Design and *In vitro* Evaluation of Oral Floating Matrix Tablets of Aceclofenac

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ABSTRACT: The purpose of this research was to prepare floating matrix drug delivery system of aceclofenac.Floating matrix tablets of aceclofenac were developed to prolong gastric residence time and increase its bioavailability. Rapid gastrointestinal transit could result in incomplete drug release from the drug delivery system above the absorption zone leading to diminished efficacy of the administered dose. Floating matrix tablets containing 100 mg aceclofenac were developed using different bees wax combinations. The tablets were prepared by melt granulation technique, using polymers such as hydroxypropylmethylcellulose (HPMC K15M), ethyl cellulose, bees wax, cetyl alcohol, glycerin monostearate alone or in combination and other standard excipients. Sodium bicarbonate was incorporated as a gas-generating agent. The effects of sodium bicarbonate on drug release profile and floating properties were investigated. The formulation was optimized on the basis of acceptable tablet properties, floating lag time, total duration of floating and *in vitro* drug release. The resulting formulation produced monolithic tablets with optimum hardness, uniform thickness, consistent weight uniformity and low friability. The results of dissolution studies, floating lag time indicated that formulations F9 exhibited good and controlled drug release. Applying the linear regression analysis and model fitting showed the selected formulation F9 showed diffusion coupled with erosion drug release mechanism, followed first order kinetics. Optimized floating matrix tablets F9 showed no change in physical appearance, drug content, or in dissolution pattern after storage at 25^{0}C/ relative humidity 65% and 40°C / relative humidity 75% for a period of 3 months.
KEYWORDS: Aceclofenac, floating tablets, melt granulation, *in vitro* release.

INTRODUCTION

Oral administration is the most versatile, convenient and commonly employed route of drug delivery for systemic action. Indeed, for controlled release system, oral route of administration has received the more attention and success because gastrointestinal physiology offers more flexibility in dosage form design than other routes. Development of a successful oral controlled release drug delivery dosage form requires an understanding of three aspects: (1) gastrointestinal (GI) physiology (2) physiochemical properties of the drug and (3) dosage form characteristics[1-2].
Until now numerous oral controlled drug delivery systems have been developed to prolong drug release. The crucial point in this respect is that the drug has to be absorbed well throughout the whole gastrointestinal tract. For drugs with a narrow absorption window in the gastrointestinal tract or acting locally in the stomach, the challenging task is not only to prolong drug release but the retention of the dosage form in the upper gastrointestinal tract. This results in a higher bioavailability, reduced time intervals for drug administration and thus a better patient compliance. Various approaches for gastro retentive dosage forms have been proposed including mucoadhesive systems, swellable and floating systems[3-7]. As for reliable retention behaviour in the stomach food effects and the complex motility of the stomach play a major role, only convincing in vivo data can validate the retention efficacy of a developed system.
Floating drug delivery systems were first described by Davis in1968. These systems were used to prolong the gastric residence time of drug delivery systems. They

remain buoyant in the stomach for prolonged period of time without affecting the gastric emptying rate of other contents. A floating dosage form is useful for those drugs that act locally in the proximal gastrointestinal tract (GIT), are unstable in lower parts of GIT, or are poorly absorbed in the intestine[8-9].

Floating dosage forms are floating due to an intrinsic density lower than that of the gastric content, which is reported as 1.004–1.010 g/cm^3, or due to the formation of a gaseous phase inside the system after contact with gastric fluid[10]. This attribute allows them to remain afloat on the surface of the gastric content for a longer period of time without affecting the rate of emptying. Thus, for the development of a floating matrix drug delivery system selecting a suitable polymer with a bulk density of less than 1g/cm^3, forming a cohesive gel barrier and the ability to dissolve slowly enough to retain the drug over a longer period of time is representing a challenge[11].

Hydrocolloids of natural or semi synthetic origin are commonly used for the development of gastric floating matrix devices. Floating matrix systems containing HPMC as the matrix forming excipient begin to swell and form a gel layer with entrapped air around the tablet core after contact with gastric fluid, whereas this gel layer controls the drug release[12-15].

Another possibility for the induction of floatation lies in the incorporation of sodium bicarbonate as gas forming agent dispersed in a HPMC hydrogel matrix as a method[16-17].

Aceclofenac (2-[(2, 6-dichlorophenyl) amine] phenyl acetoxyacetic acid) is a newer non-steroidal anti-inflammatory drug (NSAID). Aceclofenac is a phenyl acetic acid derivative showing effective anti inflammatory and analgesic properties mainly used in osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis. Aceclofenac is rapidly and efficiently absorbed after oral administration but has a short half life of 3-4 h and requires multiple dosing for maintaining therapeutic effect throughout the day. The most frequent adverse side effects occurring with aceclofenac are gastrointestinal (GI) disturbances, peptic ulceration and GI bleeding, hence there is a potential need for a floating matrix dosage form for this drug to minimize gastric erosion side effect[18-21]. Its biological half-life on the other hand is very short, sustaining its anti-inflammatory activity only for a few hours and associated adverse effects; it is considered an ideal model drug for floating matrix drug delivery.

