International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 1 Jan-Feb 2022, pp: 14-23 www.ijprajournal.com ISSN: 2249-7781

Formulation and Evaluation of Floating Tablet of Aceclofenac

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Submitted: 01-01-2022 Accepted: 10-01-2022

ABSTRACT

Formulation development is an important part of drug design and development. Bioavailability and bioequivalence are totally dependent on formulation development. Now-a-days formulation development is done by following QbD (Quality by design). The aim of present study to formulate floating tablet of Aceclofenac by using different polymer. Floating tablets of Aceclofenac were formulated by employing the direct compression method.The prepared floating tablets were evaluated for various parameters like weight variation, hardness, friability, disintegration time, drug content, floating time, in-vitro drug release, and FTIR. Pre-formulation studies of Aceclofenac drug were performed. The FTIR studies revealed that there is no chemical interaction with excipients. Percentage weight variation and drug content uniformity were found to be within the approved range of all the formulations. Evaluation parameters like hardness and friability indicated good mechanical resistance of the tablets for all the formulations. The Floating Tablet were subjected to various post compressed evaluation parameters and based on that, it was concluded each formulation was found to be an optimized formulation, except for F1 & F2, providing a quick onset with faster absorption, showing a better therapeutic effect.

Keyword: Floating Tablets, Aceclofenac, Inflammation

I. INTRODUCTION

The oral route is considered as the most promising safe and effective route of drug delivery. Effective oral drug delivery may depend upon the factors such as gastric emptying process, gastrointestinal transit time of dosage form, drug release from the dosage form and site of absorption of drugs.(1)

Floating drug delivery systems (FDDS) are invented to retain the drug in the stomach and applicable for drugs with poor solubility and low stability in intestinal fluids. The basis behind FDDS is making the dosage form less dense than the gastric fluids to make it float on them. FDDS are hydro-dynamically controlled low-density systems with sufficient buoyancy to float over the gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. The residual system is emptied from the stomach with the release of the drug. This results in enhanced gastric residence time and good control over plasma drug concentration fluctuations. The principle of buoyant preparation offers a simple and practical approach to achieve increased gastric residence time for the dosage form and sustained drug release.(2) Prolonging the gastric retention of a delivery system is desirable for achieving the greater therapeutic efficacy of the drug substance under certain circumstances. For example, drugs which show better absorption at the proximal part of the gastrointestinal tract and drugs with low solubility and get degraded in alkaline pH found efficient in prolonging gastric retention. In addition, for sustained drug delivery to the stomach and proximal small intestine in treating certain ulcerative conditions, prolong gastric retention of the therapeutic moiety and hence offer numerous advantages including improved bioavailability and therapeutic efficacy with reduction of dosing frequency.(3)

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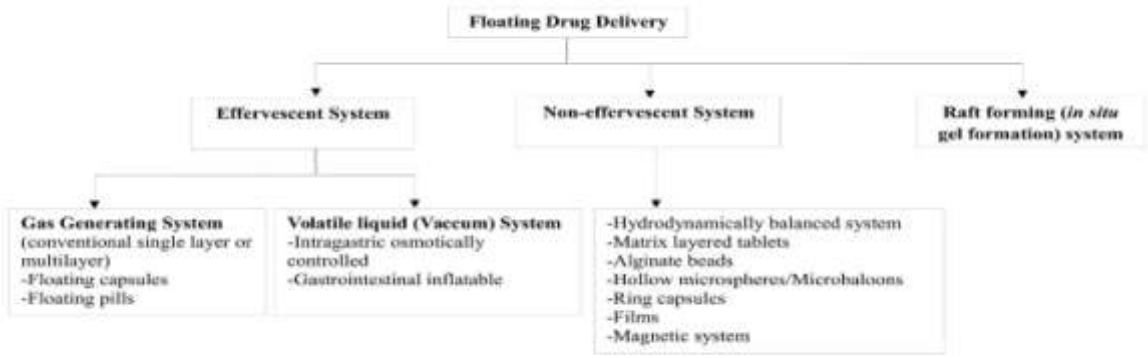

