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Formulation and Evaluation of Floating Tablet of Flurbiprofen

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ABSTRACT

In the present study, Flurbiprofen was used for preparing Floating dosage form that are designed to retain in stomach for a long time and have developed as a Floating drug delivery system by using various polymers like Carbopol 940 and HPMC K4M to enhance the bioavailability and therapeutic efficacy of Flurbiprofen. The mechanism of action of Flurbiprofen is Non selective COX inhibitor which inhibits the prostaglandin synthesis. Sodium bicarbonate and citric acid was incorporated as a gas generating agent. The direct compression method is used in present work. The formulation was optimized on basis of acceptable tablet properties like optimum hardness, uniform thickness, consistent weight uniformity and low friability. The prepared formulation shows better and significant result all the evaluated parameter.

Keywords: Flurbiprofen, Floating drug delivery system, HPMC K4M, Carbopol 940.

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INTRODUCTION

Gastro retentive dosage forms containing suitable drug candidates which would remain in the stomach and/or upper part of gastrointestinal tract for a prolonged period of time there by maximizing the drug release at desired site within the time before gastro-retentive dosage forms left the stomach and upper part of the gastrointestinal tract, has provoked a great deal of increase interest in the formulation of such drugs as floating drug delivery system.[1]

Floating drug delivery system (FDDS), also called hydro-dynamically balanced system, is an effective technology to prolong the gastric residence time in order to improve the bioavailability of the drug. This technology is suitable for drugs with an absorption window in the stomach or in the upper part of the small intestine, drugs acting locally in the stomach and for drugs that are poorly soluble or unstable in the intestinal fluid. Effervescent floating drug delivery systems generate gas (CO_2), thus reduce the density of the system and remain buoyant in the stomach for a prolonged period of time and released the drug slowly at a desired rate.[2]

Flurbiprofen drug exhibit anti-inflammatory, analgesic, and antipyretic activities in animal models. The mechanism of action of flurbiprofen is non selective COX inhibitor which inhibits the prostaglandin synthesis.[3]

MATERIALS AND METHOD

Materials

Flurbiprofen, HPMC K4M, Carbopol 940, was purchased from Balaji drug supplier., Gujarat, India. All other ingredients was purchase from Central drug house., NewDelhi & those were the laboratory grade.

Method

Preparation Method of Flurbiprofen Floating Tablets

Table 1. Formula for preparation of Flurbiprofen floating tablet

Formulation code Ingredients	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)
Flurbiprofen	200	200	200	200
HPMC K4M	100	75	50	25
Carbopol 940	25	50	75	100
Sodium bicarbonate	50	50	50	50
Methyl cellulose	75	75	75	75
Citric acid	25	25	25	25
Lactose	25	25	25	25
Magnesium stearate	5	5	5	5
Talc	10	10	10	10

The ingredient were weighed accurately as given in (Table 1) and mixed thoroughly. To this sodium bicarbonate, lactose, citric acid, were added to mortar and pestle according to their geometric dilution and finally make up the total weight (515) of tablet using micro crystalline cellulose and the powder was passed through 60 mesh sieve (60 micrometer size). Finally the sample which is obtained after passing from the sieve is re- triturated and required amount of talc and then compressed by using single punch tableting machine fitted with a 6mm round flat punches.

EVALUATION OF FLOATING TABLET

Thickness

Thickness of tablets was determined using Screw gauze. Three tablets from each batch were used, and average values were calculated.[5]

Weight variation

To study weight variation, 20 tablets of each formulation were weighed using an electronic balance, and the test was performed according to the official method.[6]

Hardness

The hardness of tablet of each formulation was measured by Monsanto hardness tester. The hardness was measured in terms of kg/cm^2.[7]

Friability

Friability is the measure of tablet strength Roche type friabilator was used for testing the friability using the following procedure. Twenty tablets were weighed accurately and placed in the tumbling apparatus that revolves at 25 rpm dropping the tablets through a distance of six inches with each revolution. After 4 min., the tablets were weighed and the percentage friability was then calculated by formula.[8]

$$\%\ loss\ = \frac{Intialwt.of tablets - Finalwt.of tablets}{Intialwt.of tablets} \times 100$$

