FORMULATION AND *INVITRO* EVALUATION OF ACECLOFENAC (NSAID) FLOATING TABLETS.

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Oral delivery of drugs is still one of the most compliant dose types. Numerous physiological constraints are present in the majority of oral dosage forms. Drugs that are poorly soluble or unstable in intestinal fluids can benefit from the use of floating oral drug delivery systems (FDDS), which are kept in the stomach. Floating drug delivery systems (FDDS) stay afloat in the stomach because their bulk density is lower than that of gastric fluids. The present study was carried out with an objective of preparation and invitro evaluation of Aceclofenac (NSAID) Floating Tablets. It was determined from the compatibility investigations that ethyl cellulose, carbopol 934p, and HPMC K15M were suitable for the formulation of Aceclofenac floating tablets because they were compatible with Aceclofenac. All formulations, F1 through F9, underwent in vitro buoyancy tests using a 0.1 N HCl solution at 37 °C. Each and every formulation floated. Compared to previous formulations, formulation F7, which contained 20 mg of HPMC K15M and 20 mg of ethyl cellulose, had a longer floating duration (17 hours). For every formulation, in vitro dissolving tests were also conducted. For 12 hours, the formulation F7 demonstrated a regulated release. Therefore, based on its outcomes, F7 was determined to be the ideal batch. Finally, it was concluded that HPMC K15M, Carbopol 934p and ethyl cellulose can be successfully used in the formulation of Aceclofenac gastro retentive floating drug delivery system.

Key words: Floating drug delivery systems, HPMC, invitro evaluation, Aceclofenac

INTRODUCTION

FLOATING DRUG DELIVERY SYSTEM

Oral delivery of drugs is still one of the most compliant dose types. Numerous physiological constraints are present in the majority of oral dosage forms, including variable gastrointestinal transit, which results in nonuniform absorption profiles, partial drug release, and a shorter duration of the dosage form's residency in the stomach due to variable gastric emptying. As the medicine passes through the absorption site, the remaining amount is not absorbed, which results in inadequate absorption of drugs with an absorption window, particularly in the upper portion of the small intestine. Wide inter- and intra-subject variability is seen as a result of many factors affecting the stomach emptying of dose forms in humans.

Human stomach emptying of dose forms is influenced by a number of factors, which results in significant intra- and inter-subject variability. This considerable variability may result in non-uniform absorption and make the bioavailability uncertain because many medications are highly absorbed in the upper gastrointestinal tract. Therefore, a delivery system that can transport medications in higher concentrations to the absorption location (i.e., upper section of the small intestine) and control and prolong the gastric emptying time would be useful.

Drugs that are poorly soluble or unstable in intestinal fluids can benefit from the use of floating oral drug delivery systems (FDDS), which are kept in the stomach. Floating drug delivery systems (FDDS) stay afloat in the stomach because their bulk density is lower than that of gastric fluids.

Limitations OF FDDS

For the medication to float in the stomach and function well, there must be an adequate amount of fluid present. For medications that have issues with solubility or stability in stomach fluid, floating systems are not practical. Since slow stomach emptying may result in decreased systemic bioavailability, medications like nifedipine, which is widely absorbed throughout the GI tract and has little first-pass metabolism, might not be the best choices for FDDS. Additionally, the use of FDDS for medications that irritate the stomach mucosa is limited.

Advantages of FDDS

1. Despite the intestinal pH being alkaline, floating dose forms like tablets or capsules will stay in the solution for an extended period of time.

2. Drugs intended for local action in the stomach, such as antacids, benefit from FDDS.
3. To maintain the drug in a floating state in the stomach and obtain a comparatively superior reaction, FDDS dosage forms are helpful in cases of diarrhea and vigorous intestinal movement.
4. HBS/FDDS formulations may be helpful for the administration of aspirin and other similar drugs since acidic substances, such as aspirin, irritate the stomach wall when they come into touch with it.

