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# FORMULATION AND EVALUATION OF ACECLOFENAC GASTRO RETENTIVE DRUG DELIVERY SYSTEM

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## ABSTRACT

In the recent years Gastro retentive drug delivery system is one of the most focusing area in the, novel drug delivery system, because this is an oral route, invasive. The present work focused mainly on formulation & evaluation of aceclofenac floating drug delivery system with a view to improve the bioavailability, patient compliance, reduce the side effects. The tablets were prepared using polymers like HPMC K4M, Carbopol 934 P grades. Total five formulations were prepared using sodium bicarbonate as effervescent material. The prepared tablets were evaluated for hard ness, friability, floating lag time, total floating time, *invitro* drug release studies. The data obtained in the *invitro* drug release studies were fitted in to various kinetic equations like, first order, peppas, and Higuchi equations. Formulation F5 shows good floating lag time (FLT), good *invitro* drug release, the kinetic data shows the values were best fit for korsemeyer peppas equation, the n value was found to be 0.7639, so it follows non fickian transport, i.e. both diffusion and dissolution ,process was involved in the drug release.

**Keywords:** floating lag time, total floating time, HPMCK4M, Carbopol 934P.

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## INTRODUCTION

Oral drug delivery remains the most user-friendly dosage form. It has the highest degree of patient compliance due to its non-invasive mode of delivery. Novel oral formulation needs to be taken once a day is perceived as "patient-friendly" for compliance. Many drugs for chronic disease conditions are still preferred for oral administration for ease of long-term use[1]. This is illustrated by the fact that oral drugs represent 84% sales of world top 50 drugs (source: IMS health). The pharmaceutical industry world over sees big opportunity in the use of novel drug delivery technologies as they strive to make their products easier to administer, more patient friendly, and more effective. it has become evident that controlled release (CR) formulations that, at present, grabs 50 - 60 per cent share of the novel drug delivery will continue to rule the roost in the years to come. Transdermal and transmucosal (buccal) systems are also enjoying prominent positions in drug delivery. The Gastro retentive drug delivery system is one of the non invasive routes the main principle involved here is prolonging release of the drug where it absorbed. The floating drug delivery approach is one of the currently utilized methods in the prolongation of gastric residence time(GRT).the floating dosage forms have the bulk density lower than that of gastric fluids, so that it can float in the stomach for a prolonged period of time there by improving bioavailability [2].

How ever, various factors affect the GRT like food, and fluids in the stomach, age, gender [3]. From the literature survey it was evident that the GRT can be increased under fed state. Nonetheless overcoming physiological adversities, such as shorter GRT and unpredictable gastric emptying time is possible utilizing gas generating component in the formulation to achieve the desired density. The present floating systems allows the controlled release of the drug from the system.

Aceclofenac, a phenylacetic acid derivative, is an NSAID related to diclofenac. It is used in the management of osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis [4]. Aceclofenac is having, rapid absorption, and shorter half-life, and hence necessitate for modified release (MR) [5] formulation.

The plasma-elimination half-life is approximately 3-4 hours. The objective of the present study is to prepare gastro retentive dosage forms which retain in the stomach for a prolonged time, where it completely absorbed.

## MATERIALS AND METHODS

Aceclofenac was obtained as a gift sample from micro labs, Hossur. Hpmc K4M, Carbopol 934P were purchased from Colorcon Asia, microcrystalline cellulose, was purchased from Qualigens, the rest of the ingredients and chemicals were pharmaceutical grade. The floating tablets were prepared by direct compression method using single punch machinery.

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**Compatibility Studies**

Compatibility with excipients was confirmed by carried out FTIR studies. The pure drug and its formulations along with excipients were subjected to FTIR studies. In the present study, the potassium bromide disc (pellet) method was employed.