Figure. 1: Classification of floating drug delivery system (FDDS)

1.1 Advantages of floating drug delivery system

- Floating dosage systems are delivery systems with gastric retentive behavior and offer several advantages in drug delivery.
- Simple and conventional technique for formulation.
- Site-specific drug delivery.
- Controlled delivery of drugs.
- Delivery of drugs for residual action at a specific site in the stomach.
- Improved drug absorption with increased GRT and excess duration of contact of dosage regimen at its target site.
- Minimizing irritation of GIT mucosa by the drugs with slow release rate. Acidic drug substances like aspirin cause irritation to gastric mucosa as it comes in contact. Hence HBS formulation would be beneficial in administration of aspirin and other similar drugs. Administration of prolonged release floating dosage forms, tablet or capsules, causes dissolution of the drug in the gastric fluid. They dissolve in the gastric fluid before getting absorbed in the small intestine with emptying stomach contents. Hence it is expected that a drug will be fully absorbed from floating dosage forms if it remains in the solution form even at the alkaline pH of the intestine.
- When there would be vigorous intestinal movement with short transit time, it might result in a certain type of diarrhea hence poor absorption is expected. Under such conditions, it is advantageous to maintain the drug in floating condition in the stomach for better efficacy.
- In treating gastroesophageal reflux disorders (GERD).
- Ease of administration with higher patient compliance. The floating drug delivery system also carries certain disadvantages which limit its applicability [4].

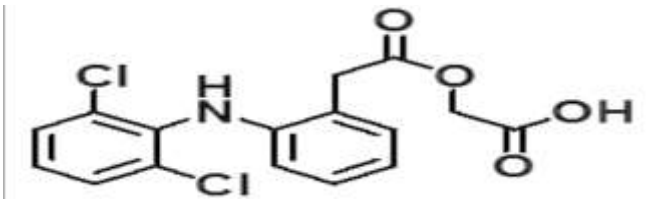

Fig 1: Structure of Aceclofenac

II. MATERIALS AND METHOD

MATERIALS:

Aceclofenac was obtained as a gift sample from Medopharm, Chennai, HPMC and Carbopol were obtained from the Otto Chemika-Biochemika reagents, Mumbai, Guar gum, Acacia gum was obtained from the Loba Chemie Pvt, Ltd, Mumbai, citric acid, sodium bicarbonate was obtained from Sisco Research Laboratories Pvt Ltd, Mumbai, magnesium stearate, and talc were obtained from U`niversal Scientific Appliances, Madurai, Chennai. All chemicals used obtained were of either AR/LR grade or the best possible pharma-grade supplied by the manufacturer.

METHODOLOGY:

PREFORMULATION STUDIES

The basic purpose of the pre-formulation activity are to provide a rational basis for the

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formulation approaches, to maximize the chances of success in formulating an acceptable product and to ultimately provide a basis for optimizing drug product quality and performance. Preformulation is defined as an investigation of physical & chemical properties of sustained release matrix tablet substance alone and when combined with excipient. A step in time saves nine, so the Preformulation studies of the new product can away the disaster that is disasters are prevented in advance.

Melting point

Melting point of drug sample was determined by using melting point apparatus. A few quantity of drug sample was taken and placed in a thin walled capillary tube; the tube was approximately 10-12 cm in length with 1mm in diameter and closed at one end. The capillary which contain sample was placed in melting point apparatus and heated and when drug sample was melted the melting point of sample powder was noted.[5],[6]

Determination of solubility

a. Qualitative Solubility

Qualitative solubility analysis of drugs were done by dissolving 5 mg of drug in 5 ml of distilled water and different solvents such as HCl (0.1N), Saline phosphate buffer (pH 7.4), Phosphate buffer(pH 6.8), ethanol, acetone and chloroform were used to determine the solubility of drug.