In context of the above principles, a strong need was recognized for the development of a dosage form to deliver aceclofenac in the stomach and to increase the efficiency of the drug, providing controlled release action. The objective of this study was to prepare floating matrix tablets of aceclofenac using hydrophobic wax materials, bees wax in combination with glyceryl monostearate, stearic acid or cetyl alcohol, sodium bicarbonate as gas generating agent and to evaluate the *in vitro* release characteristics and to predict and correlate the release behavior of aceclofenac from the matrix.

MATERIALS AND METHODS
Materials
Aceclofenac was obtained as gift sample from Lupin Research Park, Pune, India, Ethyl cellulose and stearic acid were purchased Ethyl cellulose was purchased from Merck Chemicals, Germany. Microcrystalline cellulose (Avicel pH 101) and cetyl alcohol were obtained as gift sample from Zydus Research Centre, Ahmedabad, India. Magnesium stearate and talc were procured from SD Fine Chemicals Ltd., Mumbai, India. All other reagents, solvents, chemicals used were of either pharamcopoeial or analytical grade.

Methods
Standard Calibration Curve of Aceclofenac
Solutions ranging from 3 to 6 µg/ml were prepared in 0.1 N HCl. Absorbance was measured for each solution at λ_{max} of 273 nm, using1601 PC Shimadzu UV Spectrophotometer. Correlation coefficient was found to be 0.9998 in 0.1 N HCl.

Drug-excipient compatibility studies
Fourier Transform Infrared (FTIR) Spectroscopy
FTIR spectra were recorded on samples prepared in potassium bromide (KBr) disks using a Shimadzu Corporation, (Tokyo, Japan) Model-1601 PC. Samples were prepared in KBr disks by means of a hydrostatic press at 6-8 tons pressure. The scanning range was 500 to 4000 cm^{-1}.

Differential Scanning Calorimetry (DSC)
DSC analysis was performed using Shimadzu DSC-60, Shimadzu Limited Japan. A 1:1 ratio of drug and excipient was weighed into aluminum crucible. And sample was analyzed by heating at a scanning rate of 20^0C over a temperature range 20^0-300^0 under nitrogen environment.

Preparation of Floating tablets by Melt granulation technique
Floating tablets, each containing 100 mg aceclofenac were prepared by a conventional melt granulation technique. The composition of various formulations of the tablets with their codes is listed in Table 1. The composition with respect to polymer combination was selected on the basis of trial preparation of tablets. The amount of bees wax was decreased gradually and the reduced amount of bees wax was replaced by cetyl alcohol. As per each formulation batch code required quantity of bees wax, cetyl alcohol, stearic acid and glycerin monostearate were weighed and melted separately in a large china dish over a water bath. The drug was added to the molten wax and mixed well. Previously weighed quantities of ethyl cellulose and sodium bi carbonate were added to the drug-wax mixture and mixed well. After thorough mixing the china dish was removed from water bath and cooled. The coherent mass was then scrapped from the china dish and was passed through sieve no.60.

Table 1: Formulae of Aceclofenac floating Tablets

Ingredients (mg/tablets)	Formulations									
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Aceclofenac	100	100	100	100	100	100	100	100	100	100
Bees wax	60	60	60	60	60	55	50	45	40	35
Ethyl cellulose	--	--	--	--	5	10	15	20	30	20
HPMC K15M	5	10	15	20	--	--	--	--	10	20
Stearic acid	10	20	30	--	--	--	--	--	--	--
Cetyl alcohol	--	--	--	--	--	--	30	40	50	20
Glyceryl monostearate	--	--	--	10	20	30	--	--	--	--
Avicel	116	96	76	86	86	71	71	61	36	71
Magnesium stearate	6	6	6	6	6	6	6	6	6	6
Talc	3	3	3	3	3	3	3	3	3	3
Sodium bicarbonate	0	5	10	15	20	25	25	25	25	25
Total weight of tablet (mg)	300	300	300	300	300	300	300	300	300	300

Evaluation of granules

Prior to compression into tablets, the granules were evaluated for properties such as;

1. Angle of repose

Angle of repose was determined by using funnel method. Powder was poured from a funnel that can be raised vertically until a maximum cone height, h, was obtained. Diameter of heap, D, was measured. The angle of repose, Θ, was calculated by formula

tan Θ = h / r

Θ = tan^{-1} (h / r)

Where, Θ is the angle of repose, h is the height in cm and r is the radius.

2. Bulk Density

Apparent bulk density was determined by pouring pre-sieved drug excipient blend into a graduated cylinder and measuring the volume and weight "as it is". It is expressed in g/ml and is given by

D_b = M / V_0

Where, M is the mass of powder and V_0 is the Bulk volume of the powder

3. Tapped density

It was determined by placing a graduated cylinder, containing a known mass of drug- excipient blend, on mechanical tapping apparatus. The tapped volume was measured by tapping the powder to constant volume. It is expressed in g/ml and is given by

D_t = M / V_t

Where, M is the mass of powder and V_t is the tapped volume of the powder.

