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Research Article

Development and Evaluation of Floating Pulsatile Drug Delivery System Using Meloxicam

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ABSTRACT
Objective: The objective of this research work was to develop and evaluate the floating– pulsatile drug delivery system (FPDDS) of meloxicam intended for Chrono pharmacotherapy of rheumatoid arthritis. Methods: The system consisting of drug containing core, coated with hydrophilic erodible polymer, which is responsible for a lag phase for pulsatile release, top cover buoyant layer was prepared with HPMC K4M and sodium bicarbonate, provides buoyancy to increase retention of the oral dosage form in the stomach. Meloxicam is a COX-2 inhibitor used to treat joint diseases such as osteoarthritis and rheumatoid arthritis. For rheumatoid arthritis Chrono pharmacotherapy has been recommended to ensure that the highest blood levels of the drug coincide with peak pain and stiffness. Result and discussion: The prepared tablets were characterized and found to exhibit satisfactory physico-chemical characteristics. Hence, the main objective of present work is to formulate FPDDS of meloxicam in order to achieve drug release after pre-determined lag phase. Developed formulations were evaluated for *in vitro* drug release studies, water uptake and erosion studies, floating behaviour and *in vivo* radiology studies. Results showed that a certain lag time before drug release which was due to the erosion of the hydrophilic erodible polymer. The lag time clearly depends on the type and amount of hydrophilic polymer which was applied on the inner cores. Floating time and floating lag time was controlled by quantity and composition of buoyant layer. *In vivo* radiology studies point out the capability of the system of longer residence time of the tablets in the gastric region and releasing the drug after a programmed lag time. Conclusion: The optimized formulation of the developed system provided a lag phase while showing the gastroretension followed by pulsatile drug release that would be beneficial for chronotherapy of rheumatoid arthritis and osteoarthritis.

Keywords: Floating – pulsatile drug delivery, Meloxicam, HPMC, *In vivo* radiology studies.

INTRODUCTION

Oral controlled release drug delivery systems offer many advantages when compared to immediate release delivery systems, such as: nearly constant drug level in plasma, minimizing peak- trough fluctuations, avoidance undesirable side effects, reduced dose, reduced frequency of administration, improved patient compliance. Controlled release systems are not so responsive to circadian rhythms. In addition, controlled release formulations are not applicable in some situations like time programmed administration of hormones and drugs. Pulsatile drug delivery system has fulfilled this requirement[1]. However pulsatile drug release pattern in which the active principle is released after pre-determined off release period i.e., lag time without drug release. No drug released from the device within this lag time is advantageous for following drugs and therapies: (i) Therapies that adapt drug needs to circadian rhythms of body functions or dieses. (ii) Avoiding degradation of drugs in upper GI tract, e.g., proteins and peptides. (iii) For time programmed administration of hormones and many drugs such as isosorbide dinitrate. (iv) To avoid pharmacokinetic drug–drug interactions between concomitantly administered drugs. (v) Drugs with an extensive first-pass metabolism, e.g., β- blockers. (vi) Drugs targeted to a specific site in the intestinal tract, e.g., to the large intestine or to the colon for the treatment of inflammatory diseases. (vii) Drugs tolerance can also be avoided etc.

Diseases like bronchial asthma, myocardial infarction, angina pectoris, rheumatic disease, ulcer, and hypertension display circadian variations that demand time based drug release for effective drug action[2]. The diagnostic criterion of the rheumatoid arthritis is morning stiffness associated with pain at the time of awakening. For rheumatoid arthritis Chrono pharmacotherapy has been recommended to ensure that the highest blood levels of the drug coincide with peak pain and stiffness[3-6]. To follow this principle one must have to design the dosage form so that it can be given at the convenient time for example bed time for the above mentioned diseases with the drug release in the morning. Meloxicam is 4-hydroxy-2-methyl-*N*-[(5-methyl- 1,3-thiazol-2-yl)-2*H*-1,2-benzothiazine-3- carboxamide-1,1-dioxide. It is a COX-2 inhibitor used to treat joint diseases such as osteoarthritis, rheumatoid arthritis and other

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musculoskeletal disorders. Using current release technology, it is possible for drugs oral delivery for a pulsed or pulsatile release, which is defined as the rapid and transient release of a certain amount of drugs within a short time-period immediately after a predetermined off-release period[7-11].

The disadvantage of these pulsatile release formulations is that they have need of a long residence time in the gastrointestinal tract. With conventional pulsatile release dosage forms, the highly variable nature of gastric emptying process can result in *in vivo* variability and bioavailability problems. The advantages for gastro-retentive pulsatile dosage forms are also pH dependent drug solubility (in this case meloxicam is good example)[12,13]. Overall, these considerations led to the development of oral pulsatile release dosage forms possessing gastric retention capabilities[14-16]. Ideally, the delivery system could result in (1) a floating dosage form with a prolonged gastric retention time and in (2) a pulsatile dosage form, in which the drug is released rapidly in a time-controlled fashion after rupturing of the pulsatile coating.