5. FDDS are beneficial for medications that are absorbed through the stomach, such as antacids and ferrous salts.

Disadvantages of FDDS

1. For drugs that have issues with solubility or stability in stomach fluids, floating systems are not practical.

2. Since late gastric emptying may result in decreased systemic bioavailability, medications like nifedipine, which is highly absorbed throughout the GI tract and undergoes extensive first-pass metabolism, would not be good candidates for FDDS.

3. One of the drawbacks of floating is that it necessitates a high enough level of stomach fluids for drug dosages to float and function effectively.

Aim and Objectives

For drugs that have local effects in the digestive tract, floating pills are beneficial. In the intestine, the lowest portions of the GIT are either unstable or poorly absorbed. A more recent non-steroidal anti-inflammatory medicine (NSAID) is aceclofenac (2-[(2, 6-dichlorophenyl) amine] phenylacetoxyacetic acid). Aceclofenac is a derivative of phenyl acetic acid that is primarily used to treat osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis. It has strong anti-inflammatory and analgesic effects. After oral administration, aceclofenac is quickly and effectively absorbed; nevertheless, it has a brief half-life of 3–4 hours and need several doses to sustain the therapeutic impact throughout the day. It is regarded as the perfect model drugs for floating matrix drug delivery because of its extremely short biological half-life, which only lasts a few hours and causes side effects. In order to maximize the drug's effectiveness and provide targeted action, a dosage form for aceclofenac delivery in the stomach must be developed. This study's goal was to create floating matrix aceclofenac tablets with guar gum, carbopol, and HPMC.

This project's goal was to design a floating aceclofenac drug delivery system. The dosage form floats on the stomach juice thanks to a floating drug delivery technology. These have the ability to stay in the stomach for a number of hours, which greatly extends the aceclofenac's gastric residence length.

Materials and Methods

100mg of Aceclofenac was accurately weighed and transferred into 100ml volumetric flask. It was dissolved and diluted to volume with 0.1N HCL to give stock solution containing 1000µg/ml. The standard stock solution was then serially diluted with 0.1N HCL to get 2 to 12µg/ml of Aceclofenac. The absorbances of the solutions were measured against 0.1N HCl as blank at 275 nm using UV spectrophotometer. The absorbance values were plotted against concentration (µg/ml) to obtain the standard calibration curve.

Preparation of Gastro Retentive Floating Tablets

Floating tablets containing Aceclofenac were prepared by wet granulation technique using variable concentrations of HPMC K15M, carboxymethyl cellulose and carbopol 934 with sodium bicarbonate.

Different tablets formulations were prepared by wet granulation method. All the powders were passed through 60 mesh sieve. Required quantity of drug, and low density polymer were mixed thoroughly. Then, granulating agent was added slowly with uniform mixing the get a wet mass. The wet mass was passed through sieve no 16 to obtain wet granules. The granules were dried at 50 º C for 5 to 6 hrs in try dryer. The dried granules were passed through sieve.no.22, after blending with lubricants were compresses into tablet compression machine (11mm diameter punches) using tablet compression machine.

Table No. 1 Formulation of Of Aceclofenac (NSAID) Floating Tablets.

