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Research Article

Design and Characterization of Aceclofenac-Loaded Microballoons using Eudragit with Hydroxypropyl Methylcellulose

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Abstract

Background: Drug delivery systems based on microballoons are one of the promising approaches for gastric retention, especially useful for drugs with site-specific absorption in the stomach. The microballoons are hollow, spherical particles under 200 micrometers, designed to float in the gastric environment. The Aceclofenac formulation of an NSAID is helpful with a half-life of 4–4.3 hours; this delivery form gives a sustained release and maintains constant plasma levels with enhanced bioavailability and decrease in dosing frequency.

Methodology: Microballoons of Aceclofenac were prepared using Eudragit RS 100 and Hydroxy Propyl Methyl Cellulose as polymers from the emulsion–solvent diffusion method. In this, the polymers impart stability along with a profile of controlled release. Here, the microballoons was evaluated for physical parameter and the release profile regarding average particle size, floatation percentage, entrapment efficiency, true tapped density, and percentage yield, and FTIR will be carried out on complexes of drug and polymer.

Results and Discussion: The prepared microballoons exhibit excellent floating properties and uniformity in size, which aided in long gastric retention. High entrapment efficiency with controlled and sustained release of the drug for an extended period was obtained. FTIR studies indicated that Aceclofenac remained stable in the polymer matrix with no considerable chemical interaction between the drug and the polymers.

Conclusion: This research shows promise in microballoons-based delivery systems that could maintain the release for a longer duration from the delivery device with respect to Aceclofenac, which enhances bioavailability and reduces dosing frequencies.

Keywords: Aceclofenac, Microballoons, NSAID, Sustain Release Medication, Eudragit RS100, HPMC

INTRODUCTION

Gastro retentive drug delivery systems developed to exhibit a prolonged gastric retention time (GRT), have sparked the interest of researchers due to their potential for controlled and targeted drug delivery [1]. Shorter half-life drugs that are simply absorbed from gastrointestinal tract (GIT) were found to be eliminated quickly from the Blood stream. Floating dosage forms will overcome these challenges since they release the medicine gently and aid to maintain a consistent drug concentration in the bloodstream for a longer length of time [2]. A few issues are being investigated in the development of controlled delivery frameworks for increased absorption and bioavailability. One such challenge is the difficulty to restrict the dosage form in the targeted region of the GI tract. It is widely assumed that the amount of medication absorbed in the gastrointestinal system is proportional to the time the drug is in connection with the small intestine mucosa [3]. Site-specific orally administered drug delivery system needs to achieve prolonged residence time to get the desired effect. Prolonged stomach retention enhances the bioavailability, decreases drug waste, extends the period of drug release, and enhances the solubility of medications that are less soluble in environments with high pH. [4]. Nonsteroidal anti-inflammatory medicines (NSAIDs), which have pain-relieving and anti-inflammatory qualities, have been widely utilized in the treatment of various illnesses since their development. NSAIDs act by blocking cyclo-oxygenase, a key enzyme in pain generation [5]. Rheumatoid arthritis (RA) is an inflammatory joint condition that causes synovial expansion and cartilage degradation. NSAIDs are first-line medications. Aceclofenac is a novel NSAID with good analgesic, anti-

inflammatory, and antipyretic properties for acute and chronic inflammation, as well as improved stomach tolerance. It was chosen as a model medication because of its short half-life (3-4 hours) and the fact that two-thirds (70-80 percent) of the dosage is eliminated by renal transport [6]. Aceclofenac is a more recent derivative of diclofenac that is an excellent choice for modified release multiple dose formulation because of its shorter biological half-life (4 hours), lower risk of GIT complications, and higher dose frequency [7]. Drug release rates from formulations in the stomach and upper section of the small intestine are being prolonged using floating drug delivery systems until the entire drug is released for the required amount of time. Rheumatoid arthritis (RA) is a long-term inflammatory condition of the joints that causes cartilage degradation and synovial development. The objective of the current work was to create an Aceclofenac hollow microballoons, to extend its retention in the upper gastrointestinal tract. This could lead to improved absorption and, ultimately, increased bioavailability [8].

MATERIALS AND METHODS

Materials

The drug sample was purchased from Aarti Drugs Ltd. Maharashtra. Eudragit RS 100 was purchased from Evonik Industries, Mumbai. HPMC and Tween 20 were purchased from Colorcon Asia Pvt. Ltd., Goa, and Maya Chemtech India Private Limited, Delhi Dichloromethane and disodium hydrogen phosphate were purchased from Yarrow Chem Products, Maharashtra. Other chemicals like ethanol, concentrated HCL, Sodium Hydroxide, N Hexanes, Glyceryl monostearate, and Polyvinyl Chloride were used in this work with proper analytical grade.

Methods

Preparation of standard curve

The primary stock solution of Aceclofenac was made by dissolving 100 mg of Aceclofenac in a tiny quantity of methanol and adjusting the volume to 100 ml with 0.1 N HCl. A range of concentration from 1-10 µg/ml was prepared by diluting the primary stock solution (1000 µg/ml). Using a UV-Visible double beam spectrophotometer, the absorbance of these solutions was measured at 275 nm against 0.1 N HCI as a blank. Then, using the X-axis for concentration and Y-axis for absorbance, a calibration curve was generated.

Preparation of standard curve of Aceclofenac in phosphate buffer of pH 6.8

Aceclofenac standard curve was produced using a pH 6.8 phosphate buffer and 100 mg of Aceclofenac. The primary stock solution was then diluted to prepare 1-10 µg/ml of solution. At 275 nm, absorbance was determined against phosphate buffer as blank. Then, using a concentration in g/ml on the X-axis and Y-axis as absorbance, a calibration curve was plotted.