Objective of this present investigation was to develop and evaluate a floating- pulsatile drug delivery system. The system consists of three different parts, a core tablet, containing the active principle, an erodible outer shell, and a top cover buoyant layer[17]. One layer is for buoyancy and the other for drug pulsatile release. The pulsatile release system with various lag times was prepared by compression with different erodible polymeric layers (dry -coated systems) as described previously[18-21]. Combined usage of hydroxy propyl methylcellulose (HPMC) and sodium bicarbonate in a gastric floating drug delivery system has been reported to improve the floating properties[22,23]. Developed formulations were evaluated for buoyancy studies, dissolution studies, erosion studies and *in vivo* radiology studies.

MATERIALS AND METHODS

Materials

Meloxicam as a gift sample from Cadilla Pharmaceuticals (Ahmadabad), Low viscosity HPMC grades (HPMC E5, HPMC E15, and HPMC E50), HPMC K4M, Sodium bicarbonate, Magnesium stearate, Talc, Crosspovidone, and Perlitol are obtained from Dr'Reddy laboratories and SD fine chemicals.

Methods

Preformulation studies

Micromeritics

The angle of repose of meloxicam and formulation mixture was determined by the fixed funnel method. The bulk density (BD) and tapped densities (TD) were determined by using a density apparatus (Serwell Instruments, Bangalore, India). The Carr's index (%) and the Hausner's ratio were calculated.

Drug- excipient compatibility studies

Infrared spectra were taken by using KBr pellet technique using a Shimadzu FT-IR 8300 Spectrophotometer (Shimadzu, Tokyo, Japan) in the wavelength region of 4000 to 400 cm−1. The procedure consisted of dispersing a sample (drug alone or mixture of drug and excipients or formulation) in KBr and compressing into discs by applying a pressure of 5 tons for 5 min in a hydraulic press. The pellet was placed in the light path and the spectrum was obtained.

Preparation of Rapid Release Tablets (RRT)

The composition of the tablets is given in Table 1. The core tablets containing drug (Meloxicam), cross PVP (with different percentages) were prepared by weighing the drug, cross PVP and mixing with Perlitol SD 200. Magnesium stearate and talc (1.5% each) were added to each blend and further mixed. The resultant blends were tableted to 100 mg using 6mm flat-faced punches using a rotary tablet machine (Tablet compression machine, Cadmach, Ahmadabad, India).

Preparation of Pulsatile Release Tablets (PRT)

RRT was taken as cores, respectively, and 200-mg coatings of HPMC E50 were used with two steps: the first 100 mg coatings were filled into the die, followed by RRT in the centre of die, and slightly pressed to fix the coatings around and under the core, and then the rest of the coatings were filled and compressed. So PRT dry-coated with 200 mg HPMC E50 was prepared.

Preparation of Floating and Pulsatile Release Tablets (FPRT)

FPRT was designed to comprise PRT and a top cover buoyant layer. PRT was taken as the layer for pulsatile release. The buoyant layer included HPMC K4M, which upon contact with gastric fluid formed a gelatinous mass, sufficient for cohesively binding the drug release layer and effervescent component such as sodium bicarbonate, which is fabricated so that upon arrival in the stomach, carbon dioxide is liberated by the acidity of the gastric contents and is entrapped in the jellified hydrocolloid. These produce an upward motion of the dosage form and maintain its buoyancy.

The buoyant powder of 80% (w/w) HPMC K4M and 20% (w/w) NaHCO3 was passed through a 210-mm sieve to obtain a well-dispersed mixture and followed by the addition of 1% (w/w) magnesium stearate. The 100-mg buoyant powder was filled into the die, followed by PRT in the die, and then compressed.

Physicochemical characterization of tablets

The thickness of the tablets (n=3) were determined using Vernier callipers. The hardness of the tablets (n=6) was determined by using the Pfizer hardness tester Electrolab, Mumbai, India. The friability (%) of the tablets (n=10) was determined using Roche friabilator (Friabilator USP EF-2, Electrolab, Mumbai, India). Weight variation test of the tablets (n=20) was carried out as per the official method.

The disintegration time of core tablets containing different percentage of crospovidone was determined by the Disintegration tester USP (ED-2AL, Electrolab, and Mumbai, India). For determining the drug content of core tablets, 3 tablets (n=3) were crushed and equivalent weight of powder was dissolved in 100 ml of methanol.

Table 1: Composition of tablets.