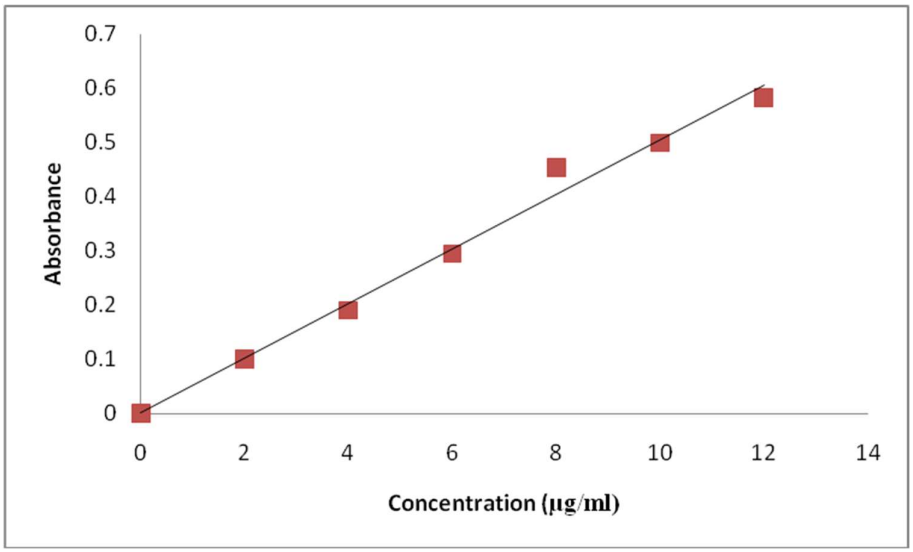
Ingredients	**F1**	**F2**	**F3**	**F4**	F5	**F6**	**F7**	**F8**	**F9**
Aceclofenac	100mg	100mg	100mg	100mg	100mg	100mg	100mg	100mg	100mg
HPMCK 15M	25m	50mg	75mg	100mg	0	150	200	250	300
Carbopol 934 P	0	25mg	50mg	75mg	75mg	75mg	75mg	75mg	75mg
Sodium bi carbonate	50mg	50mg	50mg	50mg	50mg	50mg	50mg	50mg	50mg
Citric acid	25mg	25mg	25mg	25mg	25mg	25mg	25mg	0	25mg
Ethyl cellulose (EC)	10mg	15mg	20mg	25mg	30mg	35mg	40mg	45mg	50mg
Mag. Stearate	5mg	5mg	5mg	5mg	5mg	5mg	5mg	5mg	5mg
Talc	2mg	2mg	2mg	2mg	2mg	2mg	2mg	2mg	2mg

Preparation of standard curve

Table 2 : STANDARD CURVE OF ACECLOFENAC.

S.no	Concentration (µg/ml)	Absorbance in 0.1 N HCl
1.	0	0.000
2.	2	0.101
3.	4	0.191
4.	6	0.295
5.	8	0.454
6.	10	0.500
7.	12	0.584
Y=0.050 R^2=0.988		

Fig 1. STANDARD CURVE OF ACECLOFENAC IN 0.1N HCl



The scanning of drug solution in UV region (200–400 nm) was carried out to find the wavelength of maximum absorption (λ_{max}). The λ_{max} was found to be at 275 nm. So the standard calibration curve of aceclofenac was developed at this wave length. The calibration curve was linear between 2 – 12 µg/ml concentration ranges. The standard calibration curve of aceclofenac was determined in 0.1 HCl, by plotting absorbance against concentration at 275 nm, and it follows the Beer's law. Results were tabulated in table no 7.3. Plotted in fig. (7.6) and). The r^2 and slope were found to be 0.988 and 0.050.

Table no. 3 KINETIC STUDY DATA OF FORMULATIONS (F1 – F9)

Formulation code	Zero order R^2	First order R^2	Higuchi R^2	Korsmeyer - peppas R^2	n	Mechanism of drug release
F1	0.997	0.938	0.918	0.955	0.961	Zero order non fickian diffusion.
F2	0.998	0.897	0.912	0.942	0.913	Zero order non fickian diffusion

F3	0.998	0.888	0.919	0.934	0.986	Zero order non fickian diffusion
F4	0.999	0.882	0.919	0.923	0.963	Zero order non fickian diffusion
F5	0.990	0.476	0.922	0.919	0.946	Zero order non fickian diffusion
F6	0.991	0.856	0.928	0.892	0.879	Zero order non fickian diffusion
F7	0.999	0.821	0.928	0.892	0.887	Zero order non fickian diffusion
F8	0.991	0.868	0.931	0.917	0.951	Zero order non fickian diffusion
F9	0.990	0.870	0.924	0.925	0.970	Zero order non fickian diffusion

In order to understand the mechanism of drug release the results obtained from the invitro release studies were plotted in different model of data treatment as follows.

1. Cumulative percent drug release Vs. time (Zero order rate kinetics).
2. Log cumulative percent drug retained Vs. time (First Order rate kinetics).
3. Log cumulative percent drug released Vs. Square root of time (Higuchi's Classical Diffusion Equation).
4. Log of cumulative % release Vs. log time (Pappas Exponential Equation).