**Preparation of Floating Tablet**

Floating matrix tablets containing Aceclofenac were prepared by direct compression technique using variable concentrations of HPMC k4m, Carbopol 934p with sodium bicarbonate[6]. All the ingredients except magnesium sterate and talc were blended in glass mortar uniformly. Mixed all the ingredients and passed through sieve no#60 and then binder, magnesium sterate, talc mixed to the above contents and again blended, then punched on 13mm flat punch. The weights of the tablets were kept constant for formulations f1 to f5.

**Evaluation of Physical Properties**

The prepared tablets were tested for weight variation friability (Roche fribilator), and hardness (Pfizer hardness tester). The content uniformity also measured and the results were compared with official limits.

**Floating Properties**

The floating lag time can be defined as the time took to emerge on the surface of the dissolution medium, and the time the tablet constantly float on the surface of the medium is known as Total floating time as evaluated in a dissolution vessel filled with 900ml of 0.1 N HCl (pH 1.2) previously set at 37± $0.5^0$ with rpm of 100.

***Invitro* Drug Release Studies**

The drug release studies were carried out using USP type II dissolution apparatus. The dissolution vessels were filled with 900 ml of the 0.1N HCl. Using paddle rotation 100 rpm the temperature was kept constant 37± $0.5^0$. The samples were withdrawn at predetermined time intervals each time fresh medium was replaced in same amount. Samples absorbance was measured spectrophotometrically at a wavelength of 275 nm [6], against 0.1N HCl as a blank. The content drug in each sample was calculated using a standard calibration curve. The *invitro* drug release was carried out in triplicate for each batch of tablets.

**Mechanism of drug release**

The results obtaining *in vitro* release studies will be plotted in different model of data as follows. Log cumulative percentage of drug retained vs. Time (First Order rate Kinetics). Cumulative percentage of drug release vs. Square root of time [8] (Higuchi's

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Classical Diffusion Equation).Log of cumulative percentage of drug release vs. log time (Peppas-koresmeyer Exponential Equation). Peppas-Korsmeyer equation [9] was given as. **% R=kt$^n$** Where R= drug release, K=constant, n=slope, t=time**.** This model is widely used when the release mechanism is not well know or when more than one type of release phenomenon was involved. The 'n' values can be used to characterize diffusion release mechanism as: 0.5 = Fickian diffusion; 0.5<n<1= Non- fickian diffusion, 1 = Class II transport. Higuchi square root of time $Q=K_Ht^{1/2}$ where Q= amt.of drug release, $K_H$ higuchi square root of time drug release constant.

## RESULTS AND DISCUSSION

Preformulation study and drug excipients compatibility study [10] was done initially and results directed the further course of formulation. IR spectra studies revealed that the drug and the polymers used were compatible.

The tablets were formulated using various concentrations of polymers such as HPMC K4M and Carbopol 934P and effervescing agent (sodium bicarbonate).

**Table 2**
**Characterization of Aceclofenac Floating Tablets**

| Code | Hardness g/cm$^2$ | Friability % | Weight Variation mg | Drug Content mg | Floating Time (h) |
|---|---|---|---|---|---|
| F1 | 5.5 | 0.96 | 565.35 | 98.9 | 10 |
| F2 | 5.9 | 0.72 | 566.21 | 96.1 | 11 |
| F3 | 6.4 | 0.91 | 565.43 | 95.8 | 11.5 |
| F4 | 7.2 | 0.86 | 566.20 | 95.2 | 12 |
| F5 | 6.7 | 0.76 | 563.85 | 96.7 | 12.6 |

The parameters like diameter, thickness, hardness, friability, weight variation and content uniformity were evaluated for all the formulated batches of tablet. The results were complies with the official specifications within the limits.