Formulations	Core tablet			Pulsatile tablets					Floating Pulsatile Tablets				
	C1	C2	C3	P1	P2	P3	P4	P5	FP1	FP2	FP3	FP4	FP5
Meloxicam	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Spray dried mannitol	64	62	61.5	61.5	61.5	61.5	61.5	61.5	61.5	61.5	61.5	61.5	61.5
Crosspovidone (%)	5	7.5	10	10	10	10	10	10	10	10	10	10	10
HPMC E5	-	-	-	250	-	-	-	-	-	-	-	-	-
HPMC E15	-	-	-	-	250	-	-	-	-	-	-	-	-
HPMC E50	-	-	-	-	-	250	200	150	200	200	200	200	200
HPMC K4M	-	-	-	-	-	-	-	-	50	70	80	90	100
Sodium bicarbonate	-	-	-	-	-	-	-	-	50	30	20	10	0
Magnesium stearate	1.5	1.5	1.5	-	-	-	-	-	-	-	-	-	-
Talc	1.5	1.5	1.5	-	-	-	-	-	-	-	-	-	-
Total weight	80	80	80	330	330	330	280	230	380	380	380	380	380

Table 2: Physical evaluation of powder blend.

Formulation code	Angle of repose	Bulk density	Tapped density	Carr's index	Hausner's ratio
C1	26.12±1.13	0.311	0.365	14.79±1.12	1.17
C2	28.39±1.21	0.329	0.383	14.12±1.2	1.16
C3	25.79±1.29	0.321	0.342	20.15±1.3	1.06
P1	30.23±1.23	0.332	0.345	23.33±1.08	1.03
P2	31.12 ±1.13	0.312	0.376	24.09±1.05	1.20
P3	29.13±1.26	0.342	0.389	24.17±1.2	1.13
P4	32.72±1.23	0.319	0.406	21.43±1.03	1.27
P5	33.12±1.84	0.365	0.461	20.82±1.04	1.26
FP1	28.12±1.13	0.344	0.378	23.21±1.21	1.09
FP2	29.13±1.26	0.332	0.422	21.33±1.3	1.27
FP3	31.61±1.91	0.315	0.398	20.65±1.03	1.26
FP4	25.72±1.23	0.312	0.341	22.19±1.29	1.09
FP5	27.23±1.4	0.316	0.397	20.4±1.01	1.25

All values represent mean ± Standard Deviation (SD), n=3

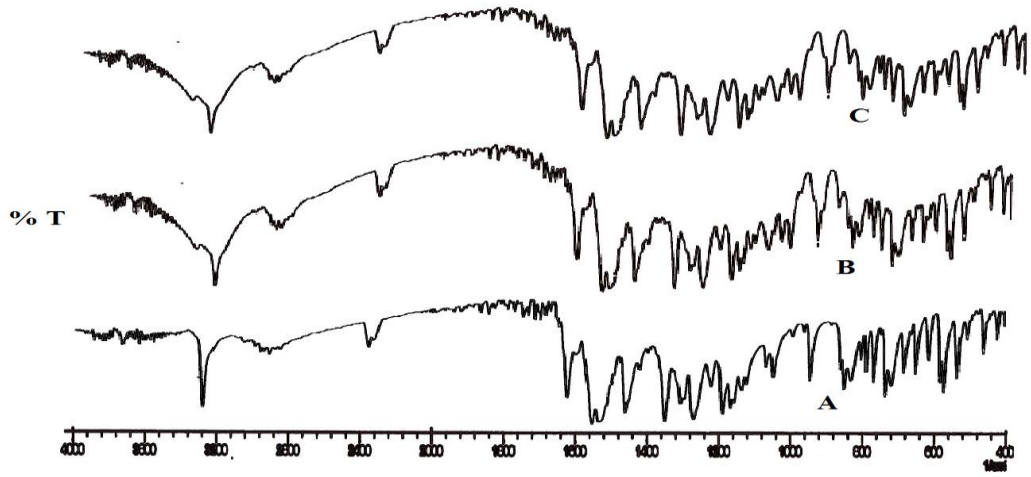

Figure 1: FTIR spectra of a) Meloxicam alone, b) Core tablet mixture (C-4) and c) Drug – polymer mixture (FP3).

The solution was then passed through a Whatmann filter and analyzed by UV–Visible spectrophotometer (UV 1601 PC, Shimadzu, Japan) at 362 nm after sufficient dilution with 6.8 pH Phosphate buffer.