4. Powder flow properties

The flow properties were determined by

i) Carr's Index (I):

It is expressed in percentage and is expressed by

I = D_t - D_b/ D_t

Where, D_t is the tapped density of the powder and D_b is the bulk density of the powder.

ii) Hausner ratio

It is expressed in percentage and is expressed by

H= D_t / D_b

Where, D_t is the tapped density of the powder and D_b is the bulk density of the powder.

Compression of tablets

After evaluation of granules were then compressed into tablet using rotary tablet press(M/s Remek, Ahmedabad, India) under hardness of 3-4 kg/cm^2.

Evaluation of tablets

Post compression parameters

1. Weight Variation

20 tablets were selected at random and average weights were determined. Then individual tablets weighed and the individual weight was compared with the average.

2. Hardness

The hardness of the tablet was determined using a Monsanto hardness tester. It is expressed in kg / cm^2.

3. Friability (F)

The friability of the tablet was determined using Roche Friabilator. It is expressed in percentage (**%**). 20 tablets were initially weighed ($W_{initial}$) and transferred into the friabilator. The friabilator was operated at 25 rpm per min for 4 mins (100 revolutions). The tablets were weighed again (W_{final}). The % friability was then calculated by

F = $W_{initial}$ - W_{final} / $W_{initial}$ * 100

4. Content uniformity

Twenty tablets were taken and amount of drug present in each tablet was determined. 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 5ml of Methanol and made up to volume

with 0.1N HCl. The sample was mixed thoroughly and filtered through a 0.45µ membrane filter. The filtered solution was diluted suitably and analyzed for drug content by UV spectrophotometer at a λ_{max} of 273 nm using 0.1 N hydrochloric acid as blank.

5. Thickness and diameter
The thickness and diameter of the tablets was measured by Vernier Calipers. It is expressed in mm.

6. *In vitro* buoyancy study
In vitro buoyancy studies were performed for all the twelve formulations as per the method described by Rosa *et al*[15]. 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 (TFT).

7. *In vitro* dissolution studies
The release rate of famotidine from floating tablets was determined using *United States Pharmacopeia* (USP) Dissolution Testing Apparatus 2 (paddle method). The dissolution test was performed using 900 ml of 0.1N hydrochloric acid, at $37 \pm 0.5°C$ and 75 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus hourly and the samples were replaced with fresh dissolution medium. The samples were filtered through a 0.45µ membrane filter and diluted to a suitable concentration with 0.1N hydrochloric acid. Absorbance of these solutions was measured at 273 nm using a UV/Visible spectrophotometer.

8. Scanning Electron Microscopy
Scanning Electron Microscopy (SEM) of intact tablet containing formulation F9 was done before and after dissolution of 24 hours. The morphological characters of these 2 scans were compared to hypothesize the mechanism of drug release and floating. The surface of the tablets was studied by SEM.

9. Drug release kinetics
To analyze the mechanism of drug release from the prepared formulations, the data obtained from *in vitro* release studies were subjected to Higuchi's model, Zero order model and Korsmeyer's model.

10. Stability studies
The promising formulation was tested for a period of 3 months at different temperatures of 25^0C and 40^0C with 60%RH and 75% RH, for their drug content.

RESULTS AND DISCUSSION
Aceclofenac is a water insoluble drug. Its poor inherent compressibility coupled with associated side effect posses a significant challenge for developing floating tablets. For developing floating tablets with desirable drug release profile, cost effectiveness and broader regulatory acceptance combination of HPMC, Ethyl cellulose, bees wax, cetyl alcohol, stearic acid was chosen as release controlling polymers. Sodium bicarbonate was added as a gas generating agent.

Compatibility study of aceclofenac by DSC
DSC thermograms of pure aceclofenac, blend of polymer/excipients with drug were determined (figure1). Pure aceclofenac showed a sharp endotherm at 155.54^0C corresponding to its melting point. There was no appreciable change in the melting endotherms of physical mixture compared to that of pure drug Aceclofenac. Absence of any new endothermic peak or disappearance or shift of endothermic peak confirms that peak in thermograms of pure drug and the blends of drug in the polymer confirms that there is no any interaction and hence the polymers and excipients are compatible with drug.

Compatibility study of aceclofenac by FTIR
FTIR spectras of pure aceclofenac, blend of polymer/excipients with drug were determined (figure2). Aceclofenac showed that the principle IR peaks Aceclofenac: 3313.3, 2970.2, 2935.5, 1716.5, 1589.2, 1506.3, 1479.3, 1344.3, 1280.6, 1255.6 and 665.4; Aceclofenac + excipients: 3278.8, 2970.2, 2935.5, 1710.7, 1589.2, 1506.3, 1479.3, 1344.3, 1280.6, 1255.6 and 665.4; The IR spectra of all the tested samples showed the prominent characterizing peaks of pure aceclofenac which confirm that interactions between the drug, polymers and excipients were unlikely to occur.

