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FORMULATION AND EVALUATION OF ACECLOFENAC FLOATING TABLET

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ABSTRACT

This study focuses on the formulation and evaluation of aceclofenac floating tablets as a novel drug delivery system to enhance gastric residence time and improve drug bioavailability. Aceclofenac, renowned for its anti-inflammatory and analgesic properties, was selected as the model drug for this research. Five formulations (AF1-AF5) were prepared using various polymers, including hydroxypropyl methylcellulose (HPMC), Carbopol 940, and guar gum, via the direct compression method. The formulations underwent comprehensive evaluation for flow properties, weight variation, content uniformity, hardness, friability, and drug release kinetics. Among the formulations, AF1, incorporating HPMC, exhibited the optimal floating time of 8 hours and a remarkable drug release of 98.4% within 24 hours. These findings underscore the potential of aceclofenac floating tablets in prolonging drug release and enhancing therapeutic efficacy. Further optimization, in vivo studies, and clinical trials are warranted to validate the effectiveness and safety of these formulations, ultimately improving patient outcomes in pain and inflammation management.

KEYWORDS: Aceclofenac, Floating tablets, Gastric residence time, Drug bioavailability, Anti inflammatory.

INTRODUCTION

Aceclofenac, a member of the non-steroidal anti-inflammatory drug (NSAID) class, is widely recognized for its potent analgesic and anti-inflammatory properties.[1] Despite its therapeutic benefits, aceclofenac encounters challenges related to its short biological half-life and erratic absorption from the gastrointestinal tract.[2] These limitations necessitate the development of innovative drug delivery systems to enhance its bioavailability and prolong its therapeutic effect.

Among various drug delivery strategies, floating tablets have emerged as promising formulations for drugs with absorption challenges in the gastrointestinal tract. Floating tablets are designed to remain buoyant on the gastric fluid, thereby prolonging gastric residence time and improving drug absorption.[3] This approach offers several advantages, including enhanced drug solubility, reduced dosing frequency, and improved patient compliance.

The formulation and evaluation of aceclofenac floating tablets represent a significant endeavor in pharmaceutical research. By utilizing suitable pharmaceutical excipients and formulation techniques, researchers aim to develop a dosage form that optimizes the therapeutic potential of aceclofenac. This involves a comprehensive assessment of various parameters such as drug release kinetics, floating behavior, tablet integrity, and stability.[4]

Aceclofenac, a potent non-steroidal anti-inflammatory drug (NSAID), has garnered considerable attention in pharmaceutical research due to its therapeutic efficacy in managing pain and inflammation.[5] However, its short biological half-life and poor aqueous solubility present challenges in achieving optimal therapeutic outcomes.[6] To address these limitations, researchers have explored various formulation strategies, with a particular focus on developing novel drug delivery systems such as floating tablets. A study by Jain et al. (2008) investigated the formulation and development of a novel floating tablet of aceclofenac. By employing hydrophilic polymers such as hydroxypropyl methylcellulose (HPMC) and sodium alginate, the researchers aimed to prolong gastric residence time and improve drug absorption.[7] The study highlighted the importance of formulation parameters such as polymer concentration and tablet hardness in modulating drug release kinetics and floating behavior.

Banerjee et al. (2006) conducted a comparative bioavailability study of aceclofenac formulated as a microemulsion and as a conventional tablet. Their findings underscored the potential of novel drug delivery systems in enhancing drug solubility and bioavailability.[8] The study emphasized the role of formulation design in overcoming the challenges associated with the poor aqueous solubility of aceclofenac. Floating drug delivery systems have emerged as promising approaches to overcome the limitations of conventional dosage forms. Streubel et al. (2002) developed floating microparticles based on low-density foam powder, demonstrating their potential for sustained drug release and improved gastric retention.[9] Similarly, Sinha et al. (2004) investigated the development of controlled-release buccoadhesive hydrophilic matrices for drugs such as diltiazem hydrochloride, highlighting the importance of optimizing bioadhesion, dissolution, and diffusion parameters.[10] Overall, the literature underscores the significance of innovative drug delivery systems in enhancing the therapeutic efficacy of aceclofenac. By prolonging gastric residence time, improving drug solubility, and controlling drug release kinetics, floating tablets offer a promising approach for optimizing the pharmacokinetic profile of aceclofenac and improving patient compliance.

