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# FORMULATION AND EVALUATION OF FLOATING TABLETS OF FLURBIPROFEN USING SOME NOVEL NATURAL AND SYNTHETIC POLYMERS

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**Abstract:**

*Floating drug delivery offers several applications for drugs having poor bioavailability because of the narrow absorption window in the upper part of the gastrointestinal tract. It retains the dosage form at the site of absorption and thus enhances the bioavailability. Flurbiprofen is a newer derivative NSAID, having short half-life of 2-4 hr, which required multiple daily doses to maintain the effective drug concentration. The long oral use of FP conventional dosage forms pronounced the drug gastro-intestinal adverse effects highly. Thus, Flurbiprofen was selected as a model drug for NSAIDs which is good candidate to be developed in sustained- release formulation. Aim of present work to develop sustained released tablets of flurbiprofen using some novel synthetic and natural polymers. The % drug content of all the formulated tablets were found within the limit. % drug content value of Flurbiprofen was within 98.65±0.14% to 99.45±0.15%.The results within the range indicate uniform of mixing. Optimized formulation (F7) showed the release of drug form gastroretentive formulation 99.45% after 12 hrs. and marketed formulation showed the release of 95.65% after 1.5 hrs. When the regression coefficient values of were compared, it was observed that '$r^2$' values of first order was maximum i.e. 0.972 hence indicating drug release from formulations was found to follow first order release kinetics.*

**Key words:** *Flurbiprofen, Gastroretentive drug delivery system, Suatain release tablets, formulation, evaluation*

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## INTRODUCTION:

Gastroretentive drug delivery system (GRDDS) is one of the novel approaches in this area. Oral controlled release dosage forms are the most commonly formulated but still offer highest attention in the area of novel drug delivery systems [2].Drugs that are easily absorbed from gastrointestinal tract (GIT) and have short half-lives are eliminated quickly from the systemic circulation. Frequent dosing of these drugs is required to achieve suitable therapeutic activity. To avoid this limitation, the development of oral sustained-controlled release formulations is an attempt to release the drug slowly into the GIT and maintain an effective drug concentration in the systemic circulation for a long time. After oral administration, such a drug delivery would be retained in the stomach and release the drug in a controlled manner, so that the drug could be supplied continuously to its absorption sites in the GIT [3].

The major objective of oral controlled drug delivery system is to deliver drugs for longer period of time to achieve better bioavailability, which should be predictable and reproducible. But this is difficult due to number of physiological problems such as fluctuation in the gastric emptying process, narrow absorption window and stability problem in the intestine. An Ideal drug delivery system should possess two main properties: (1) It should be a single dose for the whole duration of the treatment. (2) It should deliver the active drug directly at the site of action [1].

Poor absorption of many drugs in the lower GIT necessitates controlled release dosage forms to be maintained in the upper GI tract, particularly the stomach and upper small intestine [4]. These drug delivery systems suffer from mainly two adversities: the short gastric retention time(GRT) and unpredictable short gastric emptying time (GET), which can result in incomplete drug release from the dosage form in the absorption zone (stomach or upper part of small intestine)leading to diminished efficacy of administered dose [5].To formulate a site-specific orally administered controlled release dosage form, it is desirable to achieve a prolong gastric residence time by the drug delivery.

Floating drug delivery offers several applications for drugs having poor bioavailability because of the narrow absorption window in the upper part of the gastrointestinal tract. It retains the dosage form at the site of absorption and thus enhances the bioavailability.

Flurbiprofen is a newer derivative NSAID, having short half-life of 2-4 hr, which required multiple daily doses to maintain the effective drug concentration. The long oral use of FP conventional dosage forms pronounced the drug gastro-intestinal adverse effects highly. Thus, Flurbiprofen was selected as a model drug for NSAIDs which is good candidate to be developed in sustained- release formulation. Aim of present work to develop sustained released tablets of flurbiprofen using some novel synthetic and natural polymers

## MATERIAL AND METHODS:

### Preparation of Flurbiprofen floating tablet

Direct compression was followed to manufacture the gas generating floating tablets of Flurbiprofen. Nine different formulations (F1, F2, F3, F4, F5, F6, F7, F8, & F9) were prepared by direct compression [6]. All the polymers selected, drug and excipients were passed through sieve no. 40 before using into formulation. The amount and ratio of drug and polymers were weighed as per given in table 1 and all the formulation were used for further evaluations parameters.