Evaluation of the precompression parameters of formulated granules
Formulation of proper powder/granule blend is the key factor in the production of tablet dosage form involving floating extended release of drug from matrix type particle. Physical parameters such as specific surface area, shape, hardness, surface characteristics and size can be significantly affect the rate of dissolution of drugs contained in a complex system. The formulated granule blends of different formulations (F1 to F10) were evaluated for angle of repose, tapped density, bulk density, Carr's index and Hausner ratio. The results of angle of repose (<30) indicated good flow properties of the entire formulated granule blend except for formulation (F7). The compressibility index value were recorded, result in good to excellent flow properties. Formulated powder blends density, porosity and hardness are often interrelated properties and are likely to influence compressibility, porosity, dissolution profile and properties of tablets made from it. The results of percentage porosity indicating that the packaging of the granule blend may range from close to loose packaging and also confirming that particle are not of greatly different sizes. All these results indicate that the formulated granule blend possessed satisfactory flow properties and compressibility (table 2).

Evaluation of the formulated floating tablets
The tablets of different formulations (F1 to F10) were evaluated for various parameters viz; thickness, diameter, hardness, friability, percentage weight variation and percentage drug content. All the formulations showed uniform thickness and diameter. In a weight variation test, the pharmacopoeial limit for the percentage deviation for the tablets of more than 250mg is $\pm$ 5%.

The average percentage deviation of all tablet formulations was found to be with in the above limit, and hence all formulations passed the test for uniformity of weight as per official requirements. Drug content was found to be uniform among different batches of the tablets, and the percentage of the drug content was more than 96%. The hardness of all the formulation was between 4.0 to 5.5kg/cm^2. The percentage friability for all the formulations was below 1% indicating that the friability is with in the prescribed limits. All the tablet formulations showed acceptable pharmacotechnical properties and complied with the in-house specifications for weight variation, drug content, hardness and friability (Table 3).

In vitro Buoyancy study

From the results of floating behaviour studies, it was found that as the concentration of effervescent mixture increase, the floating lag time, floating duration and matrix integrity decreased and vice versa. A reverse trend was observed on increasing the polymer concentration. The initial batches of F1 prepared without sodium bicarbonate did not show any sign of floating. Therefore, sodium bicarbonate was used as a gas-generating agent in order to float the tablet. The sodium bicarbonate induces CO_2 generation in the presence of dissolution medium (0.1 N HCl). The gas generated is trapped and protected within the gel formed by hydration of the polymer, thus decreasing the density of the tablet below 1 gm/mL, and the tablet becomes buoyant. To study the effect of sodium bicarbonate concentration on floating lag time, batches F2 to F6 were selected. It was found that as the amount of sodium bicarbonate increases, the floating lag time decreases. Thus, sodium bicarbonate 25 mg was essential to achieve optimum in vitro buoyancy (ie, floating lag time of 4 to 5 minutes and floating duration of 12 hours). Further increase in concentration of sodium bicarbonate does not show any significant effect on floating behavior. Moreover, the increased amount of sodium bicarbonate caused a large amount of effervescence, which in turn resulted in pore formation, which led to rapid hydration of the polymer matrix and thereby to rapid drug release. Thus 25 mg concentration of sodium bicarbonate was kept constant for batches F6 to F10, which showed floating lag time between 4 and 6 minutes and remained floating for 12 hours. Therefore the concentration of the effervescent mixture was chosen so as not to compromise the matrix integrity with the possible shortest lag time and floating duration upto 12 h. It was observed that all tablets (except F1) ascended to the upper one third of the dissolution vessels within a short time and remained floated until the completion of release studies. The relationships between the amount of gas generating agent and the floating lag time as well as the duration of floating are shown in figure 3. It was observed that the floating lag time for this system is in the range of 15 to 4 min and floatation was achieved maximum at gas generating quantity of 25 mg within 4 min. also the system was afloat over the entire dissolution period (table 4).

In Vitro Dissolution Studies

The results obtained from *in vitro* dissolution studies of all the ten formulations were given in figure 4 and 5. In batch F1, aceclofenac tablets were prepared using HPMC K15 M in the absence of sodium bicarbonate. The tablet failed to float and did not remain intact; moreover, 50 % of the drug was released within 1 hour at this low concentration of HPMC K15M. Hence the concentration of HPMC K15M was increased for batch F2, which showed matrix integrity, but the release of drug was too rapid. In batches F2 to F6, the concentration of sodium bicarbonate was increased in order to get the desired floating behavior.

Tablets F1 and F2 released 30 % and 34 % respectively, of their aceclofenac content at the end of 2 hours. Formulations F1 and F2, containing bees wax failed to sustain release beyond 50 % at the end of 12 hours. These formulations remained impermeable, probably due to less water penetration in the matrix. Figure 4 indicates that F3, F4, F5 and F6 released 55%, 60%, 65% and 68% at the end of 12 hours, respectively. Figure 4 and 5 indicates that F7, F8, F9 and F10 released 70 %, 75%, 90% and 80% at the end of 12 hours, respectively. Incorporation of higher amount of cetyl alcohol in F7, F8, F9 and F10 was found to be more suitable to give good drug release characteristics. Batches F9 and F10 showed greater retardation of drug release because of the high concentration of polymer.