METHODS

PREFORMULATION STUDIES

Preformulation is defined as application of biopharmaceutical principles to the physicochemical properties of the drug. It is a phase of R & D process.[11-12]

FTIR Spectroscopy

IR spectra of aceclofenac, was obtained by a Perkin-Elmer Fourier transform infrared spectrophotometer using KBr pellets.[13]

Melting point

Aceclofenac MP was measured by capillary tube method.

Loss on drying

10gms Aceclofenac was heated to a temperature of 105ºC in hot air oven until it remains constant weight. The formula was.

$$\text{Percentage LOD} = \frac{\text{Initial weight - Final weight}}{\text{Initial weight}} \text{ X } 100$$

Angle of repose

It was measured by fixed funnel technique. In this technique a funnel containing aceclofenac was kept at a fixed height, and it was allowed to flow to the surface which contains graph paper. This is due to gravitational force. The height and radius of the heap formed was measured. The formula for angle of repose (θ) was

$\theta = \tan^{-1}(h/r)$

Bulk density & Tapped density

Bulk densities of granules were determined by pouring gently 20 gm of sample through a glass funnel into a 100 ml graduated cylinder. The volume occupied by the sample was recorded. Bulk density and tapped density were calculated by the formula.

$$\text{Bulk Density} = \frac{\text{Mass of Powder}}{\text{Volume of Powder (Untapped)}}$$

$$\text{Tapped Density} = \frac{\text{Mass of Powder}}{\text{Volume of Powder (Tapped)}}$$

Compressibility Index

CI of the powder was determined from the bulk and tap density as follows.

$$\text{Percentage Compressibility Index} = 100 \text{ X } \frac{(\text{Tapped Density - Bulk Density})}{\text{Tapped Density}}$$

Hausner's ratio

$$\text{Hausner ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

It was calculated as

COMPATIBILITY STUDIES

IR Spectroscopy

IR spectra of pure aceclofenac, polymer and combination of aceclofenac with polymers were obtained by using Perkin-Elmer Fourier transform infrared spectrophotometer. The scanning range used was 4000 to 400cm^{-1}.

STANDARD GRAPH OF ACECLOFENAC

Standard graphs of the drug were prepared using standard aceclofenac solution in acid buffer pH 1.2, phosphate buffer pH 6.8 & pH 7.4 containing 5 to 50µg. The absorbance was measured at 275nm. Linear relationship was observed with absorption to concentration of drug. The values of absorbance related to concentration were given in table and graphs were given in figure.

FORMULATION

Table 5: Formulation trails of Aceclofenac floating tablets (AF1 – AF5)

S.NO.	INGREDIENTS	AF1 (mg)	AF2 (mg)	AF3 (mg)	AF4 (mg)	AF5 (mg)
1.	Aceclofenac	200	200	200	200	200
2.	HPMC	200	_	_	100	100
3.	Carbopol 940	_	200	_	100	_
4.	Guar gum	_	_	200	_	100
5.	Citric acid	20	20	20	20	20
6.	Sodium CMC	20	20	20	20	20
7.	Sodium bicarbonate	20	20	20	20	20
8.	Magnesium stearate	5	5	5	5	5
9.	Talc	5	5	5	5	5
Total Weight		470	470	470	470	470

Aceclofenac floating tablets were prepared by direct compression method using excipients and polymers to release the drug sustainably after administration.

Accurately weighed quantities of excipients were placed in a mortar and gradually mixed with constant kneading to ensure homogenous mass. Then the homogenous powder was passed through sieve number 40 and the powder was retained on sieve number 100. Then the powder was lubricated with magnesium stearate and talc. Then the powder was directly compressed into tablets on a tablet punching machine.

EVALUATION OF FLOATING TABLETS

Standard graph of Aceclofenac

The λ max of aceclofenac in 0.1 N HCl was scanned to be 275 nm using UV spectrometer. The standard graph of aceclofenac was dissolved in required quantity of 0.1N HCl and made up the volume 100 ml using 0.1N HCl. To obtain the stock solution of concentration 1mg/ml, from this 1 ml was taken and diluted to 100ml using 0.1N HCl to obtain working stock solution of concentration. From the above solutions 5, 10, 15, 20,2 5ml was taken to dilute to 10ml using 0.1N HCl to obtain the concentration of 5,10,15,20,25µg/ml.