**Table .No. 1 Composition of Intragastric Buoyant Tablets of Aceclofenac (in mgs)**

| Ingredients | F1 | F2 | F3 | F4 | F5 |
|---|---|---|---|---|---|
| **Aceclofenac** | 200 | 200 | 200 | 200 | 200 |
| **HPMC K4M** | 165 | 190 | - | - | 110 |
| **Carbopol 934P** | - | - | 165 | 190 | 110 |
| **Micro crystalline cellulose(MCC)** | - | 25 | 50 | 25 | 105 |
| **Citric acid** | 50 | 10 | 10 | 10 | - |
| **Sodium Bicarbonate** | 10 | 50 | 50 | 50 | 10 |
| **PVP K30** | 50 | 75 | 75 | 75 | 50 |
| **Magnesium Stearate** | 75 | 5 | 5 | 5 | 75 |
| **Talc** | 5 | 5 | 5 | 5 | 5 |

* Total Weight of the Tablet 565 mg

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Buoyancy lag time, Total floating time, Tablet density, swelling index studies showed satisfactory results for batch F1, F2, F3, F4 and F5.The F4 was selected for further studies. Since it had sustained release and good buoyancy lag time (40 sec).

**Table .3**
**KINETICS VALUES OBTAINED FROM DIFFERENT PLOTS OF FORMULATION F1-F 5**

| Code | First Order Plot | Higuchi's Plot | Koresmeyer Plot | |
|---|---|---|---|---|
| | Regression Coefficient ($R^2$) | Regression Coefficient ($R^2$) | n | ($R^2$) |
| **F1** | -0.9127 | 0.9834 | 0.723551 | 0.9832 |
| **F2** | -0.9418 | 0.9974 | 0.729901 | 0.9974 |
| **F3** | -0.8607 | 0.9619 | 0.79897 | 0.9909 |
| **F4** | -0.9832 | 0.9979 | 0.591088 | 0.9949 |
| **F5** | -0.9912 | 0.9807 | 0.7639 | 0.9926 |

**Fig .1. Floating of tablet after 45 sec.**

**Fig .2 Floating of tablet after 12 Hrs**

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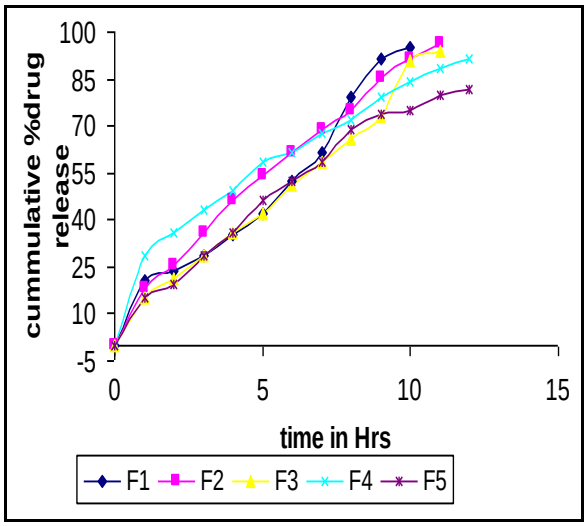


**Fig .3 Dissolution profile of aceclofenac in different formulations**

Results of *invitro* drug release studies using USPXXIII dissolution apparatus indicated that the F4 (Carbopol 934 P-195 mg, Sodium bicarbonate-50 mg) had good sustained release. From the in-vitro dissolution data it was found that formulation F1 and F2 containing HPMC K4M released 95.31% and 96.47% of drug within 10, 11hr of the study indicating that the polymer amount is not enough to control the drug release. The formulation F3 which contains Carbopol (165 mg) has total floating time of 11 Hrs with *invitro* drug release of 94.2. F4 containing Carbopol 934 P (195 mg) alone released 91.55% of drug with in 12 hrs. It concludes F4 had better-sustained release than the other formulation (F1, F2, F3& F5).

The cumulative percentage of drug release as a function square root of time (Higuchi plot) was linear and it suggested that the release of Aceclofenac, Carbopol 934P and HPMC K4M was diffusion controlled. The 'n' values obtained from the peppas-korsemeyer equation suggested that, all the formulation showed drug release by non-fickian diffusion mechanism. From the above results the floating tablet of aceclofenac may increase the bioavailability with once daily dosage form.

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