In formulation F9, which contained maximum amount of ethyl cellulose and minimum of HPMC, cetyl alcohol and drug release was found to be more than F10 and F8. Hence it was concluded that F9 was the best among the ten formulations with a sustained release of 90 % at the end of 12 hrs.

Scanning Electron Microscopy

The SEM images of the tablet were taken before and after dissolution. Figure 6 showed intact surface without any perforations, channels, or troughs. After dissolution, the solvent front enters the matrix and moves slowly toward the center of the tablet. The drug diffuses out of the matrix after it comes in contact with dissolution medium. The images of the tablet showed a network in the swollen polymer through which the drug diffused to the surrounding medium. Thus, it was concluded that the drug was released from matrix by diffusion mechanism.

Kinetic modeling of drug release

Formulation F9 was selected for further studies as an optimized formulation because it gave the best results in terms of the floating lag time (4 min), total duration of floating (> 12 hrs), *in vitro* release (90% at the end of 12 hrs).

The regression coefficients obtained for first order Kinetics were found to be higher (0.9988) when compared with those of zero-order kinetics (0.9832) indicating that drug released from all the formulations followed first-order kinetics (Table 5). Release of the drug from a matrix tablet containing hydrophilic polymers generally involves factors of diffusion. To evaluate drug release mechanism from the tablets, plots

of percent released vs. square root of time as per Higuchi's equation were constructed. These plots were found to be linear with all the formulations (R^2: 0.9968) indicating that the drug release from the tablets was diffusion controlled. To confirm the diffusion mechanism, the data were fit into Korsmeyer-Peppas equation. The formulations F9 showed good linearity (R2: 0.9986), with slope (n) vaues 0.7181. This 'n' however, appears to indicate a coupling of diffusion and erosion mechanisms- so-called anomalous diffusion. Hence, diffusion coupled with erosion may be the mechanism of aceclofenac release from F 9.

Stability studies on *in vitro* release

The selected formulation F9 was subjected upto 3 months stability study as per ICH guidelines at room temperature ($25^0C\pm2^0C$ at 60%±5%RH) and accelerated condition ($40^0C\pm2^0C$ at 75%±5%RH) to find out the effect of aging on release pattern. At the end of the testing period, the floating matrix tablets were observed for changes in physical appearance, analyzed for drug content, and subjected to *in vitro* drug release studies. No visible changes in the appearance of the floating matrix tablets were observed at the end of the storage period.

The result of the stability study does not indicate any significant alteration in the *in vitro* release pattern of the drug optimized tablet formulation F9 before and after stability study (figure 7). Indicating that the formulation could provide a minimum shelf–life of 2 years. However, a detailed investigation is necessary to determine the exact shelf- life.

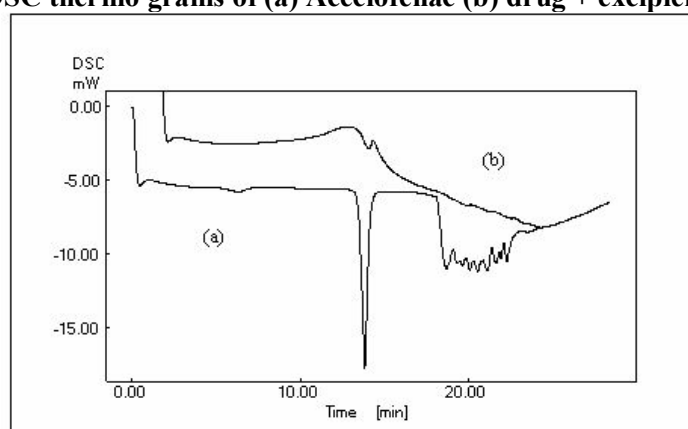**Figure 1: DSC thermo grams of (a) Aceclofenac (b) drug + excipients (1:1 ratio)**