EVALUATION OF PHYSICAL PROPERTIES

Weight variation

Weigh 20 tablets selected at random and calculate the average weight. Not more than two of the individual weights deviate from the average by more than the percentage shown in table below and none deviates by more than twice that percentage.

Friability

20 tablets were weighed and placed in the Roche friabilator where the tablets were exposed to rolling and repeated shocks resulting from free falls within the apparatus, after 100 revolutions, the weighed again. The friability was determined as the percentage loss in the weight of the tablets. A loss of less than 0.5 to 1% in weight is generally considered acceptable.

Hardness

Hardness was measured using Pfizer hardness tester which measure the pressure required to break the diametrical placed tablets by the pressure with coiled spring.

Content Uniformity

It is the amount present in each formulation for formulation (or tablets).

Tablets from formulation was taken and dropped in 100ml 0.1N HCl in a beaker. After 24 hrs or when the drug is released completely the same sample was withdrawn (about 1ml) and diluted to 10ml with 0.1N HCL and absorbance was taken at 275nm using UV spectrometer. From the standard graph % drug release was calculated.

Thickness

The thickness of the tablet is measured by using screw gauge. It gives the changes in weight variation of the tablet.

Floating lag time

The floating lag time is determined in order to assess the time taken by the dosage to float on the top of the dissolution medium, after placing the dosage form in the medium.

Floating time

It is the time the tablet constantly floats on the dissolution medium (i.e. duration of floating) in the dissolution medium.

Dissolution studies

Aceclofenac floating tablets were kept in dissolution medium 0.1N HCl (900ml) for initial 2 hours and operated at temperature 37±0.50C and rotated at 75 rpm. Then pH 6.8 phosphate buffer (900ml) was used as dissolution medium. Freshly prepared dissolution medium is used always. Type paddle apparatus is used. About 5ml of the dissolution medium was pipetted out for every 15, 30, 60, 120, 240, 480, 960 mins and the volume was adjusted using by replacing with 5ml of 0.1N HCl or with pH 6.8 phosphate buffer. The samples collected were analysed using UV spectrometer at 275nm.

RESULTS AND DISCUSSION

Preformulation Studies

In preformulation studies drug characteristics was performed and results were complying with pharmacopeial values.

Standard graph of Aceclofenac: The dissolution studies for the floating tablet have to be conducted in 0.1N HCl. Hence, UV spectrum of aceclofenac in 0.1N HCl was recorded on Elico spectrophotometer. The spectrum has shown λmax of 275nm which is selected for the construction of standard graph of aceclofenac in 0.1N HCl.

A plot of absorbance Vs concentration of aceclofenac in 0.1N HCl is found to be linear in the concentration range of 5-25µg/ml indicating a perfect relation between drug concentration and absorbance.

Table 6: Standard plot of Aceclofenac.