Water uptake and erosion studies

Water uptake and erosion studies were conducted similar

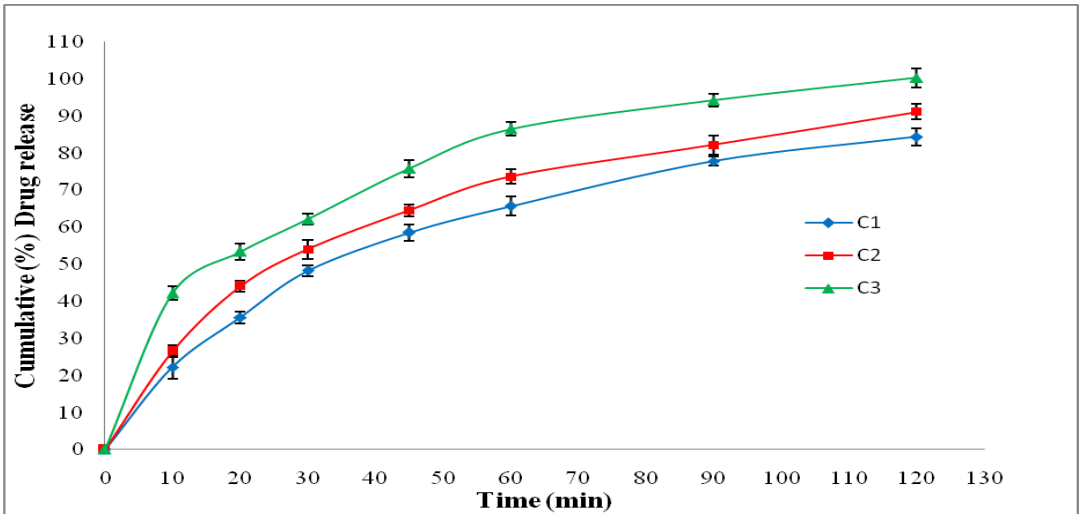

Figure 2: in vitro release profile of rapid release (meloxicam) tablets.

Table 3: Physical evaluation of tablets.

Formulation code	Hardness Kg/cm²*	Friability (%) **	Deviation in weight variation(mg) ***	Thickness(mm) *	Drug content (%) *
C1	2.3±0.6	0.43 ±0.1	99.2±0.7	2.25±0.5	99.1 ±0.8
C2	2.4±0.8	0.38 ± 0.04	100.5±1.9	2.4±0.7	102.8 ±0.2
C3	2.5±0.5	0.34 ±0.07	99.8±1.6	2.5±0.9	98.1 ± 1.2
P1	5.3 ±0.8	0.28 ±0.06	351.5±0.9	4.2±0.8	101.2 ±0.8
P2	5.6 ± 0.2	0.40 ±0.08	348.9±2.1	4.1±0.9	100.8 ± 0.4
P3	6.1 ±0.5	0.31 ±0.04	349.4±1.5	4.3±0.8	97.5 ± 0.9
P4	5.5 ±0.7	0.27 ±±0.2	249.5±1.9	3.5±0.5	98.6 ±1.9
P5	5.9 ±0.4	0.25 ±0.06	299.9±1.2	3.1±0.4	100.4 ± 0.9

***** All values represent mean ± Standard Deviation (SD), n=3
****** All values represent mean ± Standard Deviation (SD), n=6
******* All values represent mean ± Standard Deviation (SD), n=20

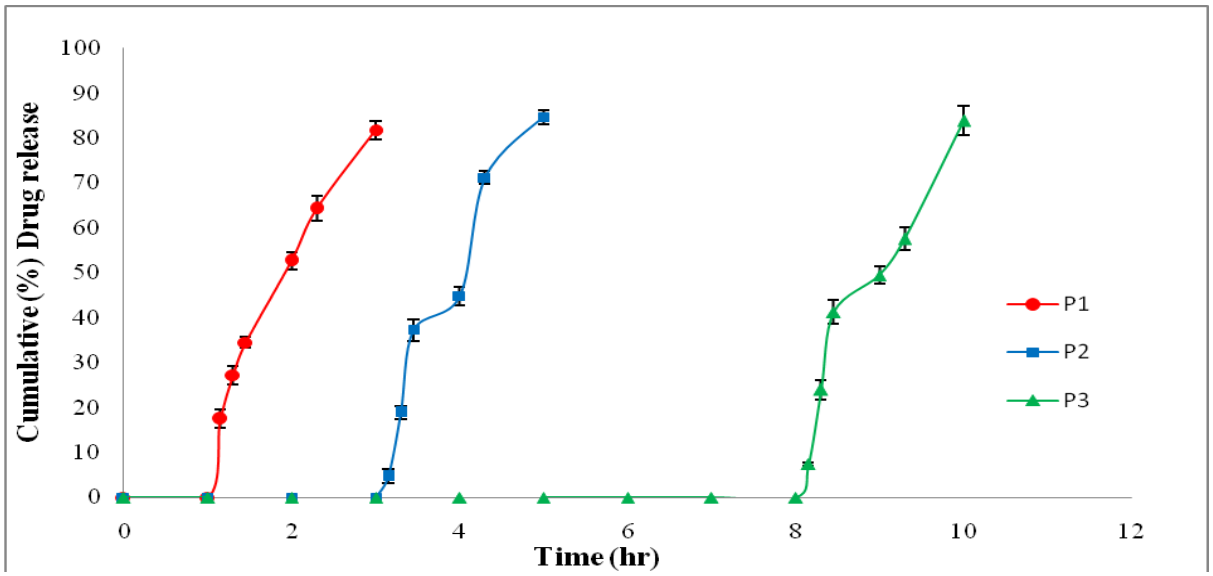

Figure 3: *In Vitro* release profile of rapid of Meloxicam from the pulsatile release tablet (PRT) coated with 250-mg different kinds of HPMC.