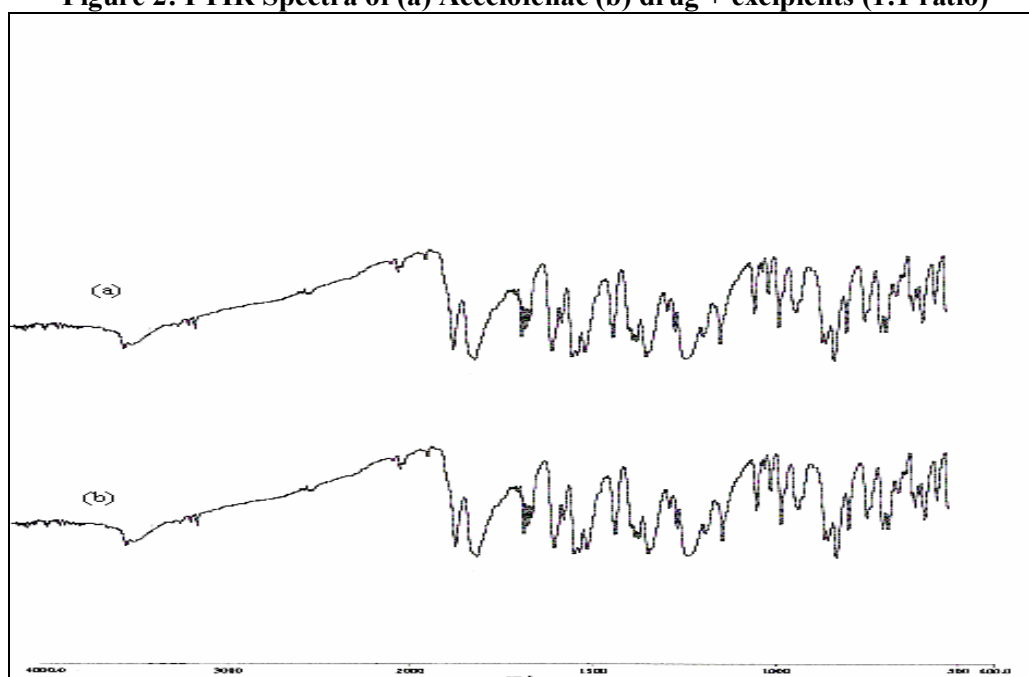**Figure 2: FTIR Spectra of (a) Aceclofenac (b) drug + excipients (1:1 ratio)**

Table 2: Precompression Properties of the aceclofenac granules

Formulation code	Angle of repose(θ)*	Bulk density (gm/cm³)*	Tapped density (gm/cm³)*	Carr's index (%)*	Hausner ratio (H$_R$)*	Bulkiness (cc/g)*
F1	28.1±0.01	0.57±0.01	0.71±0.04	19.0±0.01	1.24±0.01	1.75±0.02
F2	26.3±0.02	0.55±0.02	0.67±0.03	16.9±0.02	1.22±0.02	1.79±0.04
F3	27.6±0.03	0.55±0.01	0.70±0.01	19.9±0.02	1.27±0.03	1.82±0.05
F4	26.9±0.04	0.54±0.03	0.73±0.03	21.5±0.01	1.35±0.01	1.72±0.01
F5	26.9±0.05	0.53±0.04	0.67±0.03	20.8±0.02	1.26±0.02	1.89±0.03
F6	28.0±0.01	0.57±0.01	0.74±0.01	23.1±0.01	1.29±0.01	1.75±0.02
F7	32.6±0.04	0.56±0.01	0.74±0.02	23.7±0.01	1.30±0.04	1.79±0.02
F8	27.3±0.05	0.57±0.02	0.73±0.02	22.8±0.01	1.32±0.02	1.75±0.03
F9	27.9±0.01	0.58±0.03	0.72±0.02	18.7±0.02	1.24±0.01	1.75±0.01
F10	26.3±0.06	0.55±0.01	0.71±0.01	19.0±0.02	1.24±0.01	1.75±0.01

*All values are expressed as mean ± SD, n=3.

Table 3: Results of Post Compression Properties of aceclofenac floating Tablets

Formulation code	Thickness (mm)*	Diameter (mm)*	Hardness (kg/cm²)*	Friability (%)***	Drug content (%)**	Weight variation (mg)**
F1	3.0±0.01	11.00±0.02	4.5±0.2	0.25±0.01	96.5±0.02	400±0.04
F2	2.9±0.02	10.9±0.02	5.0±0.1	0.30±0.06	98.0±0.01	399±0.02
F3	2.8±0.03	11.1±0.02	4.5±0.12	0.45±0.04	99.0±0.01	402±0.02
F4	3.0±0.01	11.2±0.01	5.0±0.16	0.55±0.02	99.5±0.05	400±0.02
F5	2.9±0.05	11.0±0.03	5.5±0.09	0.21±0.03	98.0±0.01	398±0.03
F6	2.7±0.01	11.0±0.04	5.0±0.08	0.35±0.03	99.0±0.01	401±0.01
F7	3.0±0.01	11.2±0.04	4.5±0.07	0.40±0.02	98.5±0.02	402±0.05
F8	3.1±0.02	10.8±0.02	5.0±0.12	0.25±0.03	99.5±0.02	400±0.01
F9	3.2±0.02	11.0±0.01	4.5±0.14	0.55±0.01	99.4±0.02	401±0.01
F10	3.0±0.02	11.0±0.01	5.0±0.09	0.65±0.01	97.0±	402±0.03

*All values are expressed as mean ± SE, n=5; **All values are expressed as mean ± SE, n=20; ***All values are expressed as mean ± SE, n=10.