CONCENTRATION (µg/ml)	ABSORBANCE
5	0.065
10	0.131
15	0.192
20	0.252
25	0.321

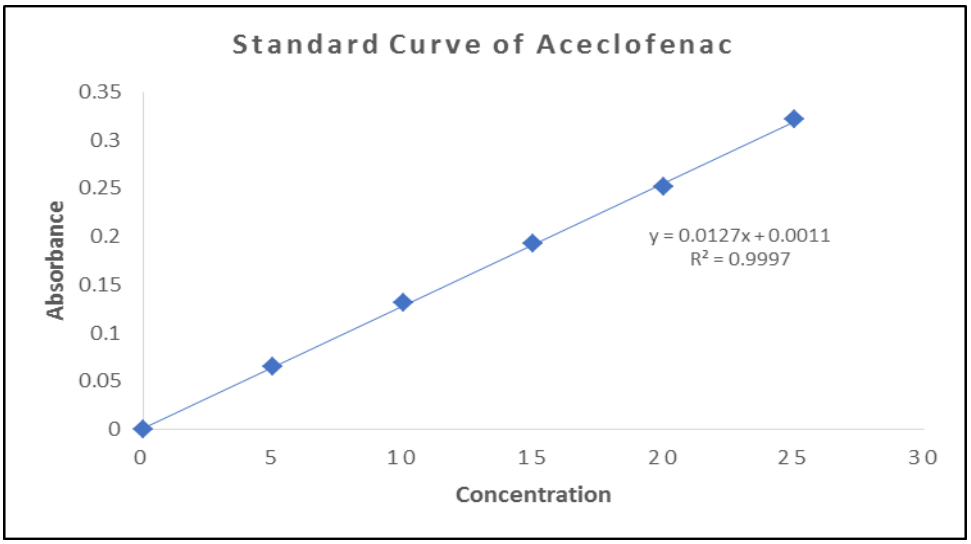

Figure 1: Standard curve of Aceclofenac.

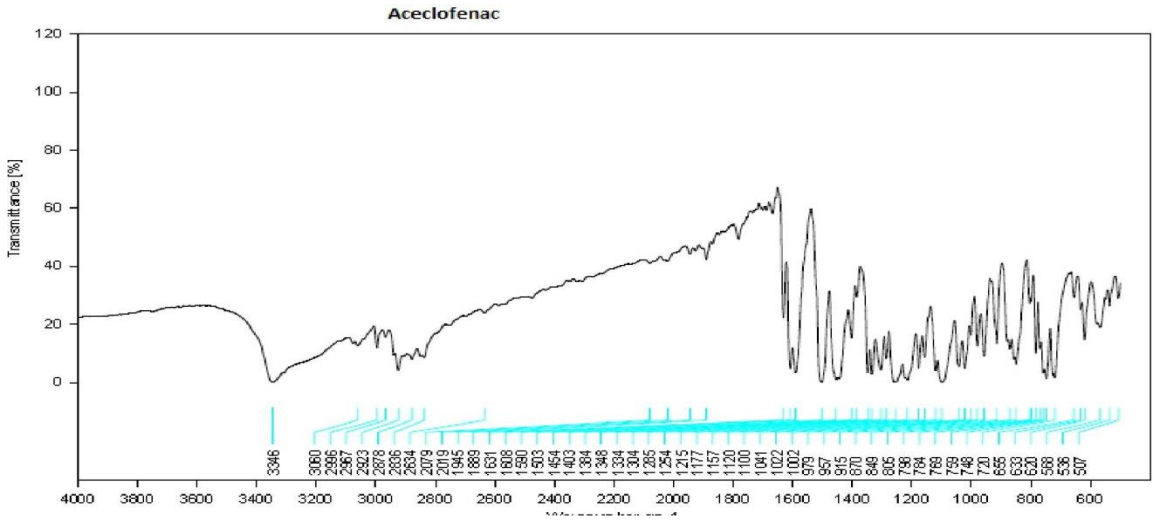

Figure 2: FTIR of Aceclofenac.