b. Quantitative Solubility

Quantitative solubility analysis of drugs were done by 5 ml each solvent and drug in gm(s) into the solvent till saturation of solvent. Different solvents were used for the solubility determination like distilled water, phosphate buffer (pH 7.4), Phosphate buffer (pH 6.8), HCl (0.1N) and NaOH (0.05N). This is done to determine the capacity of the solvent for dissolving the drug in it. The concentration of drug is measured by UV spectrophotometer.[8]

Partition coefficient

10 mg drug was added in 50 ml of n-Octanol (pre saturated with water) and it was shaken and then 50 ml of distilled water (pre saturated with n- Octanol) was added and was shaken the mixture by mechanical shaker for 24 hours. After 24 hour both phases are separated. Absorbance was taken of both the phases and calculated the concentration in each phases Po/w = Coil/Cwater.[9],[10]

Determinations of λ max & prepare standard curve

Preparation of 0.1 N HCL

8.5 ml of concentrated hydrochloric acid was diluted with distilled water and the volume was made upto 1000 ml with distilled water.

Preparation of standard stock solution in 0.1N HCL

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.

Drug excipient compatibility by FTIR

FTIR study of drug sample and identification studies was performed by potassium bromide (KBr) dispersion method (Shimadzu). Samples were prepared with KBr pellets (2 mg sample in 200 mg KBr) with a hydrostatic force of 5.2 N cm-2 for 3 minutes. The scanning range was 400 to 4000 cm-1 and the resolution was 4 cm-1.

Formulation of Aceclofenac Floating tablet :

This was formulated using direct compression method. Following formulation table was followed during the preparation of Aceclofenac tablet.

S.No.	Ingredients	AF1 (mg)	AF2 (mg)	AF3 (mg)	AF4 (mg)	AF5 (mg)	AF6 (mg)
1	Aceclofenac	25	25	25	25	25	20
2	HPMC	25			12.5	12.5	10
3	Carbopol 940		25		12.5		10
4	Guar gum			25		12.5	10
5	Citric acid	15	15	15	15	15	15
6	Sodium CMC	15	15	15	15	15	15
7	Sodium bicarbonate	15	15	15	15	15	15
8	Magnesium	3	3	3	3	3	3

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	stearate						
9	Talc	2	2	2	2	2	2
Total Weight		100	100	100	100	100	100

Post composed evaluation parameter

Weight variation

Twenty tablets were randomly selected and individually weighed. The average weight of 20 tablets was calculated. The individual tablet weights were compared to the average weight.

IP Standards for uniformity of weight

S.no.	Average weight of tablet	Percentage of deviation ,
1.	< 80 mg	10
2.	80 – 250 mg	7.5
3.	>250mg	5

Hardness The hardness of the tablet was defined as the force required breaking a tablet in a diametral compression test. The hardness of the tablet was measured on a Monsanto hardness meter in a range between 7 and 9 kg / cm2. The hardness of the tablet reflects the differences in density and porosity of the tablet, which should produce different drug release patterns influencing the rate of dissolution liquid penetration on the tablet surface. (51)

Friability

The tablets require a certain amount of strength or hardness and strength to withstand the mechanical shock of handling in production, packaging and shipping. A pre-weighed sample (20 tablets) was placed in the crusher and run for 100 revolutions, then the tablets were weighed again and the friability percentage was calculated using the formula**.**

F = 1 – Wo/ W× 100

Where, Wo=Weight of tablet before test, W= Weight of tablet after test

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.

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**.** (52)

Floating

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±0.50 C 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.

III. RESULTS AND DISCUSSION

Organoleptic Evaluation: Aceclofenac API was white powder and found to have white colour with a slightly bitter in taste. It didn't have any odour associated with it.

Melting Point: Melting point of drug sample was determined by using melting point apparatus. A few quantity of drug sample was taken and placed in a thin walled capillary tube; the tube was approximately 10-12 cm in length with 1mm in diameter and closed at one end. The capillary which contain sample was placed in melting point apparatus and heated and when drug sample was melted the melting point of sample powder was noted. The melting point of came out to be 149^0C.