to the *in vitro* dissolution studies. At selected time intervals, an individual tablet was withdrawn using the basket. The basket and the tablet were blotted to remove excess liquid and then weighed on an analytical balance. The wetted tablets were then dried in an oven at 105 ◦C for 3 h, cooled in a desiccators and weighed again. This

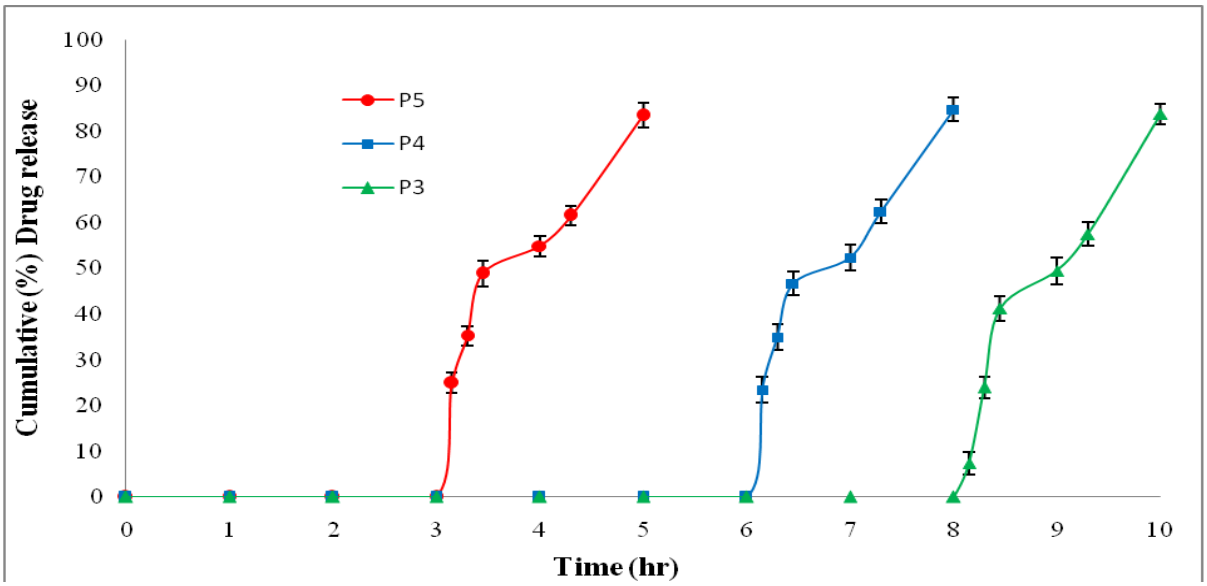

Figure 4: *In Vitro* release profile of rapid of Meloxicam from the pulsatile release tablet (PRT) coated with different amount of methocel E50.

Table 4: The Composition of the Buoyant Layers for Floating Testing, Expressed as mg per Tablet.

Ingredients	No.				
	FP1	FP2	FP3	FP4	FP5
HPMC K4 M	50	70	80	90	100
Sodium bi carbonate	50	30	20	10	0

Table 5: Floating Ability of Various Formulations (granules) of the Floating–Pulsatile Release Tablet (FPRT).

Formulation	Floating Onset Time (min)	Floating Duration (h)	Integrity
FP1	<1	<3	Broken
FP2	<1	>12	Intact
FP3	<1	>12	Intact
FP4	<1	>12	Intact
FP5	2-3	>12	Intact

procedure was repeated until constant weight was achieved (final dry weight). Three different tablets were measured for each time point and fresh tablets were used for each individual time point.

The extent of erosion (*E*) was determined from

$$E\,(\%) = 100 \times \frac{(W_i - W_f)}{W_i}$$

Where *W*i and *W*f are the initial starting dry weight and final dry weight of the same dried and partially eroded tablet, respectively. The increase in weight (uptake) due to absorbed liquid (*A*) was calculated at each time point from

$$A\,(\%) = 100 \times \frac{(W_w - W_f)}{W_f}$$

Where *W*w is the mass of the wet tablet before drying.

Floating lag time and buoyancy time

Floating lag time and floating time of FPRT was studied by placing them in 900 mL containers (0.1 N HCl). The floating onset time (time period between placing FPRT in the medium and buoyancy beginning) and floating duration of FPRT were determined by visual observation.

In vitro dissolution studies

The dissolution testing of core tablet was carried out using a USP Type II dissolution apparatus (TDT-06P, Electrolab, Mumbai, India) at 37±0.5 ℃ in 900 ml dissolution medium simulated intestinal fluid (without enzymes) at a speed of 50 rpm.