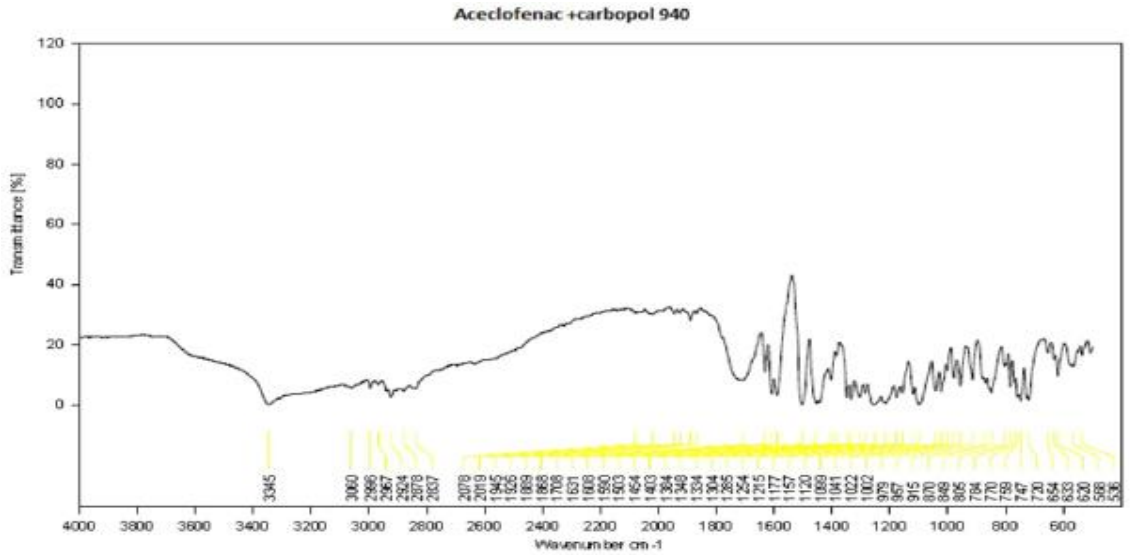

Figure 2: FTIR of Aceclofenac + Carbopol 940.

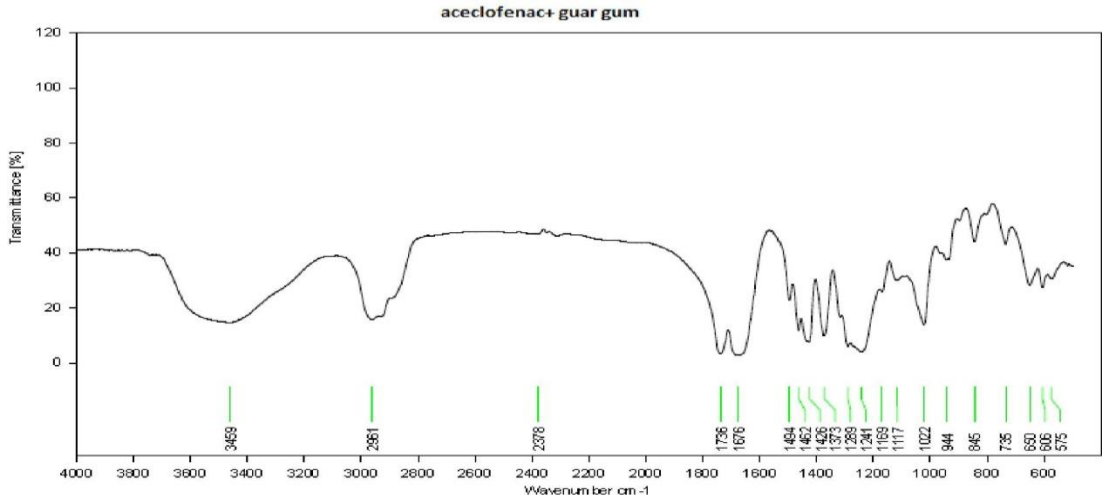

Figure 3: FTIR of Aceclofenac + guar gum.

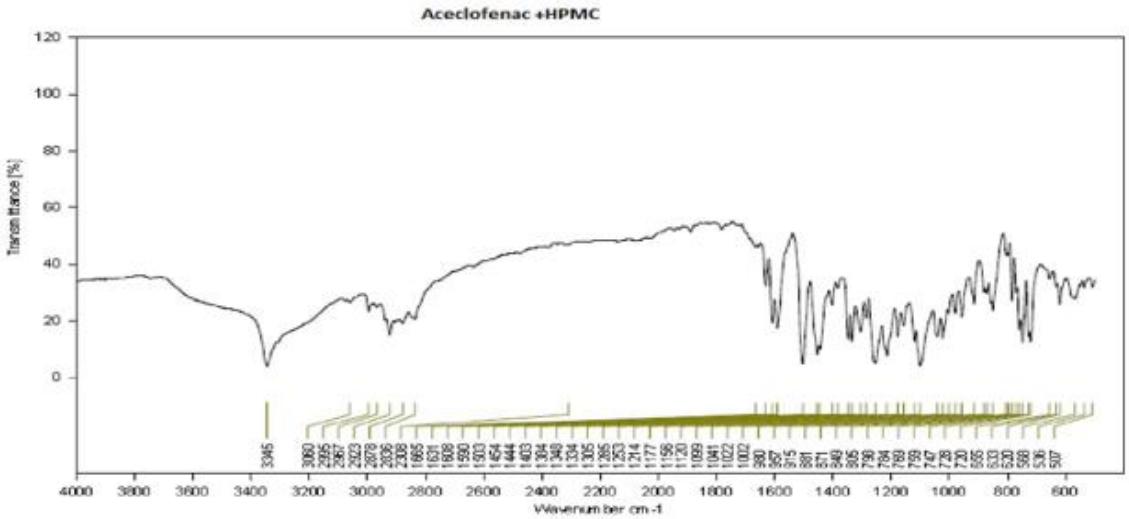

Figure 4: FTIR of Aceclofenac + HPMC.