Preparation of microballoons following quality by design approach

Defining the Quality Target Product Profile (QTPP) and Critical Quality Attributes (CQAs)

As the first step towards Quality by Design (QbD)-based product development for floating microballoons of Aceclofenac, the definition of the patient-centric QTPP included a review of the drug product's quality attributes in order to produce a delayed release profile for medication delivery. A number of Quality Attributes (QAs) were identified in order to meet the QTPP, including EE (indicative of drug loading in the hollow microspheres), particle size (imperative for discerning the drug release and absorption potential through GI tract), percentage of drug release in 12 hrs. (i.e., Q12h) and time required for 60% drug release (i.e., T60%) (marker of drug release from microballoons). Various elements of QTPP for development of floating microballoons of Aceclofenac have been summarized in **Table 1**, while **Table 2** enlists the respective justification(s) of selecting each CQA.

Table 1: Quality target product profile (QTPP) for GR hollow microballoons of Aceclofenac

QTPP Element	Target	Justification
Dosage form type	Gastroretentive microballoons	Helps in maintaining the therapeutic effect of drug for prolonged periods of time by retaining the formulation in GIT for extended time periods
Drug delivery type	Microballoons	Selection of GR floating microballoons help in enhancing the residence time of drug formulation in stomach and upper GIT leading to complete absorption of drug within its absorption window
Route of administration	Oral	Recommended route for delivery of Aceclofenac is oral and the available marketed formulations (i.e., tablets) are also meant for oral intake only
Dosage strength	150 mg	It is the unit dose of Aceclofenac which needs to be incorporated for once-a-daily administration
Packaging	Hard gelatin capsules	The microballoons can easily be delivered by filling in hard gelatin capsules with improved patient compliance, portability, and manufacturing ease
Stability	At least 24 months at room temperature	To maintain therapeutic potential of the drug during storage period

Table 2: Critical quality attributes (CQAs) for GR hollow microballoons of ITH and their justifications

Quality attributes of drug product	Target	Is this a CQA?	Justification
Physical attributes Color Odor. Appearance	Acceptable to patients No unpleasant Odour Acceptable to patients	No	Color, odor, and appearance were not considered as critical, as these are not directly linked to patient efficacy and safety.
Drug content	100%	No	Drug content is a vital parameter for any pharmaceutical dosage form for attaining maximal plasma concentration of the drug. Unlike tablets, microballoons are not the unit dose formulations, thus it was regarded as moderately critical.
Percentage buoyancy	100%	No	Higher value of percent buoyancy is required for longer residence time of the drug formulation in the gastric region. As the developed GR microballoons were hollow in nature having inherent ability to completely float up to 24 h, hence it was taken up as less critical.
Particle size	Low	Yes	As the microballoons are administered through oral route, the particle size was thought to exert significant influence in attaining prolonged gastric retention of the drug formulation, and thus its therapeutic performance. Hence, it was considered as critical.
Entrapment efficiency	100%	Yes	Higher values of entrapment efficiency are vital for accomplishing maximal drug release regulation from the dosage form and hence the therapeutic concentration of the drug. Thus, it was considered as critical.
Time required for 60% drug release (T60%)	8 hrs	Yes	This parameter is an indicator of sustained release profile of drug release from the prepared microballoons formulations, thus was taken up as highly critical.
Cumulative amount of drug release in 12 h (Q12h)	80.0%	Yes	Cumulative drug release should be greater than 80% after 12 hrs to achieve the targeted sustainable release.

Table 3: Formulation composition of GR hollow microballoons prepared as per central composite design

Sl. No.	Formulation Code	Aceclofenac (gm)	Eudragit RS 100 (gm)	HPMC (gm)	Monostearin
1	F_1	0.1	+1	-1	0.5
2	F_2	0.1	0	-1	0.5
3	F_3	0.1	-1	-1	0.5
4	F_4	0.1	+1	0	0.5
5	F_5	0.1	0	0	0.5
6	F_6	0.1	-1	0	0.5
7	F_7	0.1	+1	+1	0.5
8	F_8	0.1	0	+1	0.5
9	F_9	0.1	-1	+1	0.5

Table 4: Translation of coded factors into physical units

Factors	Coded Levels		
	-1	0	+1
Eudragit RS 100	0.4	0.5	0.6
HPMC	0.2	0.3	0.4

Optimization of GR microballoons using experimental design

Systematic optimization of GR microballoons was accomplished employing Central Composite Design (**Table 3** and **Table 4**) using the highly influential CMA/CPPs selected using the factor screening and risk assessment studies. The design matrix as per CCD containing a total of nine different formulations prepared employing different concentration of Eudragit RS100 and HPMC as the CMA/CPPs at three different levels, i.e., low (-1), intermediate (0) and high (+1) levels. All the prepared formulations were evaluated for various CQAs viz. EE, particle size, Q12h and T60%, respectively.

Evaluation of microballoons

Particle size analysis

In assessing the release properties and floating properties, particle size analysis is crucial. Microballoons diameters were determined using a series of conventional sieves with sizes ranging from 14, 16, 18, 22, 30, and pan. From top to bottom, the sieves were stacked in increasing order. The microballoons were run through several sieves, and the number of microballoons maintained on every sieve was weighed to determine the percent weight of microballoons retained by each sieve. The mean particle size can be obtained by applying the formula [9,10].

Mean particle size = Total weight of the formulation / % Total weight of microballoons.

Floating property of microballoons

100 mg of microballoons were dissolved in 300 mL of 0.1 N HCI with 0.02 % Tween 20 followed by stirring at 100 rpm. After 1, 2, 4, and 6 hours, the buoyant microballoon layer was pipetted and filtered out. The microballoons were collected and dried overnight in a desiccator [10].