Solubility: The solubility of the drug Aceclofenac is seen freelysoluble in ethanol and acetone where as is insoluble.

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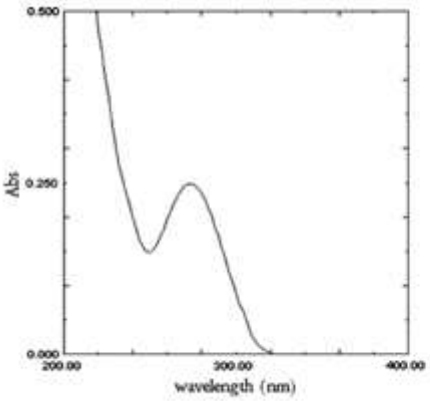
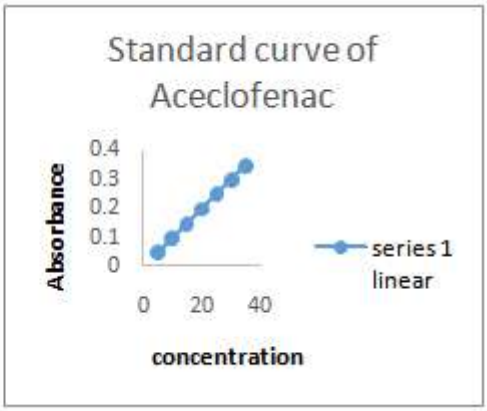
Partition coefficient: The partition coefficient of Aceclofenac is calculated as mean± SD and the results were

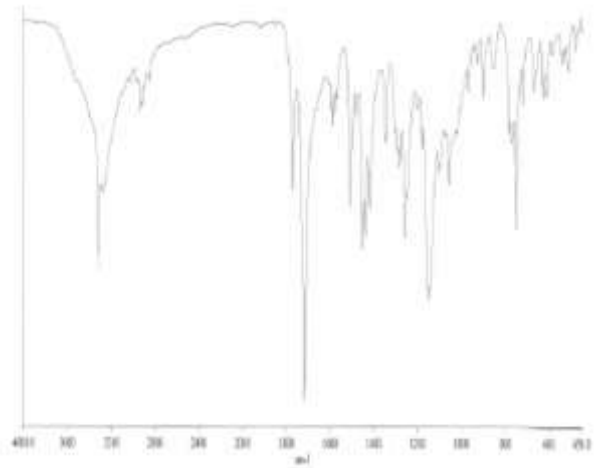
Concluded as 1.30± 0.3

λ max and Standard curve of Aceclofenac





Drug Compatability Studies:



FTIR of Aceclofenac

FTIR Spectra of Aceclofenac + HPMC + Carbopol 940 + Guar gum

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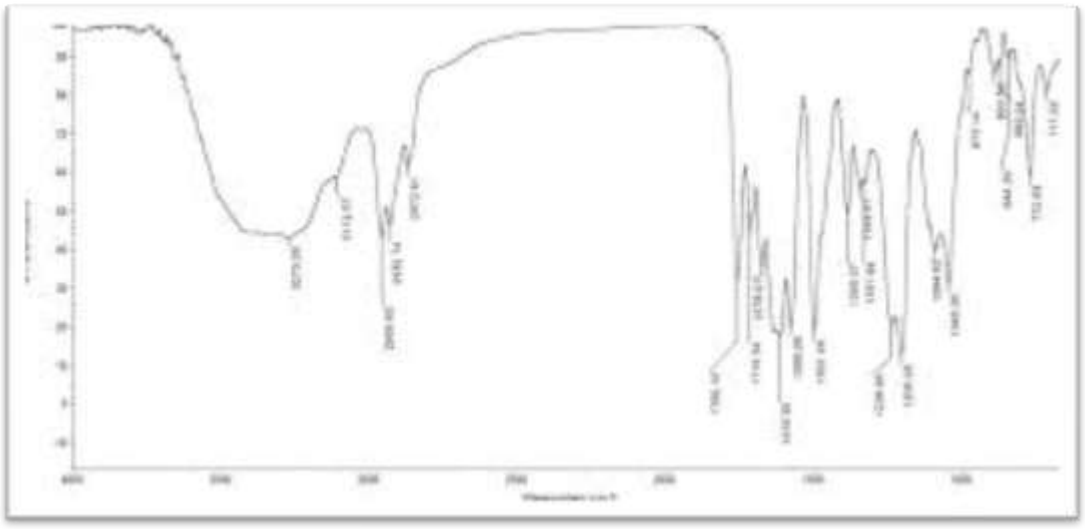
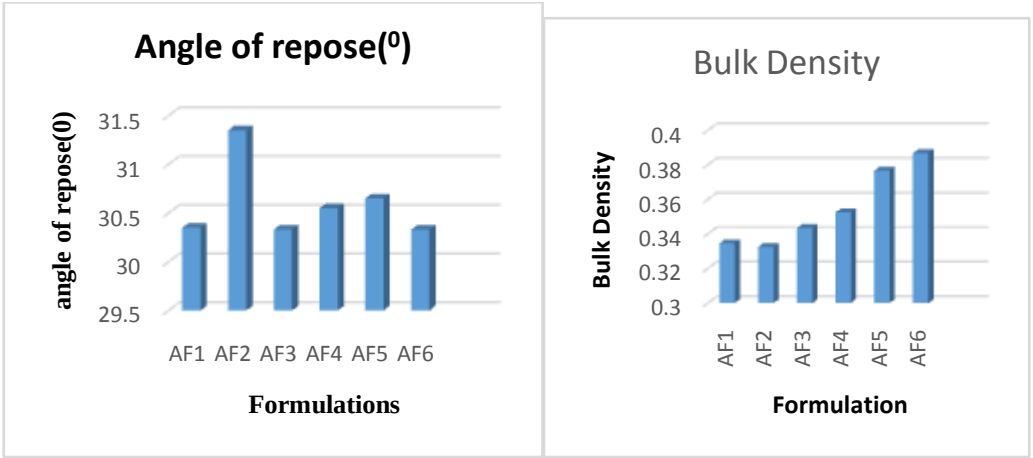


Pre-compressed evaluation studies: Factors including density, porosity drug content, and flowability were studied. Results are tabulated below**:**

Pre-evaluation parameters of Aceclofenac

S.No.	Formulation	Angle of Repose (θ)	Bulk Density (gm/cm^3)	Tapped Density (gm/cm^3)	Car's Index	Hausner Ratio (HR)
1	AF1	30.35	0.3346	0.4456	24.91	1.33
2	AF2	31.35	0.3324	0.4343	23.46	1.30
3	AF3	30.33	0.3434	0.4563	24.74	1.32
4	AF4	30.55	0.3524	0.4362	19.21	1.23
5	AF5	30.65	0.3767	0.4456	15.46	1.18
6	AF6	30.33	0.3867	0.4365	11.58	1.12



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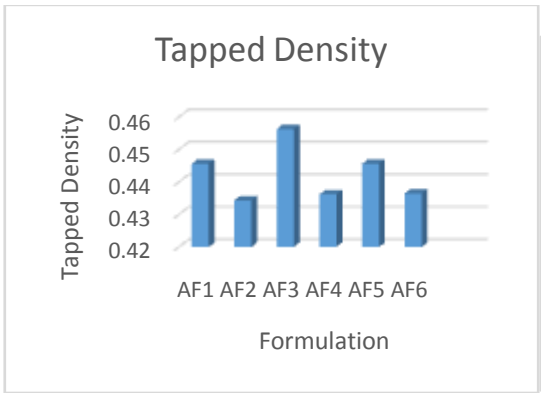