Evaluation of Floating Tablets

It is always necessary that the dosage forms prepared have to be evaluated for their characteristic properties. Hence quality control tests of tablets are performed to assess various properties of tablets.

Table: Preformulation.

Formulation	Angle of repose (θ)	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Hausner ratio (HR)
AF1	28.1±0.01	0.57±0.01	0.71±0.04	1.24±0.01
AF2	26.3±0.02	0.55±0.02	0.67±0.03	1.22±0.02
AF3	27.6±0.03	0.55±0.01	0.70±0.01	1.27±0.03
AF4	26.9±0.04	0.54±0.03	0.73±0.03	1.35±0.01
AF5	26.9±0.05	0.53±0.04	0.67±0.03	1.26±0.02

i. Weight variation: Tablets exhibit variation due to improper filling of die cavity, uneven distribution of ingredients in the compression and variation in compressional pressure.

The total weight of each formulation is not maintained constant but the weight variation is in the range of +/-5% w/w indicating good control of compression process.

S.NO.	FORMULATION	WEIGHT VARIATION (mg)
1.	AF1	460±0.12
2.	AF2	462±0.34
3.	AF3	460±0.33
4.	AF4	460±0.33
5.	AF5	457±0.42

ii. Friability: It is a measure of tablet strength. It is related to tablets ability to withstand both shock and abrasion without crumbing during the handling of manufacture, jacking, shipment and consumer use.

The friability was determined as the percentage loss in the weight of the tablets. A loss of less than 0.5 to 1% in weight is generally considered acceptable.

Table: Percentage Friability for (AF1-AF5)

S.NO.	FORMULATION	FRIABILITY (%)
1.	AF1	0.25±0.01
2.	AF2	0.30±0.06
3.	AF3	0.45±0.04
4.	AF4	0.55±0.02
5.	AF5	0.21±0.03

iii. Hardness: Hardness was measured using Pfizer hardness tester which measure the pressure required to break the diametrical placed tablets by the pressure with coiled spring.

iv. Thickness: The thickness of the tablet is measured by using screw gauge. It gives the changes in weight variation of the tablet.

Table: Hardness for (AF1-AF5).

S.NO.	FORMULATION	HARDNESS
1.	AF1	4.5±0.2
2.	AF2	5.0±0.1
3.	AF3	4.5±0.12
4.	AF4	5.0±0.16
5.	AF5	5.5±0.09

Table: Thickness for (AF1-AF5).

S.NO.	FORMULATION	THICKNESS (mm)
1.	AF1	3.0±0.01
2.	AF2	2.9±0.05
3.	AF3	3.1±0.02
4.	AF4	3.2±0.02
5.	AF5	3.0±0.02

v. Floating lag time: The floating lag time is determined in order to assess the time taken by the dosage to float on the top of the dissolution medium, after placing the dosage form in the medium.

Table: Floating lag time (sec) & Floating time (hrs) for (AF1-AF5)

S.NO.	FORMULATION	FLOATING LAG TIME (sec)	FLOATING TIME (hrs)
1.	AF1	30	8
2.	AF2	120	9
3.	AF3	40	6
4.	AF4	75	6
5.	AF5	240	9

vi. Drug content

Table: Percentage Drug content for (AF1-AF5)

S.NO.	FORMULATION	DRUG CONTENT (%)
1.	AF1	98.5±0.1
2.	AF2	97.2±0.2
3.	AF3	98.1±0.6
4.	AF4	97.5±0.5
5.	AF5	98.3±0.1

vii. Dissolution studies: Freshly prepared dissolution medium i.e. 900ml 0.1N HCl in each dissolution vessel of dissolution paddle apparatus maintained at temperature 37+/-0.50°C and rotated at 75 rpm. The tablets of aceclofenac were placed in dissolution medium. About 5ml of the dissolution medium was pipetted out for every 15, 30, 60, 120, 240, 480, 960 min and the volume was adjusted using by replacing with 5ml of 0.1N HCl. The above samples i.e. 5ml (7 samples) were collected in a volumetric flask and make up the volume to 10ml with 0.1N HCl. Finally, the absorbance of the solution was taken using UV spectrometer at 275 nm.