Figure 3: Comparison between floating lag time, duration of floating and amount of sodium bicarbonate (F1 to F6).
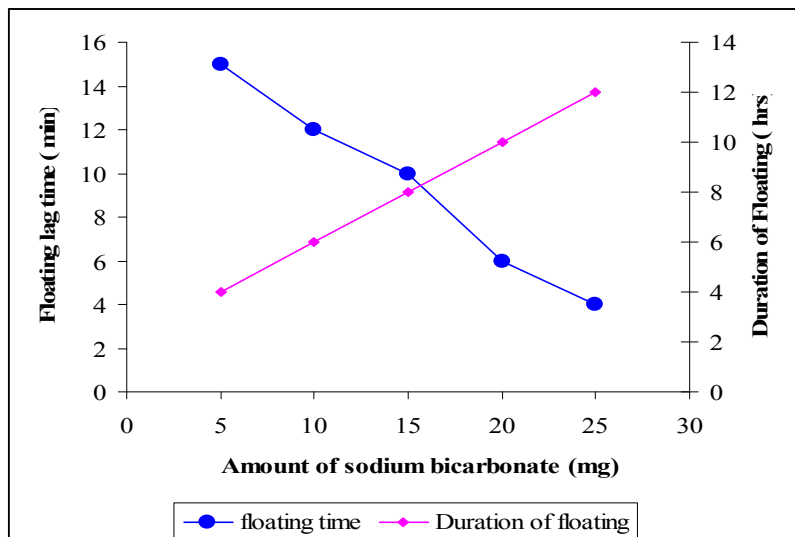
Table 4: Results of *In vitro* Buoyancy study of aceclofenac Floating Tablets

Formulation code	Buoyancy Lag Time (min)	Total Floating Time (hrs)	Matrix integrity
F1	Did not float	Did not float	--
F2	15 min	4 hrs	+
F3	12 min	6 hrs	+
F4	10 min	8 hrs	+
F5	6 min	10 hrs	+
F6	4 min	12 hrs	+
F7	5.0 min	12 hrs	+
F8	5.0 min	12 hrs	+
F9	4.0 min	12 hrs	+
F10	4.5 min	12 hrs	+

Figure 4: comparison of *In Vitro* Dissolution profiles of F1 to F8
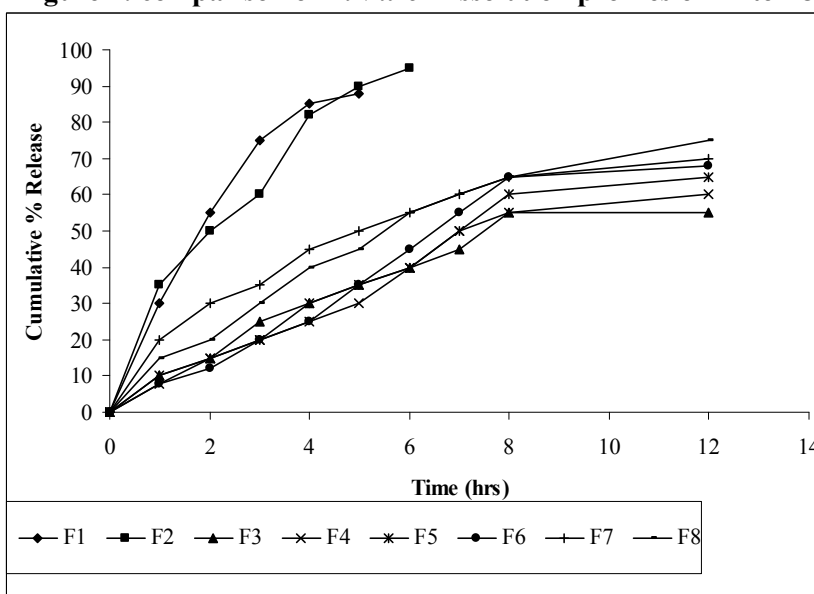
Figure 5: comparison of *In Vitro* Dissolution profiles of F9 to F10
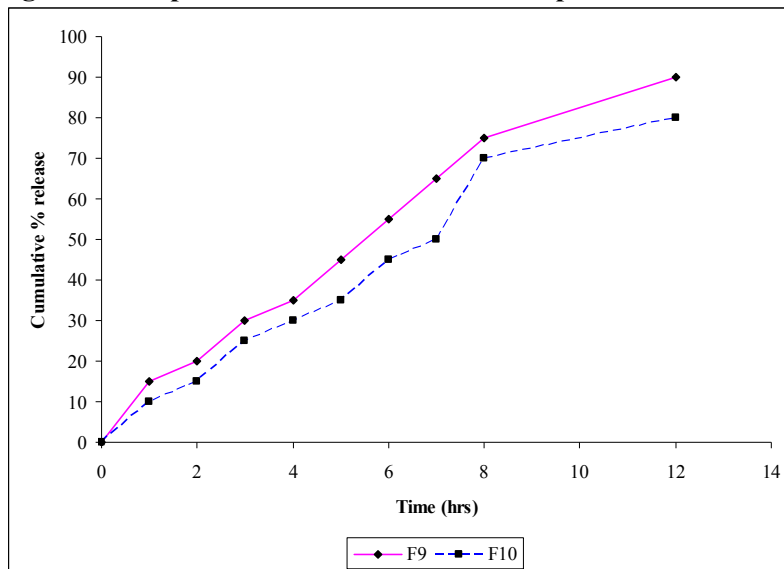
Table5: **Mathematical modeling and drug release mechanisms of optimized formulation (F9)**

