the granulations was mixed thoroughly using transparent plastic envelop for 2-3 minutes. Five different granulations were prepared with different percentage of excipients code as F1, F2, F3, F4 and F5. The flow properties & physical compatibility of the granulations were evaluated [11, 12].

## Method of Preparation

The Diclofenac floating tablets were prepared by dry granulation method. Diclofenac, HPMC, MCC, PVP, citric acid and sodium bicarbonate were mixed evenly with isopropyl alcohol used as granulating agent, sieved through a 16 mesh sieve and dried for 1 h at 30 °C in a tray dryer. After the granules are completely dry, add magnesium stearate, powder and stir for 2-3 minutes. The granules were compacted into tablets having an average weight of 375 mg using a rotary tablet punching machine [2]. Five different tablet formulations were prepared with different percentage of excipients code as F1, F2, F3, F4 and F5.

## Post-compression Evaluation Parameters

The compressed diclofenac floating tablets were subjected to different quality control tests includes, hardness, friability, weight fluctuation, drug content determination, Invitro buoyancy & Invitro dissolution study [8, 13, 14, 15].

## Drug Content Determination

100 mg of standard Diclofenac sodium was dissolved in 100ml of methanol, 1ml of the solution was transferred in 100ml volumetric flask and made up to 100ml with methanol (10mcg/ml). The absorbance of the solution was measured at 276 nm. The experiment was repeated in triplicate, $A_{Std}$ was recorded as 0.286 [4, 6]. The drug content was calculated as follows

**Drug Content = $A_{test}$ /$A_{Std}$ X $C_{std}$**

$C_{std}$ = 100mg of std Diclofenac Sodium

10 compressed Diclofenac floating tablets were selected, triturated to fine powder in a mortor & pestle. Weighed quantity equivalent to 100mg of diclofenac sodium was taken suitably diluted with methanol and absorbance of the test sample ($A_{test}$) was measured at 276nm. Drug content was calculated.

## *In-vitro* buoyancy studies

The compressed Diclofenac floating tablets were placed in a 250 ml conical flask containing 0.1 N HCl as the medium. The floating lag Time (FLT) was calculated as the time required for the tablet to rise to one third of the surface in 0.1N HCl, and Total Floating Time (TFT) was calculated as the time required for the tablet to rise on the surface & stay floating in the medium [1, 2, 3].

## *In-vitro* dissolution study

Standard Absorbance ($A_s$): *In vitro* dissolution studies were carried out in a United States Pharmacopoeia (USP) type I apparatus (basket) at a rotational speed of 100 rpm. 150mg of diclofenac was filled in empty hard gelatin capsule & placed in the basket of a dissolution vessel with 900 ml of 0.1 N HCl as the dissolution medium and maintained at 37 ± 0.5 °C. 5 ml of the sample was removed after one hour & diluted to 100ml in a volumetric flask with 0.1N HCl (conc. 0.0083mg/ml). The absorbance was measured at 276nm. The standard absorbance9 ($A_s$) was calculated using $A^{1\%}_{1cm}$ of Diclofenac sodium. $A^{1\%}_{1cm}$ of Diclofenac sodium was reported as 286 [4, 8, 9]. $A_s$ was calculated as follows

$10/286 = 0.0083/A_s$

$A_s = 0.238$

Test Absorbance ($A_t$): The procedure was repeated with compressed Diclofenac floating tablet having 150mg of diclofenac. The Test absorbance ($A_t$) was measured. The % Drug Release was calculated using following equation

**% Drug Release = $A_t$ / $A_s$ X 100**

*In-vitro* dissolution study was performed for 12 hour & was done in Duplicate.

## Results and Discussion

Five granulations of diclofenac sodium sodium was formulated and coded as F1 to F5 (Table 1). The granulations were evaluated for flow properties and physical compatibility. The flow properties of all five formulations were found free flowing. The values for flow properties are presented in Table 2

In tablet dosage form, the drug is in close contact with one or more excipients, which can affect the stability of the drug. Therefore, knowledge of drug-excipient interactions is very useful for formulators in selecting the right excipient. Diclofenac sodium was thoroughly mixed with excipients according to the tablet formula as per table 1 and a small portion of the mixed powder was stored in cleaned and dried clear glass bottles in a stability chamber at 40 °C / 75°RH. Visual physical observations were carried out for seven days. There was no visible evidence of precipitation, discoloration found in all five formulations.

Diclofenac floating tablets produced were off- white in color, smooth and flat in shape(Figure 1). The results of quality control test carried on all five formulations were presented in Table 3. The average weight of each formulation is reported. The results are almost the same in the parameters. The tablet values varied from 373.94 ± 1.1 to 374.26 ± 0.2 mg. The resulting floating diclofenac tablet passed the weight variation test because the weight percent deviation was within the pharmacopoeia of ± 5 weight percent. The hardness of all formulations is in the range of 6.5 ± 0.8 to 6.5 ± 0.9 kg/cm2, which indicates that the hardness of all formulations is almost the same and has good mechanical strength. The friability of the resulting tablet is below 1%, which indicates that the tablets of all formulations are compact and resistant to mechanical impact and abrasion. The five formulas were tested for homogeneity of their contents. Drug content was found 98-99% in all five formulations.