Microballoons were determined using the subsequent formula:

% Microballoons = (Weight of microballoons / Initial weight of microballoons) × 100

Drug entrapment

Microballoons were passed through a drug entrapment test to check the amount of drug present in the prepared formulation. Microballoons samples (50 mg each) of different batches were taken and powdered to dissolve in a small amount of ethanol. The volume was composed to 100 ml using 0.1 N HCl. The solution was then filtered followed by double dilution to prepare a concentration of 1µg/ml and at 275 nm, The absorbance was measured in relation to a blank of 0.1 N HCI. The percentage of drug entrapment was calculated by the following equation [11].

% Drug entrapment = (Calculated drug concentration / Theoretical drug concentration) × 100

Determination of true density

The liquid displacement technique was introduced to determine the true density of microballoons using a pycnometer and n-hexane as the solvent. First, the weight of the pycnometer was recorded (a), followed by the addition of 25 ml of n-hexane and the recording of the weight (b). The pycnometer was emptied, the weight amount of the microballoons was added and weight (c) was recorded. Now n-hexane was added to fill the vacant areas within the microballoons until the volume, i.e., 25 ml, was occupied by the microballoons and n-hexane. Final weight (d) was taken and true density was calculated using the formula [12].

$$\text{The density of liquid } (\rho) = \frac{b-a}{25}$$

$$\text{True density} = \frac{c-a}{25-\left[\frac{d-c}{\rho}\right]}$$

Determination of tapped density

It is the proportion of a particular mass of microballoons to the volume of the microballoons after tapping. The tapping method was used to estimate the density of microballoons. An exact weight of microballoons was placed into a 10 ml measuring cylinder. After viewing the initial volume of floating micro spheres, tapping on a hard surface was maintained until no further volume change was seen and the tapped density was calculated using the formula [11,13].

Tapped density = (Mass of microballoons / Volume of microballoons after tapping)

Percentage compressibility index

The percentage compressibility index was calculated using the same tapping approach.

$$\%\ \text{Compressibility index} = \left[1-\frac{V}{V_0}\right] \times 100$$

The volumes of the sample after and before standard tapping are V and V_0, respectively [12].

Percentage yield

By weighing the microballoons after drying, the percentage yield of various formulations was calculated using the formula [14].

% Yield = (Total weight of microballoons / Total weight of drug and polymer) × 100

Angle of repose

The angle of repose of the floating microspheres is commonly used to determine the flow characteristics of microballoons. It is the highest angle between the free-floating surface of a heap of floating micro balloons and the horizontal plane that can be achieved. The fixed funnel method was used to estimate the angle of repose of microballoons. The microballoons were free to tumble down a funnel until the conical pile's peak just brushed the funnel's tip.

The angle of repose ϕ was determined according to the following formula [14,15].

$$\phi = \tan^{-1} h/r$$

[Where, h = height of pile, r = radius of the pile formed by the microballoons]

FT-IR analysis

For the examination of drug-polymer interaction and drug stability throughout the microencapsulation process, a Fourier transform infrared analysis was performed. Pure Aceclofenac, Eudragit RS 100, HPMC, and microballoons were analysed using the Fourier transform infrared spectrum [15].

Stability Study

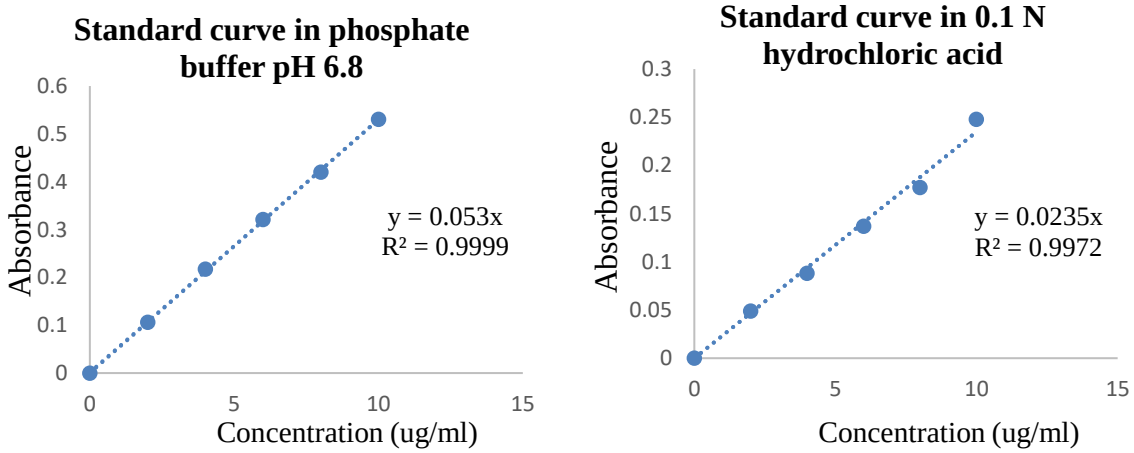
The ideal formulation (F_4) was selected for stability studies. The produced formulation (F_4) was kept for 45 days at ambient temperature (27±2°C), oven temperature (42±2°C), and refrigerator temperature (5-8°C) in borosilicate screw-capped glass containers. At two-week intervals, the samples were tested for drug content [16].