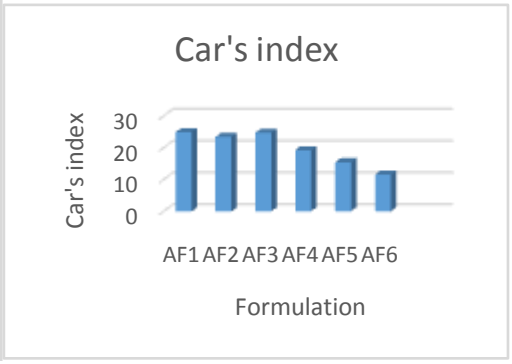

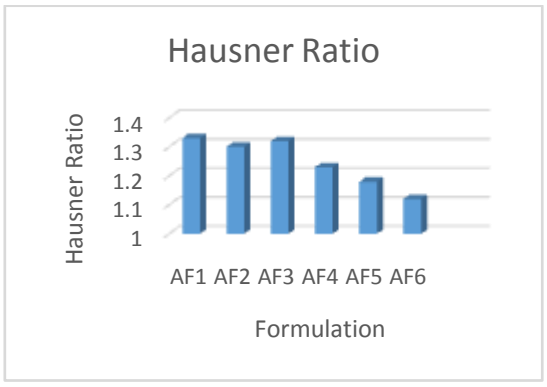

Graphs of Pre evaluation reading

Post compressional evaluation studies:

These factors were evaluated for the Aceclofenac for the quality test of the tablet. Results were tabulated below:-

S.No.	Formulation	WEIGHT VARIATION (mg)	Hardness (Kg/cm2)	FRIABILITY (%)	THICKNESS (mm)	Drug content (%)	Floating lag/time sec
1	AF1	97 ± 0.45	3.0 ± 0.03	0.19 ± 0.04	3.0 ± 0.02	97.5 ± 0.1	43 ± 2.6
2	AF2	102 ± 0.15	3.5 ± 0.06	0.22 ± 0.03	2.9 ± 0.01	98.2 ± 0.3	42 ± 3.4
3	AF3	98 ± 0.25	3.2 ± 0.07	0.26 ± 0.06	3.1 ± 0.02	99.3 ± 0.4	34 ± 2.8
4	AF4	101 ± 0.30	3.5 ± 0.06	0.28 ± 0.43	2.8 ± 0.05	96.8 ± 0.6	32 ± 2.6
5	AF5	102 ± 0.35	3.3 ± 0.04	0.26 ± 0.34	3.2 ± 0.04	97.5 ± 0.4	28 ± 1.2
6	AF6	99 ± 0.15	3.1 ± 0.02	0.38 ± 0.33	3.3 ± 0.03	98.6 ± 0.3	30 ± 2..2

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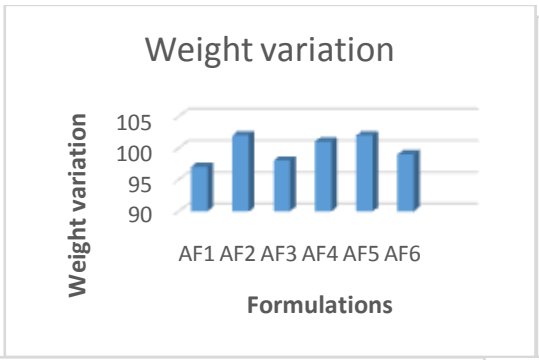