Determination of Swelling Index

The swelling index of tablets was determined in 0.1N HCl (pH 1.2) at room temperature. The swollen weight of the tablet was determined at predefined time intervals over a period of 24 h. The swelling index (SI), expressed as a percentage, and was calculated from the following equation. The percentage weight gain by the tablet was calculated by the formula.[9]

$$Swelling\ \ index\ (S.I.) = \{\frac{Wt - Wo}{Wo}\} \times 100$$

Where, S.I. = Swelling index

Wt = Weight of tablet at time t

Wo = Weight of tablet before immersion

***In-vitro* buoyancy studies**

The randomly selected tablets from each formulation were kept in a 100ml beaker containing simulated gastric fluid, pH 1.2 as per USP. The time taken for the tablet to rise to the surface and float was taken as floating lag time (FLT). The duration of time the dosage form constantly remained on the surface of medium was determined as the total floating time.[10]

Drug content uniformity*:*

Five tablets from each formulation were weighed and taken in mortar and crushed to make powder. A quantity of powder weighing from this equivalent to 20 mg of Flurbiprofen was taken in 100 ml volumetric flask diluted up to 100 ml with 0.1 N HCl. It was then shaken vigorously on a Magnetic stirrer for 2 hr & filtered into 50 ml volumetric flask up to the mark by using Whatman filter paper. Further appropriate dilutions were made & absorbance was measured at nm 248 nm.[11]

***In-vitro* dissolution studies**

In-vitro drug release of all formulations was carried out using USP- type II dissolution apparatus. The dissolution medium 900 ml 0.1 N HCl Buffer was placed into the dissolution flask maintaining the temperature of 37 ± 0.5^0C & rpm of 50. One Flurbiprofen tablet was placed in the dissolution apparatus. Dissolution studies were carried out for 12 hr. 5ml of the Aliquot was taken at intervals of 1, 2, 3, 6, 9, 12, hrs. After collecting the sample, the dissolution medium was replenished with the same volume of fresh medium, and the sample was filtered 1ml of the filtrate was diluted to 10 ml with 0.1 N HCl and analyzed spectrophotometrically at 248 nm.[12]

RESULTS AND DISCUSSION

Thickness

The thickness of floating tablets were measured by Screw Guaze of formulation F1 toF4 and were range between 2.81±0.08 to 3.40±0.02 mm (Table 2).

Table 2. Evaluation of floating tablets

Formulation	Thickness (mm)	Hardness Kg/cm^2	Average weight mg	Friability% loss	Drug content%
F1	2.81±0.08	5.5±0.16	498.15±0.66	0.19	97
F2	2.93±0.04	5.8±0.37	499.13±0.28	0.34	96
F3	3.20±0.06	6.2±0.48	501.19±0.71	0.48	92
F4	3.40±0.02	6.5±0.56	502.11±0.81	0.55	93

Weight variation

All the formulation tablet F1 to F4 passed the weight variation test as the percent weight variation was within the pharmacopeia limit of 5% of average weight (Table 2).

Hardness

The hardness of the floating tablet was measured by the Monsanto tester of formulation F1 to F4 and were controlled between 5.5 to 6.5 kg/cm^2 .The standard hardness of the tablet is 5 kg/cm^2 (Table 2).

Friability

The friability of the floating tablet was measured by The Roche Friabilator of formulation F1 to F4 and were controlled between 0.19 to 0.55%. The standard friability of the tablet is below 0.8% according to IP and 1% according to USP (Table 2).

Drug content uniformility

The percent drug content of formulation F1 to F4 was found to be 92.00 to 97.00% of Flurbiprofen in which was within the acceptable limit, the standard drug content uniformity 100±10% (Table 2).

***In-vitro* buoyancy studies**

On immersion of tablets of different formulations from F1 to F4 in 0.1N HCl solution at 37±5°C, the tablets floated, and remained buoyant without disintegration, the results of the buoyancy lag time (BLT) and total floating time (TFT) were shown in Table. Buoyancy lag time (BLT) and total floating time (TFT) of different formulation were noted. With reference to buoyancy studies results it can be concluded that as the amount of HPMC polymers increase, the formulation showed good buoyancy lag time (BLT) and total floating time (TFT). The formulation of F1 to F4 buoyancy lags time (sec.) between 120 to 180 sec. and total floating time (hr) 16 to 24 hr. or more (Table 3).

Table 3. Evaluation of floating tablets

Formulation	Buoyancy lag time(sec.)	Total floating time (hr.)	Swelling index after 6 hr (%)
F1	120	> 16	55.40±0.36
F2	168	>20	62.52±0.11
F3	140	>18	58.34±0.55
F4	180	>24	65.00±0.18

Swelling index study

The Swelling Index for different formulations was shown in table. Formulation F4 shows max swelling index comparing to other formulation after 24 hrs. while formulation F1 shows less swelling index as concentration of Carbopol 940 increases may be due to high viscosity and hydrophilic nature (Tablet 3).