For Pulsatile tablets and floating pulsatile tablets two sets of dissolution studies were carried out using USP Type I dissolution test apparatus. Volume of dissolution medium (900 ml), stirring speed (100 rpm) and temperature of medium (37±0.2 ◦C) were kept same for all dissolution studies. In one set of dissolution studies, simulated gastric fluid without enzymes (SGF) was used as dissolution medium and dissolutions were performed for 6 h. The second set of dissolution studies were performed using SGF for time period equivalent to floating time which varied for each formulation and then subsequently in simulated intestinal fluid, w;;;ithout enzymes (SIF) till complete release of drug. At appropriate time intervals, 5 mL of the solution was withdrawn, filtered, and assayed by a UV spectrophotometer at 362 nm, while an equal volume of fresh dissolution medium was added into the apparatus. Dissolution tests were performed in triplicate. The lag time was determined by extrapolation of the upward part of release profile to the time axis.

In vivo radiographic studies

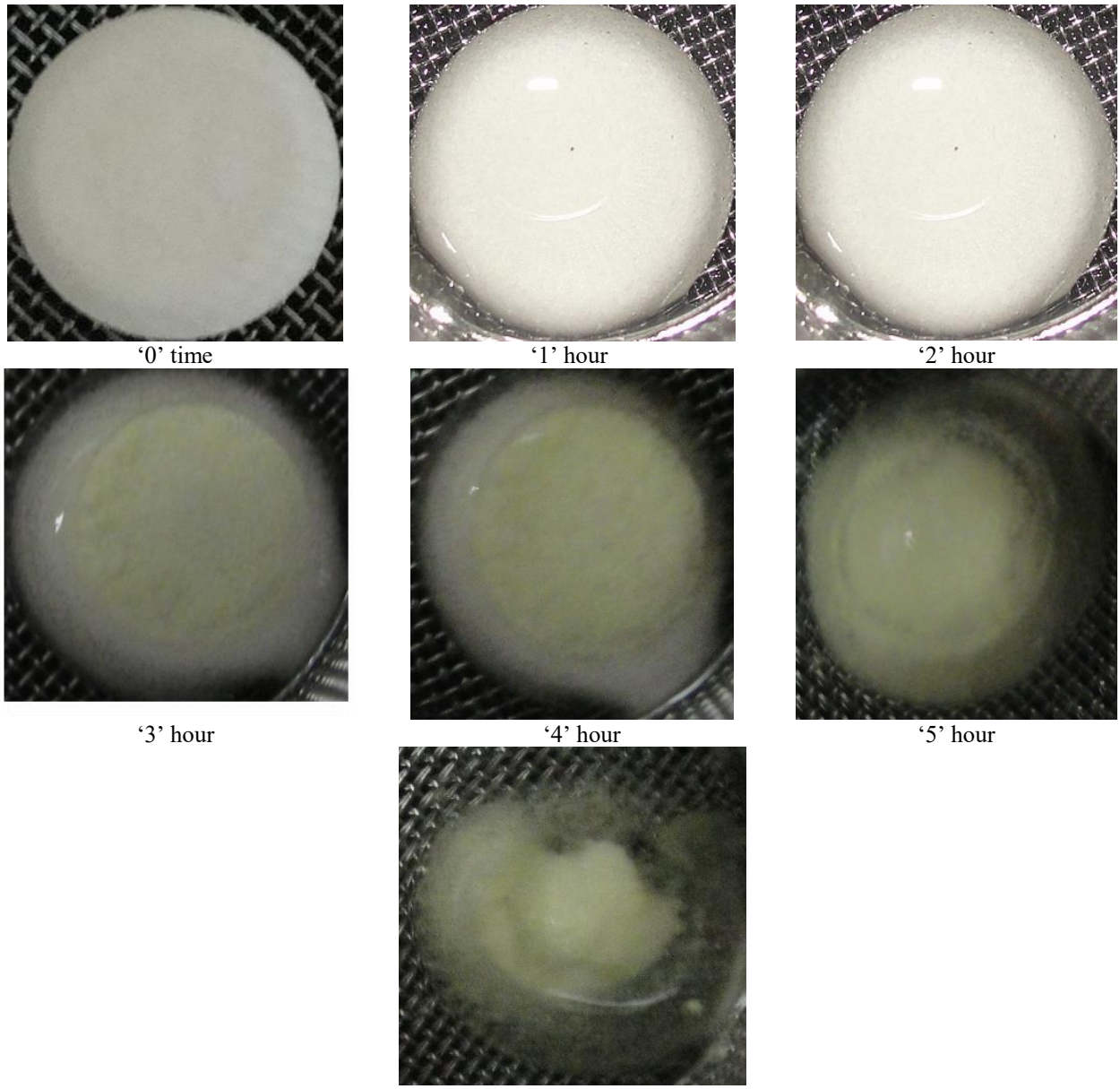

Figure 5: Morphological changes of pulsatile release tablets during dissolution.

In vivo radiology studies were conducted for examination of internal body system. This is the simplest method for studying the gastro retentive behaviour of dosage forms *in vivo*. The radiographic study protocol of Meloxicam floating-pulsatile tablets was approved by the Institutional Human Ethics Committee (IHEC), bearing No: 1007/SPIPS/WGL/IHEC/2011, Warangal, India.