RESULTS AND DISCUSSION

The standard curve of Aceclofenac in 0.1 N HCL follows a linear equation where y = 0.0235x and R^2 value is = 0.9972 and the same drug in Phosphate buffer at pH 6.8 follows a linear equation where, y = 0.053x and R^2 value is = 0.9999 The standard curve in both the medium was showed in **Figure 1(a)** and **1 (b).** The absorbance at different concentration is given in **Table 5.**

Table 5: Concentration vs Absorbance table

Sl. No.	Concentration (µg/ml)	Absorbance at 0.1 N HCl at 275 nm	Absorbance at Phosphate Buffer pH 6.8 at 275 nm
1.	0	0	0
2.	2	0.049	0.106
3.	4	0.088	0.217
4.	6	0.137	0.321
5.	8	0.177	0.420
6.	10	0.248	0.530



1(a) **1(b)**

Figure 1(a): Standard curve of 0.1 N hydrochloric acid and **1(b):** standard curve of the model drug in Phosphate buffer at pH 6.8

Particle size analysis

Particle size determination was performed by the sieving method. In general, if the magnitude of the micro balloons is less than 500 microns, the drug release rate will be high and the floating ability will be reduced, but if the size is between 500 and 1000 micron, the floating ability will be greater and the drug release rate will be sustained. The mean particle size of micro balloons was in the range of 603 – 858 µm

Floating property of microballoons

To simulate stomach fluid, microballoons were distributed in 0.1 NH_4Cl containing tween 20 (0.02% w/v). The floating ability of various formulations was identified to change depending on the Eudragit and HPMC ratios. In 6 hours, F_1-F_4 formulations had the best floating ability (90.47-72.17%). The floating ability of the F_5-F_9 formulation was lower (60.12-25.61%) than that of the F_5-F_7 formulation. By increasing the HPMC ratios, the floating ability of the microspheres was decreased. Percentage buoyancy for different formulations is discussed in **Table 6**.

The % Buoyancy decreased for a different formulation was represented in Figure 3.

Table 6: Percentage buoyancy for different formulations

Formulation Code	Time (hours)			
	1	2	4	6
F_1	99.46	98.28	95.83	91.67
F_2	99.23	96.78	94.27	89.54
F_3	99.63	95.58	85.48	77.62
F_4	99.76	93.56	81.42	73.22
F_5	99.83	89.95	73.29	62.34
F_6	89.36	78.57	61.18	56.82
F_7	88.34	76.44	56.08	46.09
F_8	82.51	66.23	46.2	27.28
F_9	81.63	63.28	43.15	25.61

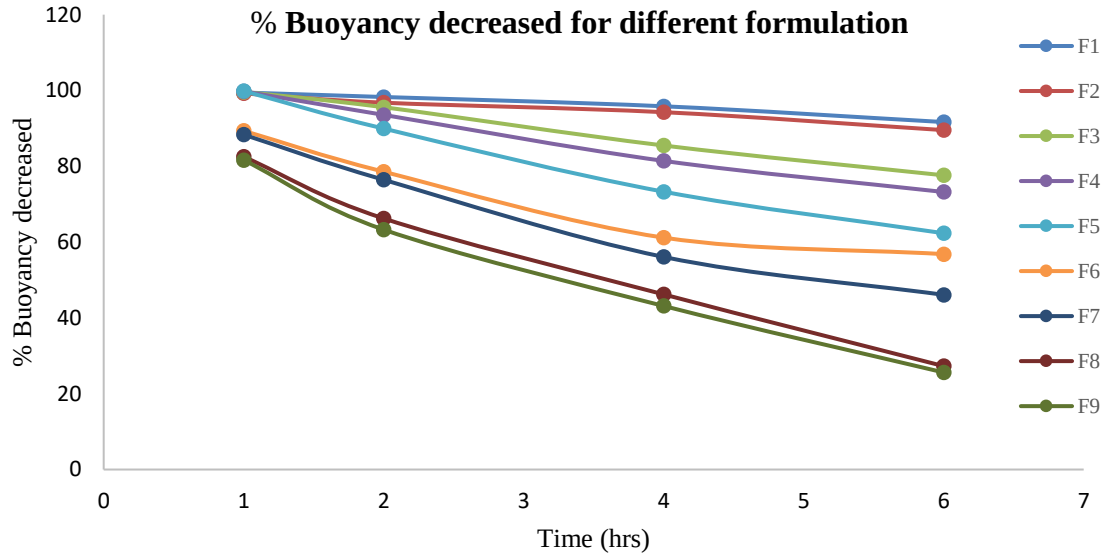


Figure 3: % Buoyancy decreased for a different formulation

Drug entrapment

The drug entrapment effectiveness of varied formulations ranged from 43.14 to 74.12% w/w. Drug entrapment effectiveness in microballoons reduces somewhat when HPMC concentration increases and the Eudragit ratio lowers. This is owing to the permeability properties of HPMC, which may enable the diffusion of some of the encapsulated drugs to the surrounding media during the production of microballoons.

Percentage yield

The percentage yield for each formulation was determined by weighing the microballoons after they had dried, and it varied from 55.10% to 84.67%.

True density

Using n-hexane as the solvent, the liquid displacement method was used to measure the true density of micro balloons. The value was determined to fall between 0.482 to 0.916 gm/cm3 which is lower than gastric fluid (1.004 gm/cm^3), indicating a good flow property.

Tapped density

The tapped density values for different formulations were found to be in the range between 0.201 to 0.405 gm/cc lower than the gastric fluid density of 1.004 gm/cm^3, indicating a good buoyancy property in the stomach.

Percentage compressibility index

The percentage compressibility index, which was determined using the tapping method, ranged from 8.34 ± 0.641% to 17.45 ± 1.01%, suggesting a good flow property. Value for all formulations is discussed in **Table 7.**

Angle of repose

Angle of repose was calculated using the fixed funnel method and ranged from 24.09º to 38.12º, suggesting a good flow property (<40º).