Effervescent technology along with matrix forming polymers was used to make the Diclofenac floating Tablets. that all floating effervescent tablets float immediately after being placed in 0.1 N HCl solution at 37.5 °C. and remain floating for 24 hours without disintegration (Figure 2). Sodium bicarbonate and anhydrous citric acid were used. to increase the buoyancy of Diclofenac floating tablets *in vitro* without damaging the integrity of the polymer matrix, with the shortest possible float delay time (FLT) and a total float time (TFT) of more than 24 hours. In an acidic environment, the interaction between sodium bicarbonate and citric acid creates carbon dioxide. The gel created by the hydration of the polymers has been shown to be responsible for trapping and protecting the gas created in the tablet, reducing the density below unity and causing the tablet to float. Compared to the other formulations F1, F3, F4 and F5, the F2 made floating diclofenac tablets had a short buoyancy delay of 25 seconds. The reduction in the floating lag time of the F2 formulation could be attributed to an increase in polymer content which creates a firm gel that traps a greater amount of carbon dioxide to provide quick buoyancy and make the tablet swim longer

*In-vitro* drug release experiments were carried out to evaluate the release of Diclofenac sodium from all diclofenac formulations in 0.1 N HCl and the percent drug release was calculated (Table 4). Drug release profiles of all five formulations were compared. By increasing the amount of polymer HPMC K100 LV, the release of the active ingredient was reduced, but not more than with Carbapol due to its high viscosity, it showed a slow release in the following order F4 <F3 <F5 <F2 <F1. *In vitro* drug release studies showed that drug release was higher at F1; 49 ± 2.2% and at least at F4, ie 23 ± 1.0% for every 6 hours.

**Table 1:** Diclofenac sodium Floating Tablet Formulations

| | Composition(mg) | | | | |
|---|---|---|---|---|---|
| Ingredient | F1 | F2 | F3 | F4 | F5 |
| Diclofenac | 150 | 150 | 150 | 150 | 150 |
| HPMC K 100LV | 80 | 100 | ____ | ____ | 55 |
| PVP | 10.5 | 10.5 | 10.5 | 10.5 | 10.5 |
| Carbapol | ____ | ____ | 55 | 85 | 45 |
| Sodium bicarbonate | 50 | 50 | 50 | 50 | 50 |
| Magnesium stearate | 3 | 3 | 3 | 3 | 3 |
| Talc | 2.5 | 2.5 | 2.5 | 2.5 | 2.5 |
| Citric acid | 9 | 9 | 9 | 9 | 9 |
| MCC | 70 | 50 | 95 | 65 | 50 |

**Table 2:** Flow Properties of dry Granulations

| Formulation No. | Angle of repose | Tapped density | Bulk density | Carr's index | Hausner ratio |
|---|---|---|---|---|---|
| F1 | 25.43±0.10 | 068±0.2 | 0.58±0.1 | 14.7 | 1.17 |
| F2 | 25.86±0.9 | 0.65±0.4 | 0.56±0.3 | 13.8 | 1.16 |
| F3 | 26.60±0.05 | 0.70±0.1 | 0.58±0.2 | 17.1 | 1.20 |
| F4 | 26.12±0.08 | 0.69±0.7 | 0.58±0.1 | 15.9 | 1.18 |
| F5 | 25.97±0.11 | 0.66±0.3 | 0.56±0.3 | 15.1 | 1.17 |

**Table 3:** Quality Control Test for Diclofenac Floating Tablets

| Formulation No. | Weight Variations | Friability (% wt loss) | Hardness ($kg/cm^2$) | Drug Content |
|---|---|---|---|---|
| F1 | 373.94±1.1 | <1 | 6.5±0.8 | 99.5±0.8 |
| F2 | 374.2±0.75 | <1 | 6.7±0.3 | 99.3±0.6 |
| F3 | 374.1±0.3 | <1 | 7.2±0.6 | 98.3±0.5 |
| F4 | 374.28±0.5 | <1 | 7.5±0.4 | 98.6±0.6 |
| F5 | 374.26±0.2 | <1 | 6.9±0.9 | 99.1±0.3 |

**Table 4:** *In vitro* Dissolution Test

| Formulation No. | Drug release at 3h (%) | Drug release at 6h (%) |
|---|---|---|
| F1 | 25±1.0 | 49±2.2 |
| F2 | 19±1.3 | 42±2.4 |
| F3 | 14±1.2 | 30±1.9 |
| F4 | 11±1.5 | 23±1.0 |
| F5 | 17±1.1 | 38±2.5 |

**Fig 1:** Compressed Diclofenc Floating Tablets

**Fig 2:** *In-vitro* buoyancy studies on Diclofenac Floating Tablets

## Conclusion

sodium bicarbonate and citric acid was used as gas producers and hydroxypropylmethyl cellulose (HPMC k100 LV), Carbapol 934 P, microcrystalline cellulose as polymer matrix, diclofenac sodium floating tablets have been successfully prepared using combination of effervescent technology and matrix tablets. Diclofenac floating tablets have been shown to be satisfactory in terms of hardness & Friability. Tablets prepared with sodium bicarbonate with a hardness of 6.5 ± 0.8

- 7.5 (kg/cm2) showed satisfactory results in terms of floating delay time, total floating time and release profile. A total of five formulations with different concentrations of HPMC, Carbapol and MCC were developed. The best formulation F4 released 23 ± 1.0 percent of the drug in 6 hours, with a levitation delay of 56 seconds and a total flushing time of more than 24 hours. Formula F2 has good swimming properties. Formulations containing carbapol reduce the buoyancy of formulations containing HPMC.

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