Preparation of tablets for radiographic studies

For this study core tablets according to the optimized meloxicam tablet formulation were prepared by replacing the drug with radio-opaque compound barium sulphate. The coating was carried out similarly to that of the optimized batch.

Six healthy males with ranging ages (25–30), weights (55–70 kg) and heights (165–186 cm) were selected. No volunteer had a history of gastrointestinal disorders. Those volunteers who were smokers abstained during the study. The protocol was approved by the local Ethics Committee. The prepared tablets were administered simultaneously to each volunteer, 30 min after dinner with 200 mL water and then supine 6 h following the dose. Through the images taken at definite intervals by X-rays a gastro-intestinal transit of the dosage forms was followed and the site and time of their break-up were assessed.

RESULTS AND DISCUSSION

Preformulation studies

Micromeritics studies

The results of micromeritics properties were shown in table 2. For direct compression of materials, it is essential to possess good flow and compacting properties. Values for angle of repose 20–30° generally indicate good flow

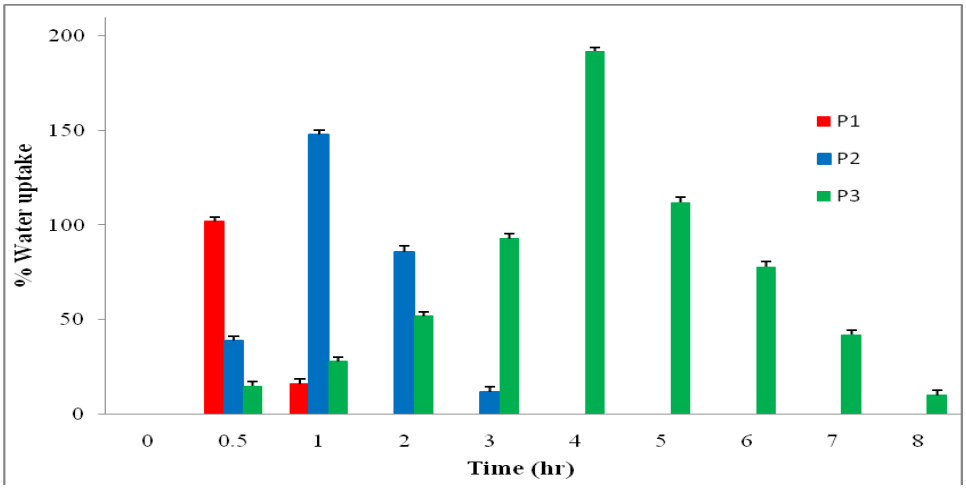

Figure 6: % water uptake studies for pulsatile release tablets coated with different viscosity grades of HPMC.

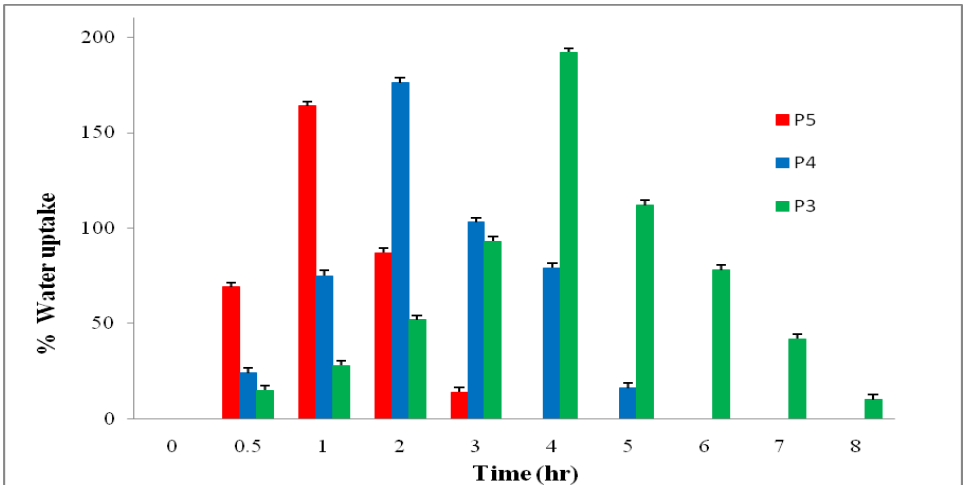

Figure 7: % water uptake studies for pulsatile release tablets with different coat level of HPMC E50.