Table 7: Micromeritics of Aceclofenac loaded microballoons

Formulation	*Drug entrapment (% w/w)	*Percentage yield (%)	*True density (gm/cm^3)	*Tapped density (gm/cm^3)	*% Compressibility index	*Angle of repose
F_1	76.78	85.18	0.474	0.21	8.095	24°.26’
F_2	73.46	81.53	0.513	0.22	9.545	25°.64’
F_3	70.23	76.89	0.584	0.262	10.305	27°.14’
F_4	69.76	72.56	0.647	0.275	11.272	26°.89’
F_5	68.98	70.34	0.672	0.312	15.064	31°.79’
F_6	53.28	68.03	0.710	0.348	20.114	36°.41’
F_7	48.27	59.44	0.852	0.379	25.593	38°.84’
F_8	44.14	55.10	0.916	0.418	25.837	39°.52’
F_9	41.25	52.34	1.025	0.468	26.478	39°.95’

*Average of three Preparation

FT-IR spectrum analysis

Aceclofenac, Eudragit RS 100, HPMC, physical mixing of drug-polymer and F_4 formulation FT-IR spectra were observed. FTIR spectra revealed the presence of Aceclofenac in formulation F_4. The distinctive peaks for pure Aceclofenac seem to be at 662.31, 1715.13. 1769.49, and 1343.21 for C – H Bending, C = O Stretching, C = O Stretching, and C – N Stretching shown in **Table 8**, due to polynuclear aromatic ring, secondary aromatic, carboxylic group, esters to the group. All these peaks were observed in the formulation and physical mixing, showing that there was no chemical interaction between Aceclofenac and the polymer. It also demonstrated the drug's stability during the microencapsulation procedure. It is depicted in Table 10. The FTIR Spectrum of HPMC, Eudragit RS 100, Aceclofenac, and F_4 Formulation were represented in **Figure 4, 5, 6, 7** respectively.

Table 8: FT-IR spectrum range of Aceclofenac

Sl. No.	Transition	Ranges (cm^{-1})	Drug	Formulation
1.	C = O Stretching	1740 – 1680	1715.13	1710.84
2.	C = O Stretching	1800 – 1725	1769.49	1768.06
3.	C – N Stretching	1350 – 1280	1343.21	1350.36
4.	C – O Stretching	1310 – 1250	1251.66	1257.38
5.	C – H Bending	900 – 625	662.31	655.16