Table: Percentage Cumulative Drug Release.

TIME (h)	% CUMULATIVE DRUG RELEASE				
Formulations	AF1	AF2	AF3	AF4	AF5
0	0	0	0	0	0
1	20.3	12.8	16.9	17.9	13.6
2	43.5	13.2	24.3	22.7	21.6
4	59.1	28.9	32.5	36.3	33.6
8	72.6	37.1	46.3	44.3	44.8
12	80.4	46.5	59.7	56.6	62.3
16	85.2	56.9	72.2	72.6	71.3
20	95.3	62.2	86.9	82.1	76.8
24	98.4	72.2	88.3	84.1	80.3

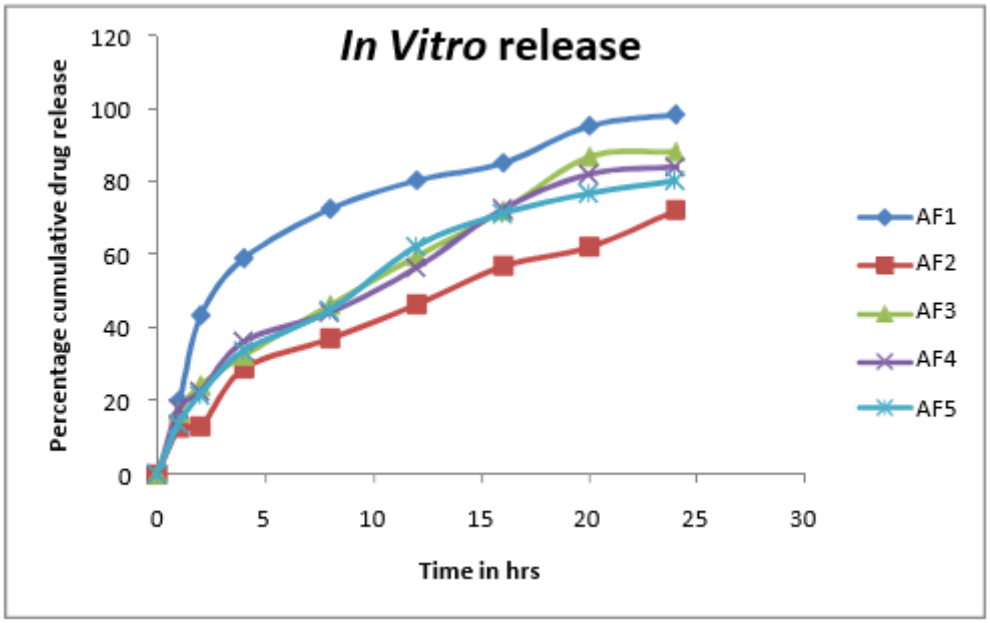

Figure 5: Cumulative % Drug Release Curve.

SUMMARY

The project aimed to develop floating tablets of aceclofenac, a drug renowned for its anti-inflammatory and analgesic properties, to enhance gastric residence time and improve drug bioavailability. Aceclofenac's effectiveness in treating inflammation, pain management, and alleviating symptoms in conditions like rheumatoid arthritis and ankylosing spondylitis underscores its importance as a model drug for this formulation. Utilizing various polymers such as HPMC, Carbopol 940, and guar gum, five formulations (AF1-AF5) were designed and prepared via direct compression method. Evaluation of the formulations revealed satisfactory flow properties, weight variation, content uniformity, hardness, and friability. Importantly, the floating lag time met the criteria for floating drug delivery systems. Among the formulations, AF1, incorporating HPMC, exhibited the best floating time of 8 hours and a remarkable drug release of 98.4% within 24 hours. These findings underscore the potential of aceclofenac floating tablets in prolonging drug release and enhancing therapeutic efficacy. However, further research, particularly in vivo studies, is warranted to validate the effectiveness of these formulations.

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CONFLICT OF INTEREST

No authors declared Conflict of Interest.

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