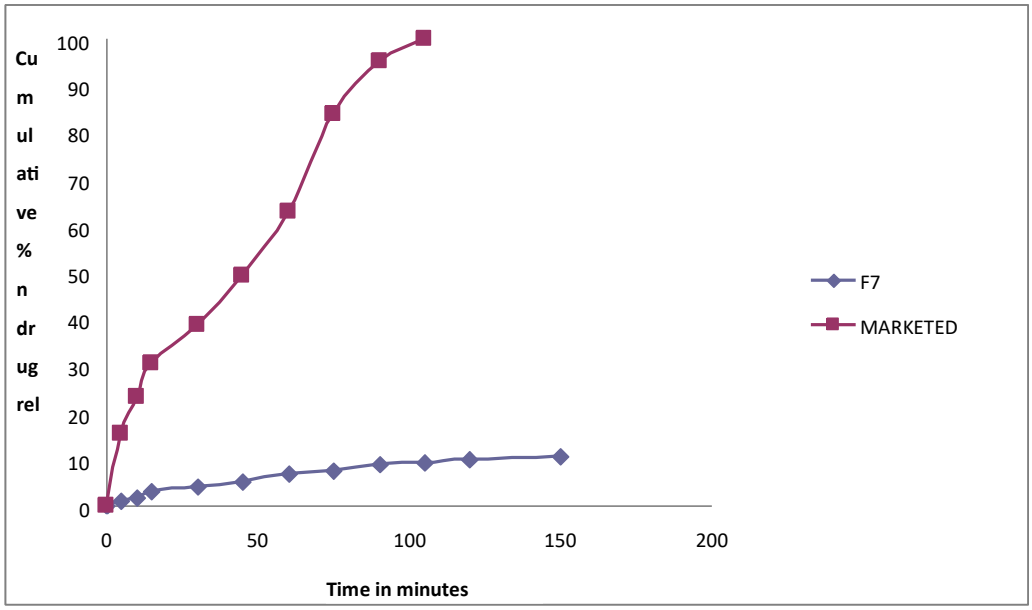
The release exponent value thus obtained was ranged from 0.879 to 0.986 all the formulations exhibited non fickian diffusion mechanism. The drug release was found following zero order kinetics.

COMPARATIVE STUDY OF OPTIMIZED BATCH WITH MARKETED CONVENTIONAL TABLET

Table no.4 *INVITRO* DRUG RELEASE STUDY

Time (min)	Cumulative % drug release of Formulation (F7)	Cumulative % drug release of marketed tablets
0	0.000	0.00
5	0.900	15.53
10	1.585	23.35
15	2.953	30.58
30	4.110	38.57
45	5.280	49.34
60	6.688	62.92
75	7.660	84.08
90	8.868	95.33
105	9.19	99.87
120	9.81	--
150	10.62	--