**Table 1: Various formulations of Flurbiprofen floating tablets**

| Excipients (mg) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| **Flurbiprofen** | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| **HPMC K 4** | 80 | 100 | 120 | - | - | - | 40 | 50 | 60 |
| **Xanthum gum** | - | - | - | 40 | 50 | 60 | 40 | 50 | 60 |
| **Guar gum** | - | - | - | 40 | 50 | 60 | - | - | - |
| **Citric acid** | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **$NaHCO_3$** | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| **$Mg(C_{18}H_{35}O_2)_2$** | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 |
| **Talc** | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| **Lactose** | 75 | 55 | 35 | 75 | 55 | 35 | 75 | 55 | 35 |
| **Total Weight** | 300 | 300 | 300 | 300 | 300 | 300 | 300 | 300 | 300 |

**Evaluation of tablets:**
All the tablets were evaluated for following different parameters which includes;

**General Appearance:**
Five tablets from different batches were randomly selected and organoleptic properties such as color, odor, taste, shape, were evaluated. Appearance was judged visually. Very good (+++), good (++), fair (+) poor (-), very poor (- -).

**Thickness and diameter:**
Thickness and diameter of tablets were determined using Vernier caliper. Five tablets from each batch were used, and an average value was calculated [7]

**Drug content:**
Twenty tablets were taken and amount of drug present in each tablet was determined [8]. The tablets were crushed in a mortar and the powder equivalent to 100mg of drug was transferred to 100ml standard flask. The powder was dissolved in 50 ml of 0.1 N HCl and made up to volume with of 0.1 N HCl. The sample was mixed thoroughly and filtered through a 0.45µ membrane filter. The filtered solution was diluted suitably and for drug content by UV spectrophotometer at λmax of 244nm using of 0.1 N HCl as blank.

**Hardness:**
For each formulation, the hardness of five tablets was determined using the Monsanto hardness tester (Cadmach).

**Friability :**
The friability of a sample of 10 tablets was measured using a Friability tester (Electro Lab). Ten tablets were weighed, rotated at 25 rpm for 4 minutes. Tablets were reweighed after removal of fines (dedusted) and the percentage of weight loss was calculated [9]

**Uniformity of weight**
Twenty tablets were randomly selected from each batch individually weighed, the average weight and standard deviation of 20 tablets was calculated.

***In vitro* buoyancy studies:**
*In vitro* buoyancy was determined by floating lag time as per the method described by Rosa *et al.*, 1994[10]. The tablets were placed separately in a 100 ml glass beaker containing simulated gastric fluid (SGF), pH 1.2 as per USP. The time required for the tablet to rise to the surface and float was determined as floating lag time.

***In vitro* dissolution rate studies**
*In vitro* drug release of the sample was carried out using USP- type II dissolution apparatus (Paddle type). The dissolution medium, 900 ml 0.1N HCl was placed into the dissolution flask maintaining the temperature of 37±0.50c and rpm of 75. One Flurbiprofen tablet was placed in each basket of dissolution apparatus. The apparatus was allowed to run for 10 hours. Sample measuring 5 ml were withdrawn after every 1 hour up to 10 hours using 10ml pipette. The fresh dissolution medium (37ºC) was replaced every time with the same quantity of the sample and take the absorbance at 244.0 nm using spectroscopy[11].

## RESULTS AND DISCUSSION:

The thickness of the tablets was reported in the micrometer (mm).The thickness of tablet indicates that, die fill was uniform. The thickness depends on the size of the punches (8 mm) and the weight of one tablet (300mg). The value of thickness ranges between 3.4±0.2 to 3.5±0.2mm.

Friability determines the strength of the tablets. The friability for all the formulations was below 1% indicating that the friability was within the prescribed limits. The results of friability test indicate that the tablet possesses good mechanical strength. The friability value ranges from 0.621±0.025 to 0.854±0.014.

The mean hardness values were measured for all the formulation using Monsanto hardness tester. The hardness value ranges from 5.6±0.1 to 5.9±0.3kg/cm2.