***In-vitro* dissolution study**

In vitro drug release studies exhibited a decrease drug release with an increase in polymer concentration which may be due to increase in viscosity of the gel as well as the gel layer with longer diffusion path. Formulations containing high viscosity grade HPMC showed slower drug release compared to formulations containing low viscosity polymers. There was no considerable effect of gas generating agents on the release of the drug. Drug release profile of batches of Flurbiprofen floating tablet F1-F4 was found 31.42%, 36.77%, 51.81%, and 54.49% respectively. F3 formulation of Flurbiprofen floating tablet shows highest release of drug among the all batches (Table 4 & Figure 1).

Table 4. In vitro dissolution floating tablet of Flurbiprofen

Time (hr)	F1	F2	F3	F4
1	1.01±0.44	2.37±0.58	2.99±0.54	4.27±0.18
2	1.09±0.30	6.49±0.72	6.31±0.23	7.26±0.66
3	3.62±0.28	7.64±0.25	8.16±0.46	9.09±0.29
4	9.46±0.66	9.16±0.65	10.01±0.24	10.99±0.80
5	13.67±0.78	11.06±0.30	11.98±0.61	12.01±0.56
6	15.62±0.80	13.88±0.24	13.98±0.32	13.94±0.90
7	18.49±0.84	15.83±0.26	20.39±0.19	18.60±0.67
8	21.39±0.22	16.90±0.18	23.31±0.66	22.39±0.12
9	22.52±0.10	19.78±0.20	30.76±0.38	30.73±0.86
10	25.46±0.76	25.39±0.17	37.39±0.25	37.35±0.88
11	27.53±0.71	29.26±0.24	48.59±0.35	47.88±0.78
12	31.42±0.26	36.77±0.33	51.81±0.19	54.49±0.49

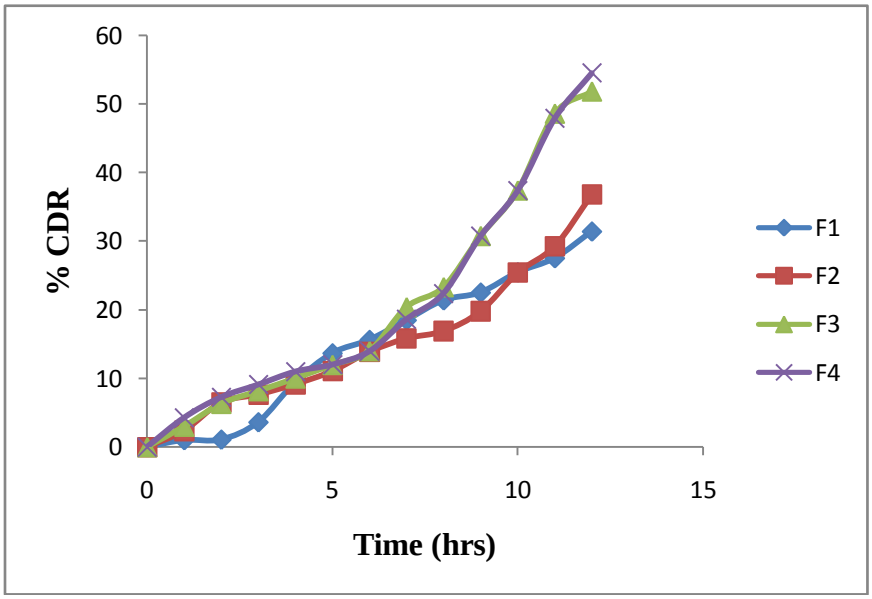

Figure 1: % cumulative drug release of Flurbiprofen floating tablet

CONCLUSION

The objective of the study was to formulate and evaluate Flurbiprofen floating tablets. The tablets were formulated using direct compression method using varying quantities of the ingredients. The formulated tablets were tested for the parameters such as weight variation, hardness, thickness, friability and drug content and were found to be with in the limits. The floating lag time and the floating duration of the tablets are the most important parameters. Hence, diffusion controlled Flurbiprofen gastro retentive tablets were formulated and evaluated and formulation F1 was concluded as the best formulation for the manufacture of Flurbiprofen gastro retentive tablets which can assure 100% bioavailability. Floating drug delivery tablets of Flurbiprofen were developed to enhance gastric residence time and there by eradication of Helicobacter pylori infection. The optimized formula F1 showed better sustained drug release and which also had good floating properties.

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