Figure no. 2 *INVITRO* DRUG RELEASE



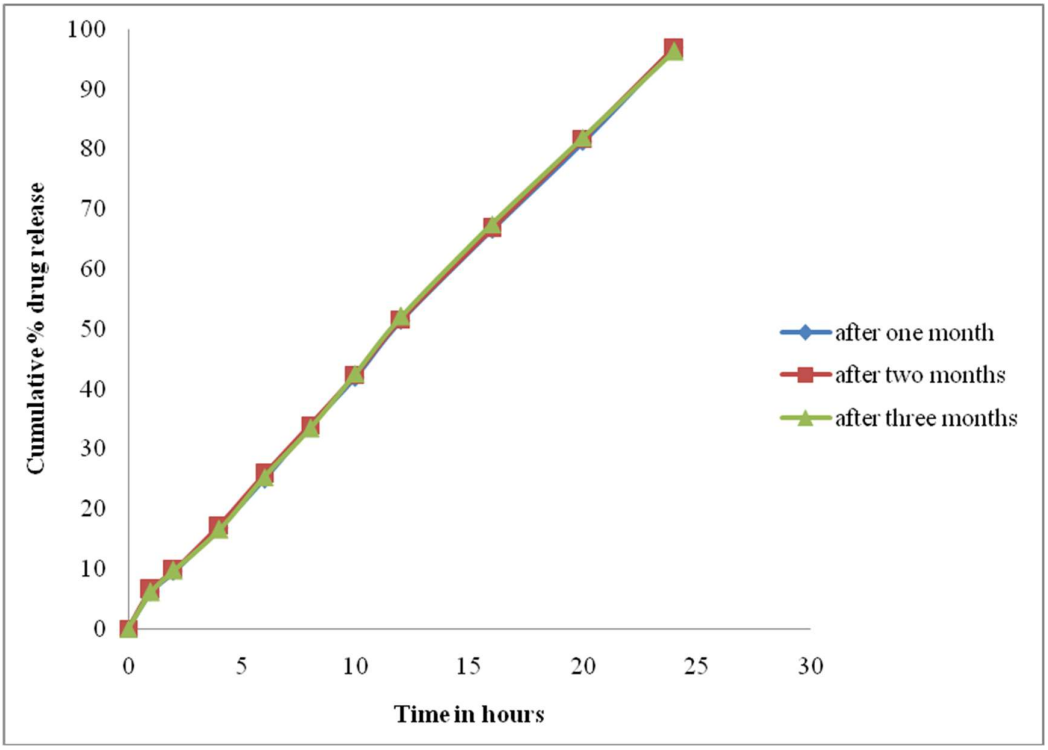
The *invitro* drug release of prepared floating tablet Formulation (F7) was compared with that of the marketed conventional tablet (aceva-tab). The marketed tablet released 99.87% within 105 minutes, whereas the prepared floating tablet (F7) released only 9.19% in 105 minutes and 10.62% in 120 minutes.

Table no. 5 *INVITRO* DRUG RELEASE STUDY FORMULATION (F7)

Time in hours	Cumulative % Drug Release after one month	Cumulative % Drug Release after two months	Cumulative % Drug Release after three months
0	0.000	0.00	0.00
1	6.075	6.53	6.08
2	9.518	9.75	9.74
4	16.823	17.28	16.60
6	24.883	25.80	25.33

8	33.705	33.95	33.49
10	41.948	42.42	42.63
12	51.403	51.66	52.09
16	66.583	66.84	67.50
20	81.250	81.74	81.95
24	96.973	96.79	96.33

Figure no. 3 *INVITRO* DRUG RELEASE STUDY



The tablets were investigated at 40°C/75%RH for 3 months. From the data, the formulation is found to be stable under the conditions mentioned before since there was no significant change in the percentage amount of drug content and drug release. Thus, it was

found that the floating tablets of aceclofenac (F7) were stable under these storage conditions at least for three months

SUMMARY AND CONCLUSION

It was determined from the compatibility investigations that ethyl cellulose, carbopol 934p, and HPMC K15M were suitable for the formulation of Aceclofenac floating tablets because they were compatible with Aceclofenac.

All formulations, F1 through F9, underwent in vitro buoyancy tests using a 0.1 N HCl solution at 37 °C. Each and every formulation floated. Compared to previous formulations, formulation F7, which contained 20 mg of HPMC K15M and 20 mg of ethyl cellulose, had a longer floating duration (17 hours). For every formulation, in vitro dissolving tests were also conducted. For 12 hours, the formulation F7 demonstrated a regulated release. Therefore, based on its outcomes, F7 was determined to be the ideal batch.

Finally, it was concluded that HPMC K15M, Carbopol 934p and ethyl cellulose can be successfully used in the formulation of Aceclofenac gastro retentivefloating drug delivery system.

- Formulate and evaluate floating tablets of aceclofenac by using different polymers.
- Provide an increased gastric residence time resulting in prolonged drug delivery in gastrointestinal tract.
- Minimize the amount of drug enter into systemic drug delivery.
- Maximum utilization of drug enabling reduction in total amount of dose administered.
- Reduction in treatment cost through improved therapy.
- Improve patient’s compliance and convenience.

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