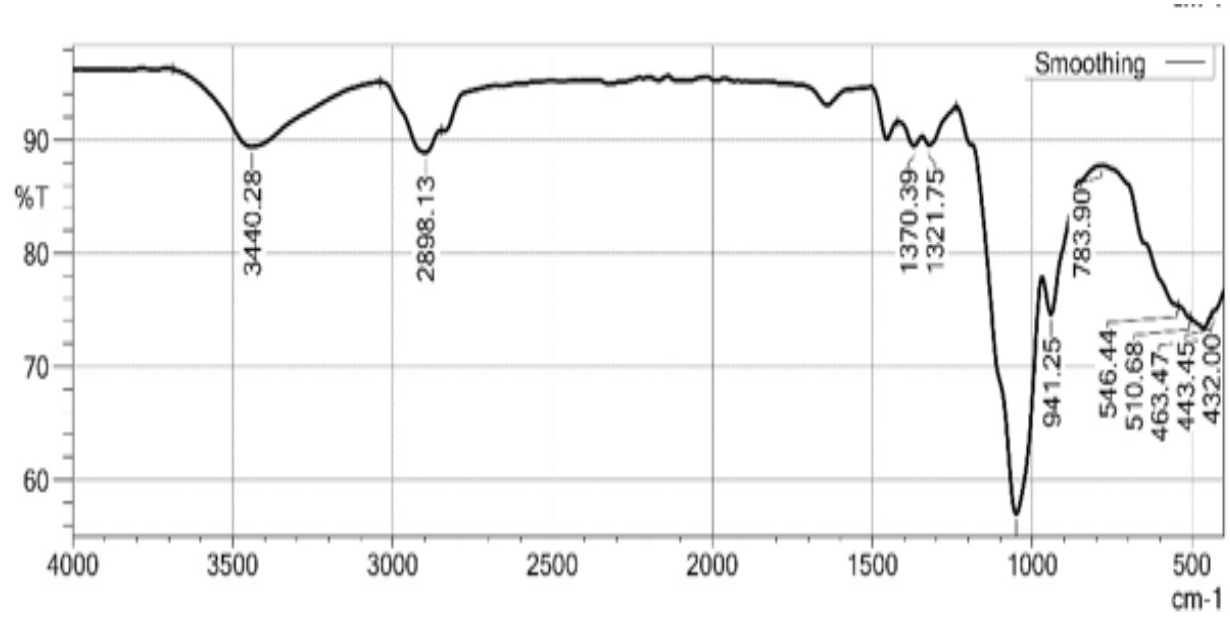


Figure 4: FTIR spectrum of HPMC

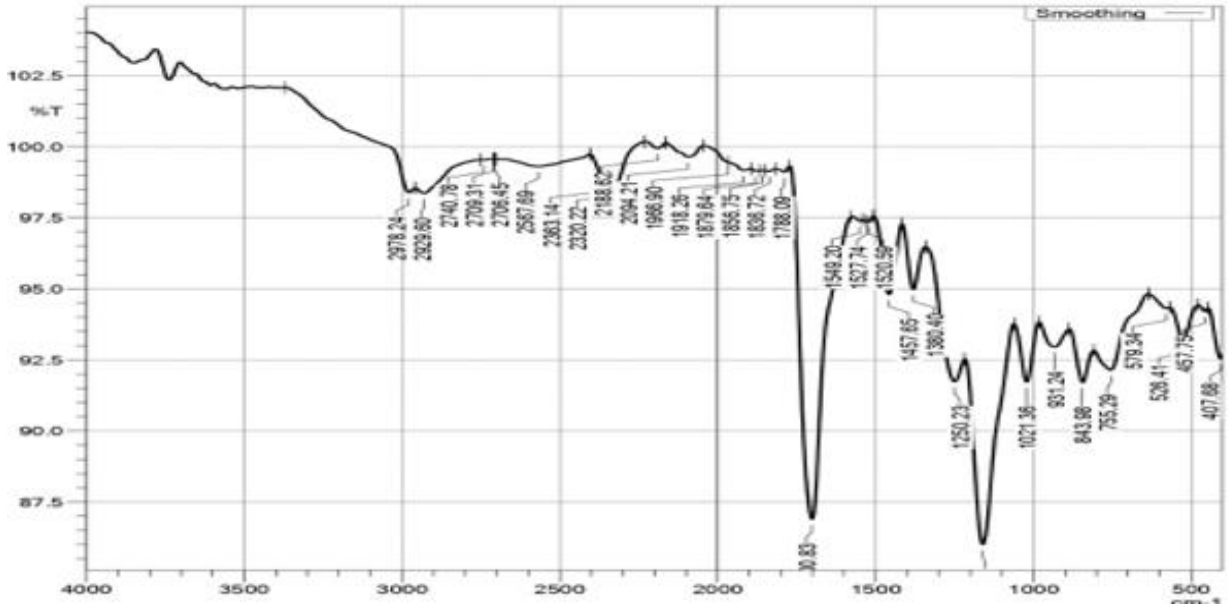


Figure 5: FTIR spectrum of Eudragit RS 100

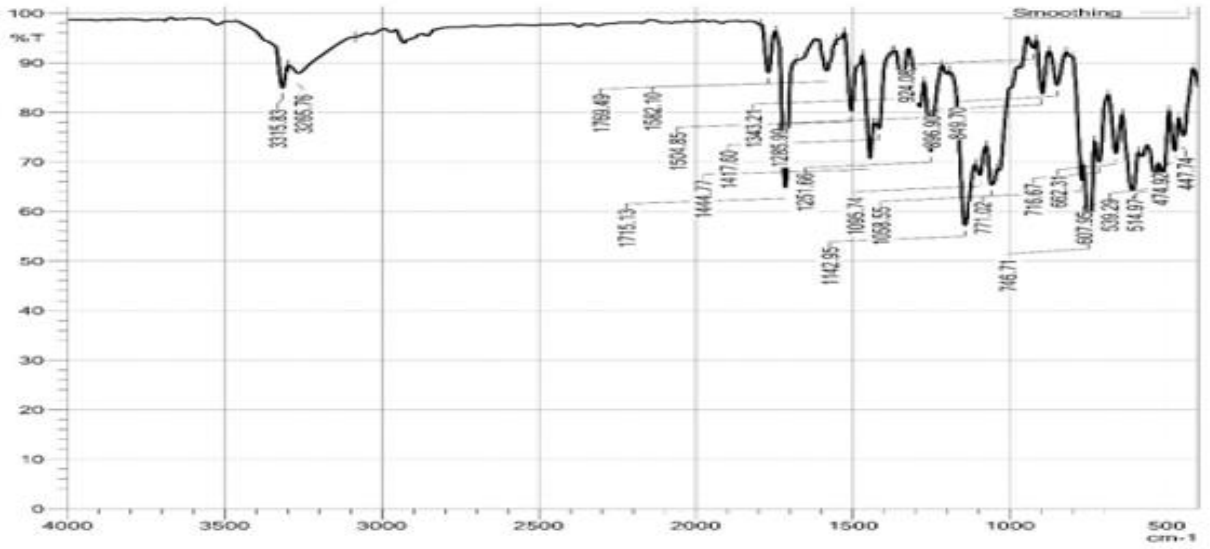


Figure 6: FTIR Spectrum of Aceclofenac pure

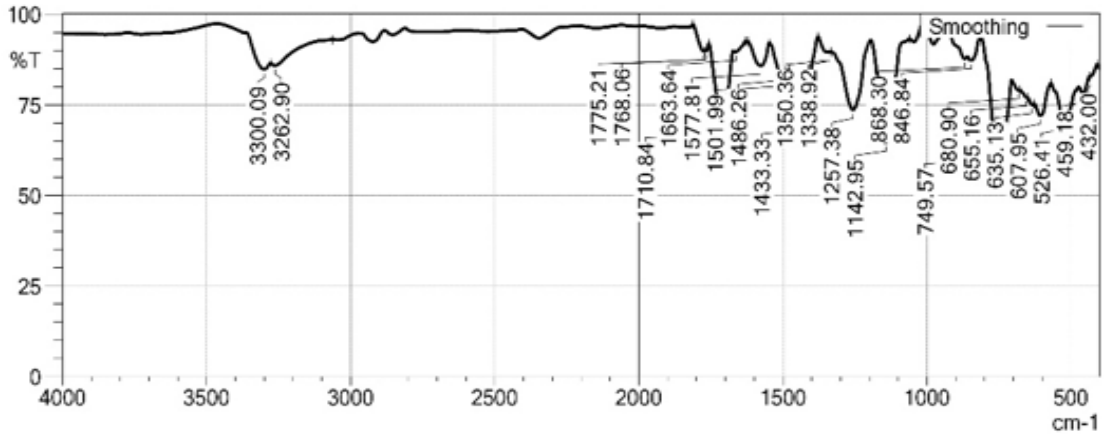


Figure 7: FTIR spectrum of Drug and polymer mixture

***In vitro* drug release study**

Table 9: %Cumulative Drug Release of all the formulations (F1-F9)