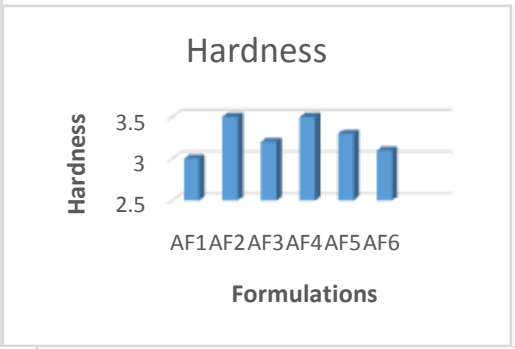

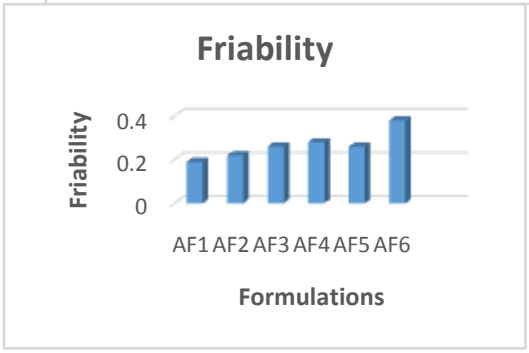

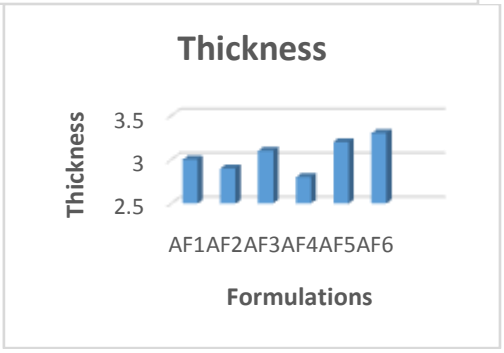

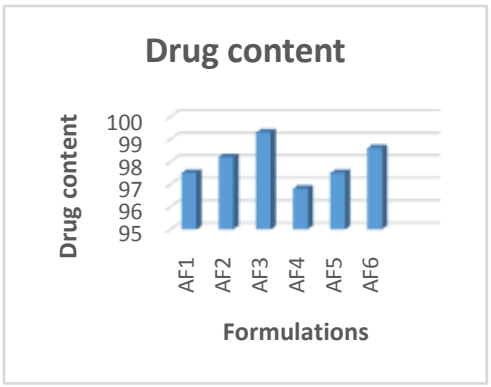

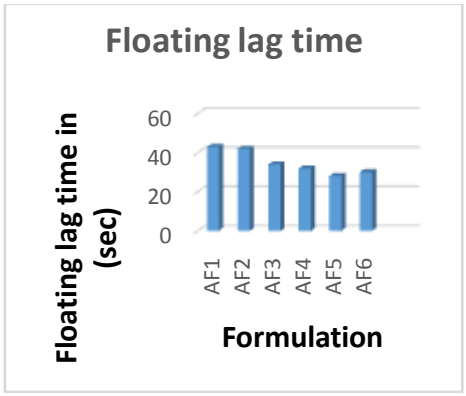

Graphs of Post compressional evaluation studies

Percentage Cumulative Drug Release

TIME(h)	**% Cumulative Drug Release**					
Formulations	**AF1**	**AF2**	**AF3**	**AF4**	**AF5**	**AF6**
0	0	0	0	0	0	0
1	20.3	12.8	16.9	15.9	13.6	15.7
2	42.5	12.2	23.3	22.7	21.5	20.5
4	58.1	28.5	31.5	35.3	33.3	40.3
8	71.6	37.1	45.3	42.3	43.8	50.4