Twenty tablets were randomly selected from each formulation and evaluated. The obtained data were almost uniform. The values of tablets average weight ranging from 295±7 to 305±5mg. All the tablets passed weight variation test as the % weight variation was within the USP Pharmacopoeia's limits of ±5% of the weight.

The % drug content of all the formulated tablets were found within the limit. % drug content value of Flurbiprofen was within 98.65±0.14% to 99.45±0.15%.The results within the range indicate uniform of mixing.

**Table 2: Results of post compression properties of Flurbiprofen floating gastroretentive tablets**

| F. Code | Thickness* (mm) | Hardness* (kg/cm2) | Weight variation* (mg) | Friability* (%) | Drug content* (%) | Total floating duration* (h) | Floating lag times* (sec) |
|---|---|---|---|---|---|---|---|
| F1 | 3.2±0.2 | 5.8±0.2 | 305±5 | 0.745±0.012 | 98.85±0.25 | MT 12 | 74±6 |
| F2 | 3.3±0.3 | 5.9±0.3 | 302±4 | 0.658±0.022 | 98.78±0.32 | MT 12 | 65±4 |
| F3 | 3.2±0.2 | 5.7±0.1 | 300±6 | 0.854±0.014 | 98.65±0.14 | MT 12 | 63±5 |
| F4 | 3.2±0.1 | 5.8±0.2 | 303±5 | 0.745±0.032 | 98.78±0.25 | MT 12 | 74±5 |
| F5 | 3.3±0.2 | 5.6±0.1 | 298±4 | 0.621±0.025 | 98.78±0.32 | MT 12 | 65±2 |
| F6 | 3.2±0.2 | 5.8±0.3 | 295±7 | 0.745±0.021 | 99.05±0.14 | MT 12 | 85±5 |
| F7 | 3.3±0.2 | 5.7±0.1 | 302±4 | 0.854±0.014 | 99.45±0.15 | MT 12 | 45±2 |
| F8 | 3.3±0.2 | 5.8±0.2 | 304±2 | 0.745±0.014 | 98.78±0.17 | MT 12 | 62±3 |
| F9 | 3.2±0.3 | 5.6±0.3 | 302±3 | 0.625±0.014 | 98.96±0.22 | MT 12 | 68±2 |

***Average of three determinations (n=3)**

**Table 3: *In-vitro* drug release study of gastroretentive floating tablets**

| Time | % Cumulative drug release | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| (hr) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 | M.F |
| 0.5 | 43.32 | 38.85 | 35.45 | 36.65 | 33.32 | 30.25 | 25.65 | 23.36 | 20.14 | 46.65 |
| 1 | 65.58 | 45.65 | 43.32 | 42.23 | 40.56 | 36.65 | 33.32 | 26.65 | 25.65 | 55.56 |
| 1.5 | 75.65 | 65.65 | 55.65 | 55.65 | 59.65 | 48.85 | 45.65 | 35.45 | 30.25 | 95.65 |
| 2 | 83.32 | 75.45 | 65.58 | 63.32 | 65.58 | 59.98 | 55.65 | 48.85 | 36.65 | |
| 3 | 98.74 | 86.65 | 78.85 | 78.89 | 76.65 | 65.58 | 63.32 | 55.65 | 43.32 | |
| 4 | | 98.78 | 95.65 | 98.38 | 89.98 | 78.85 | 75.65 | 63.32 | 52.32 | |
| 6 | | | 99.74 | | 99.45 | 89.98 | 83.32 | 75.65 | 65.58 | |
| 8 | | | | | | 98.95 | 96.65 | 84.45 | 73.32 | |
| 12 | | | | | | | 99.45 | 91.45 | 84.45 | |

**M.F-marketed Formulation**

**Table 4: Regression analysis data of Flurbiprofen floating tablets**

| Batch | Zero Order | First Order | Higuchi model | Korsmeyer peppas model |
|---|---|---|---|---|
| | $r^2$ | | | |
| **F7** | 0.839 | 0.972 | 0.948 | 0.971 |

## CONCLUSION:

In house tablet optimized formulation (F7) showed the release of drug form gastroretentive formulation 99.45% after 12 hrs. and marketed formulation showed the release of 95.65% after 1.5 hrs. When the regression coefficient values of were compared, it was observed that '$r^2$' values of first order was maximum i.e. 0.972 hence indicating drug release from formulations was found to follow first order release kinetics.

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