Time (hrs.)	F_1	F_2	F3	F4	F5	F6	F7	F8	F9
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
0	0	0	0	0	0	0	0	0	0
2	28.12 ± 0.05	32.12 ± 0.21	42.13 ± 0.29	21.64 ± 0.18	28.13 ± 0.13	31.08 ± 0.45	18.1 ± 0.21	22.18 ± 0.23	28.32 ± 0.24
4	40.32 ± 0.15	45.21 ± 0.18	58.02 ± 0.42	34.28 ± 0.26	40.16 ± 0.46	44.1 ± 0.13	30.18 ± 0.42	35.24 ± 0.32	40.24 ± 0.36
6	52.36 ± 0.28	58.18 ± 0.17	70.06 ± 0.23	48.24 ± 0.24	52.26 ± 0.48	56.13 ± 0.21	41.28 ± 0.19	47.28 ± 0.15	52.12 ± 0.48
8	66.28 ± 0.28	70.14 ± 0.26	82.28 ± 0.17	64.28 ± 0.45	66.22 ± 0.21	73.07 ± 0.58	52.18 ± 0.36	63.48 ± 0.18	66.24 ± 0.47
10	82.36 ± 0.19	86.15 ± 0.28	96.24 ± 0.16	80.64 ± 0.37	82.09 ± 0.78	85.12 ± 0.49	65.24 ± 0.74	84.24 ± 0.23	82.1 ± 0.18
12	97.36 ± 0.54	98.26 ± 0.24	97.08 ± 0.32	98.27 ± 0.43	97.14 ± 0.26	96.14 ± 0.17	82.13 ± 0.54	97.18 ± 0.28	97.48 ± 0.27

Here, Average of six tablets is taken and at SD (Standard deviation) is calculated

From the above results given in **Table 9.** it has been observed that formulation F_4 and F_7 gives the better results than other formulations when physical characteristics and drug release is considered as per **Figure 8**. F_4 gives better appearance of microballoons and Formulation F_7 shows best sustainability as the concentration of both Eudragit and HPMC is higher in this formulation. But % buoyancy of F_7 formulation not showed good results so F_4 is considered best among both the formulations. Further stability study results of F_4 formulation proved it to be a robust formulation.

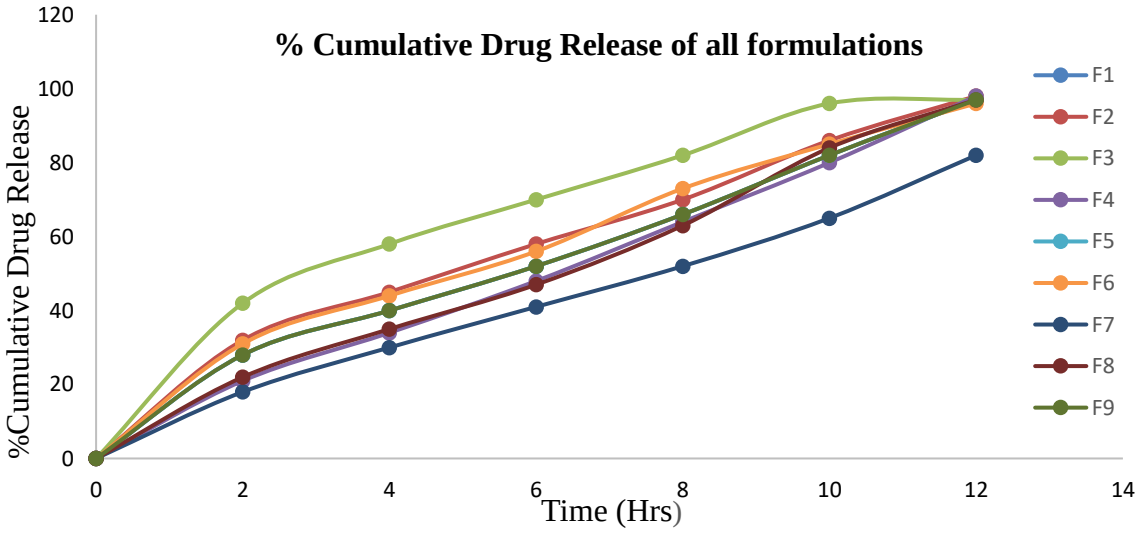
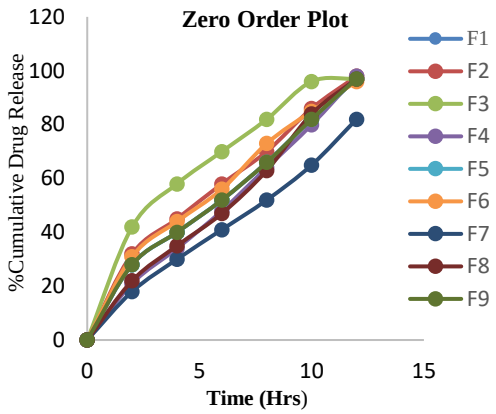


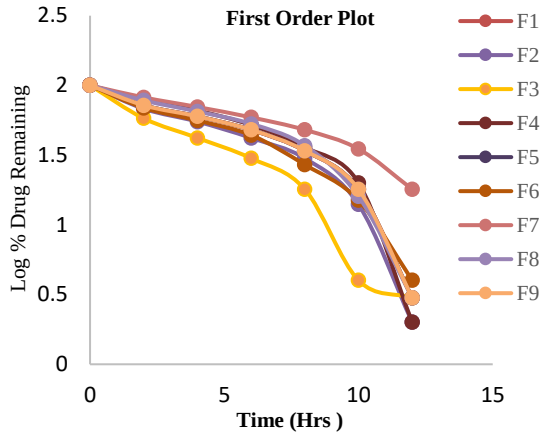
Figure 8: % Cumulative Drug Release of all formulations (F_1-F_9)

Drug release kinetics

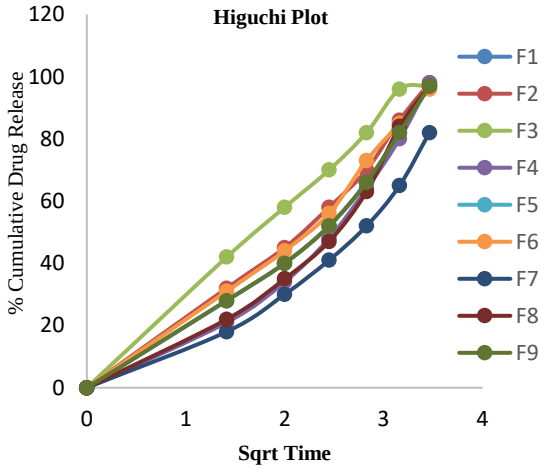
The drug release kinetics of all the formulation was checked which comprises of Zero Order (**Figure 9a**), First Order (**Figure 9b**), Higuchi Plot (**Figure 9c**), and Korsmeyer Peppas Plot (**Figure 9d**) from where the diffusional exponent was calculated.