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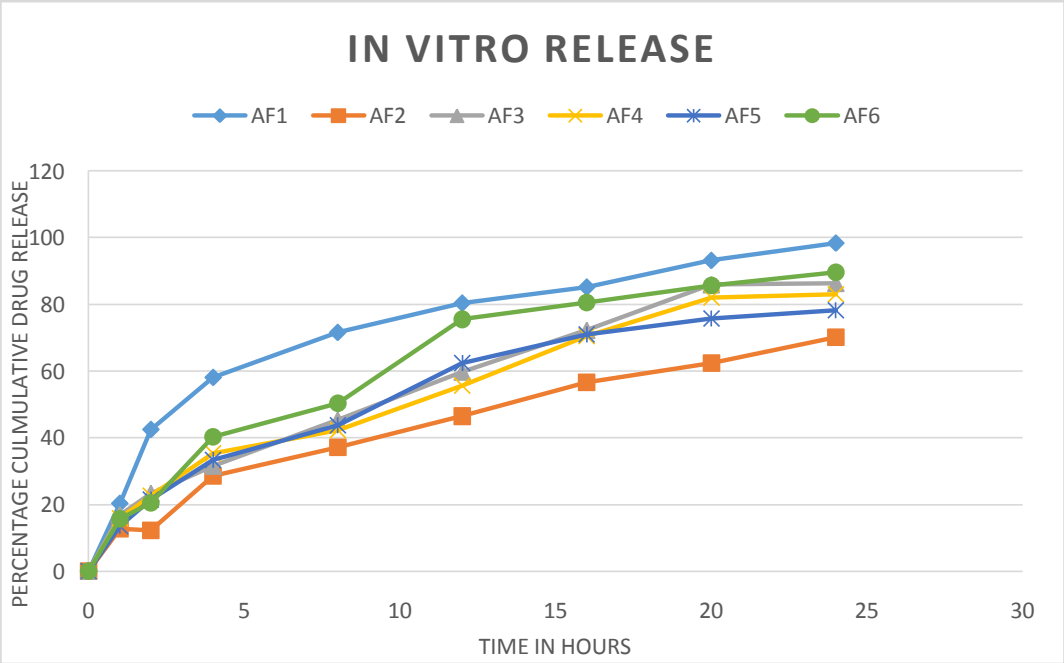
12	80.4	46.5	59.7	55.6	62.5	75.5
16	85.2	56.6	72.2	70.6	71.1	80.5
20	93.2	62.2	85.9	82.1	75.8	85.6
24	98.4	70.2	86.3	83.1	78.3	89.6



IV. SUMMARY AND CONCLUSION

Floating drug delivery systems prolongs the gastric residence time which in turn produces increased drug bioavailability. Due to its less density than the aqueous medium, it floats in the gastric fluid. These drug delivery systems are suitable in the stomach or in upper small intestine due to its narrow absorption window.

Inflammation is part of the complex biological response of vascular tissues to harmful stimuli, such as pathogens, damaged cells, or irritants. Inflammation is a protective attempt by the organism to remove the injurious stimuli and to initiate the healing process. In this present project, aceclofenac was used as a model drug for the floating tablets. Aceclofenac is used in the treatment of inflammation, and it is used as analgesic, anti-arthritic agent also.

Aceclofenac decrease pain and suppresses the disease severity and improves the therapeutic efficiency. It reduces pain in joint inflammation, pain intensity and the duration of morning stiffness in patients with rheumatoid arthritis. The duration of morning stiffness and pain intensity are reduced and spinal mobility improved, by aceclofenac in patients with ankylosing spondylitis.

Floating tablets of aceclofenac were developed to prolong gastric residence time and increase its bioavailability.

Floating tablets of aceclofenac were prepared using individual and combination of polymers. The polymers HPMC, Carbopol 940 and guar gum were used in different ratios. Totally seven formulations (AF1-AF6) were designed and formulated. The flow properties bulk density, tap density, angle of repose for the granules was determined and the results were found to be within the limit for all the formulations. The aceclofenac floating tablets were prepared by direct compression method. The direct compression method is easy, simple and ime consuming. These formulations (AF1-AF6) were evaluated for

various tests like weight variation, content uniformity, friability, hardness and dissolution studies.

The hardness and friability of the tablets were within the limits for all the formulations.

The weight variation of the tablets was found to be within the limits. The content uniformities of the prepared tablets were found to be within the limits. The floating lag time for the prepared formulation was ideal for the floating drug delivery systems.

The percentage drug release of the formulations AF1, AF2, AF3, AF4, AF5, and AF6, was 98.4, 70.2, 86.3, 83.1, 78.3, and 89.6 and up to 24 hour.

The formulation (AF1) prepared with HPMC showed good floating time and formulation (AF2) with carbopol 940 showed good floating time.

The formulation (AF1) with hydroxypropylmethyl cellulose was found to be best formulation with floating time of 8 hrs and drug release of about 98.4% at the end of 24th hour.

This present research work focuses on the floating tablets of aceclofenac, and succeeded in the formulation. But still research to be continued to in vivo studies to prove the effectiveness of the prepared aceclofenac floating tablets.

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