Formulation	Regression coefficient(r^2)	Korsmeyer's plot		
	Zero order	First order	Higuchi equation	n	r^2
F9	0.9832	0.9988	0.9968	0.7181	0.9986

Figure 6: Scanning electron microscopy images of tablet surfaces before and after dissolution.
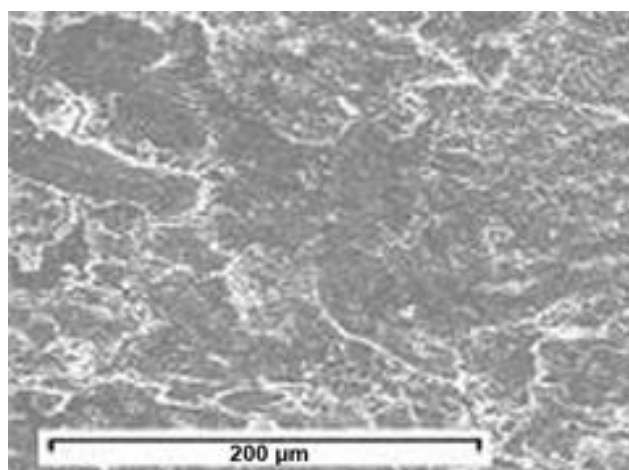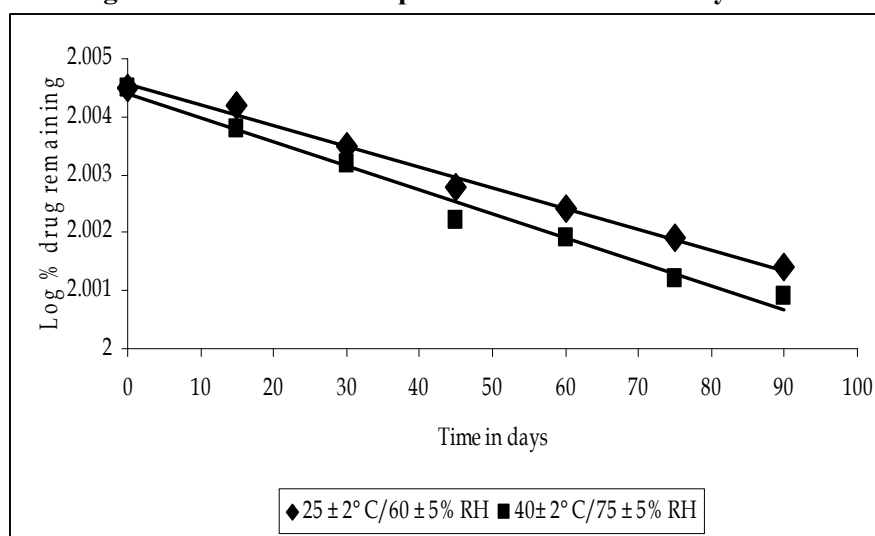**Before Dissolution (0 hrs)   After Dissolution (12 hrs)**
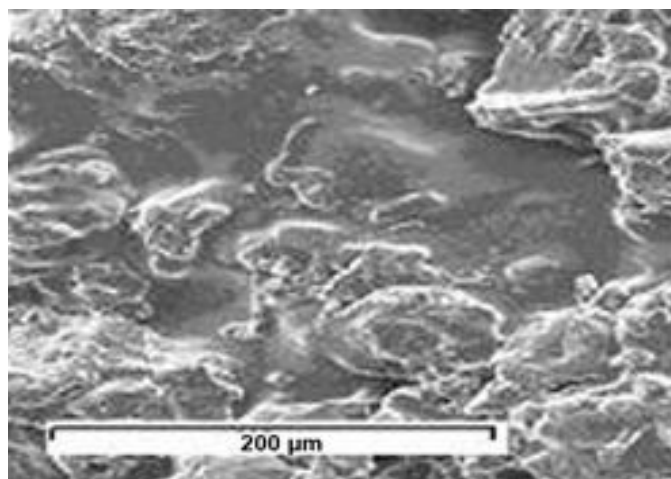
Figure 7: *In vitro* release profile of F9 after stability studies

CONCLUSION

The present study was aimed at developing an oral floating system for aceclofenac with the use of wax materials, swellable polymer, release retardant and an alkalizing agent which proved to be an ideal formulation, as it released the drug in a controlled manner for extended period of time by maintaining the buoyancy. The study reveals that, the release of water soluble drug, aceclofenac exhibited diffusion dominated mechanism. The optimized formulation gives the best result in terms of the floating lag time (4 minutes) and floating duration of 12 hours, and drug release (90%) at the end of 12 hours. This result is encouraging, because a longer gastric residence time is an important condition for higher bioavailability of the drugs included in the floating matrix dosage forms. The dose can be reduced and possible incomplete absorption of the drug can be avoided.

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