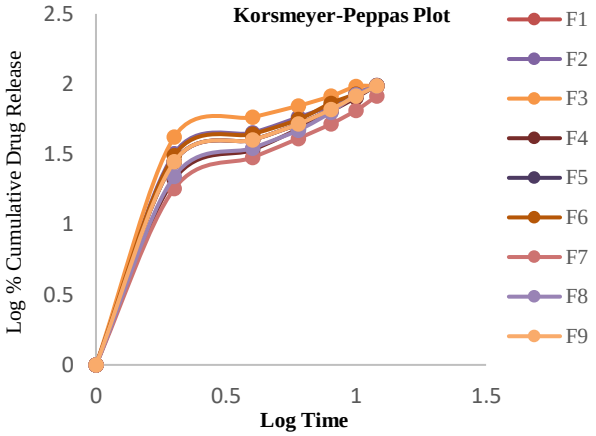
(a) Zero order Plot



(b) First Order Plot



(c) Higuchi Plot



(d) Korsmeyer- Peppas Plot

Figure 9: Drug release Kinetics of all formulations include **(a)** Zero order Plot, **(b)** First order Plot, **(c)** Higuchi Plot, and **(d)** Korsmeyer Peppas Plot

Since the diffusional exponent (n) is coming below 0.45 (**Table 10**)., hence it can be concluded that the drug release mechanism followed Fickian diffusion and the drug release kinetics mechanism followed Korsmeyer-Peppas model with initial first order release rate followed by zero order-controlled release.

Table 10: Drug release diffusional exponent from Korsmeyer Peppas Plot

	F1	F2	F3	F4	F5	F6	F7	F8	F9
K	1.8723	1.8251	1.8034	1.7195	1.5000	1.496	1.4876	1.4892	1.496
n	0.2055	0.1948	0.2000	0.1901	0.1842	0.1802	0.1716	0.1603	0.1445
R^2	0.9989	0.9993	0.9992	0.9983	0.9990	0.9991	0.9986	0.998	0.997

Stability study

A different range of temperatures was used to perform the stability study for F_4 formulation for 45 days. Drug content was checked at regular intervals and no remarkable change was found. The details are given in **Table 11**.

Table 11: Stability study data for F_4 formulation

Sl. No	Days	% Drug remaining 2-8°C	% Drug remaining 25 ± 2°C	% Drug remaining 40 ± 2°C
1.	0	100 ± 00	100 ± 00	100 ± 00
2.	14	99.6 ± 0.015	99.9 ± 0.003	99.4 ± 0.041
3.	28	99.5 ± 0.013	99.8 ± 0.027	99.2 ± 0.036
4.	45	99.4 ± 0.15	99.6 ± 0.012	99.1 ± 0.02

CONCLUSION

Gastro retentive dosage forms are a promising approach for prolonged and predictable drug delivery in the upper gastrointestinal tract to control the gastric residence time. Because of their low density, microballoons have good floating qualities and the benefits of multiple-unit systems, making them one of the most effective buoyant medication delivery devices. Moreover, the drug is released slowly at the desired rate when it floats over gastric contents resulting in reduced fluctuations in plasma drug concentration. It is supposed to be an efficient means of enhancing bioavailability. Biocompatible and cost-effective polymers like HPMC in combination with Eudragit RS100 were used to formulate an efficient floating microparticulate system. Hence, it can be concluded that the prepared floating microballoons of Aceclofenac proved to be a potential and promising candidate for multiple-unit delivery devices adaptable for safe and effective sustained drug delivery. The importance of gastro-retentive dosage forms, especially floating microballoons for drugs Aceclofenac, is relevant nowadays due to increasing demand for targeted, controlled, and precise drug delivery systems. These classes of dosage forms prolong and stabilize the drug release profiles, which are especially advantageous for the agent that can be only absorbed in the high gastrointestinal tract or that have a narrow absorption window, by prolonging the retention times of the drugs inside the stomach. Such technologies have successfully been able to make an impact in the current healthcare scenario in which optimizing therapeutic efficacy and patient compliance are a top priority. They float on top of the stomach solution to release the drug over a prolonged period and therefore it lessens the need for frequent doses and stabilize plasma drug concentrations. Drugs like Aceclofenac are usually prescribed for chronic conditions like arthritis and inflammatory disorders, where consistency in effects is very important. Using these biocompatible and inexpensive polymers, like HPMC and Eudragit RS100, would support the current tendency towards more affordable and patient-friendly health care. This will not only ensure better patient adherence but also broader access. It would, therefore, be a part of future drug delivery to better tailor therapies to needs while keeping them effective and adaptive and patient-cantered, based on the trends related to personalized medicine and emphasis on sustained and localized delivery.

Authors Contribution

Souvik Biswas: Conceptualization, original draft preparation, figure preparation

Sindhuja Sengupta: Original draft preparation, Editing

Padmanath Pegu: Review and editing

Nikita Dey: Secondary editing and Scientific evaluation

Amartya Sen: Primary editing, design

Biplab Debnath: Supervision and Project administration

Mrinmoy Nag: Conceptualization and study design

Nurul Amin: Collection and sorting of data

Arijit Das: Software applications for study design

Soumya Datta: Investigation, Data curation

Amlan Bishal: Supervising the work, conception, and Project administration

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