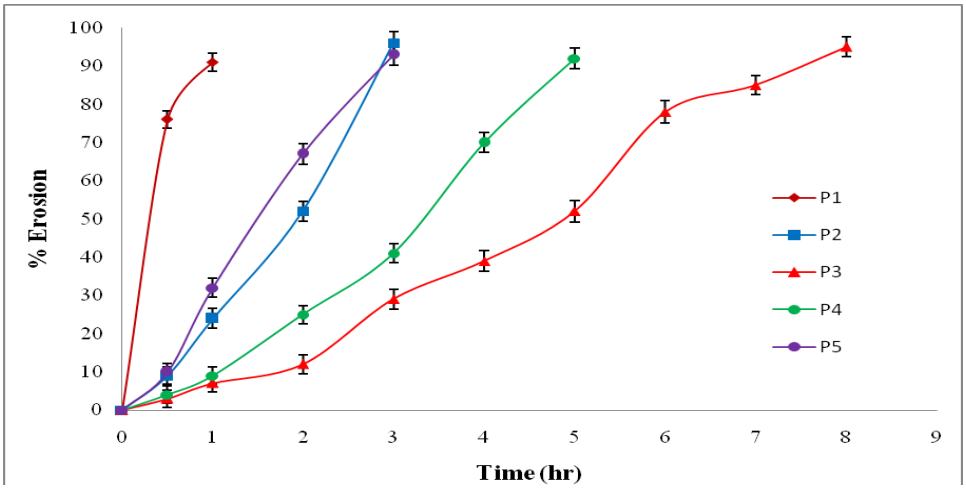

Figure 8: % Erosion studies for pulsatile release tablets.

property. A Hausner ratio of less than 1.25 and Carr's index of 12–16 indicate good flow The drug meloxicam exhibited angle of repose of 34.54±0.48° indicating poor flow property. The Carr's index (23.26±1.06%) and Hausner ratio (1.294±0.017) values were also high. All the prepared powder mixtures showed good flow properties as indicated by low values of angle of repose, Carr's index and Hausner ratio.

Drug-excipients compatibility studies

Drug-excipients compatibility studies were carried out by FTIR spectroscopy and differential scanning colorimetry (Thermal analysis). The FTIR spectra of pure meloxicam their physical mixtures with other excipients are shown in

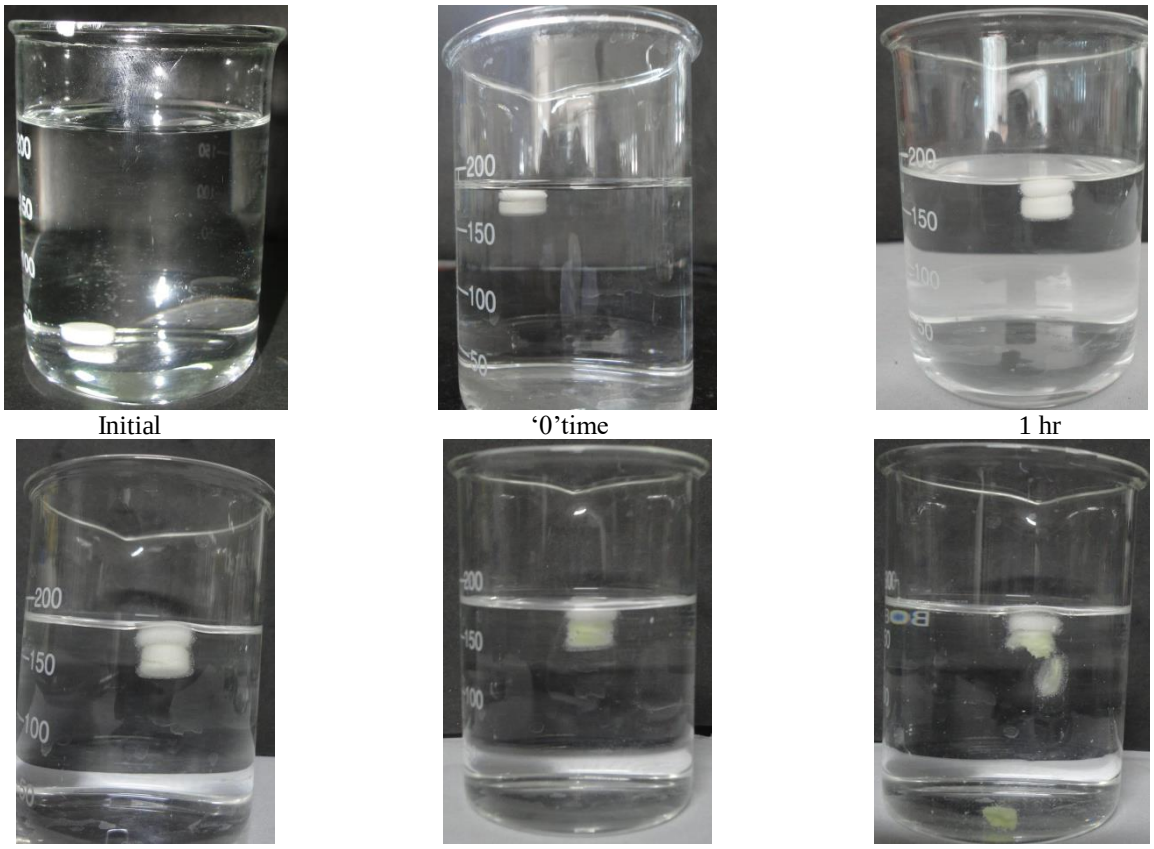

Figure 9. *In vitro* buoyancy studies

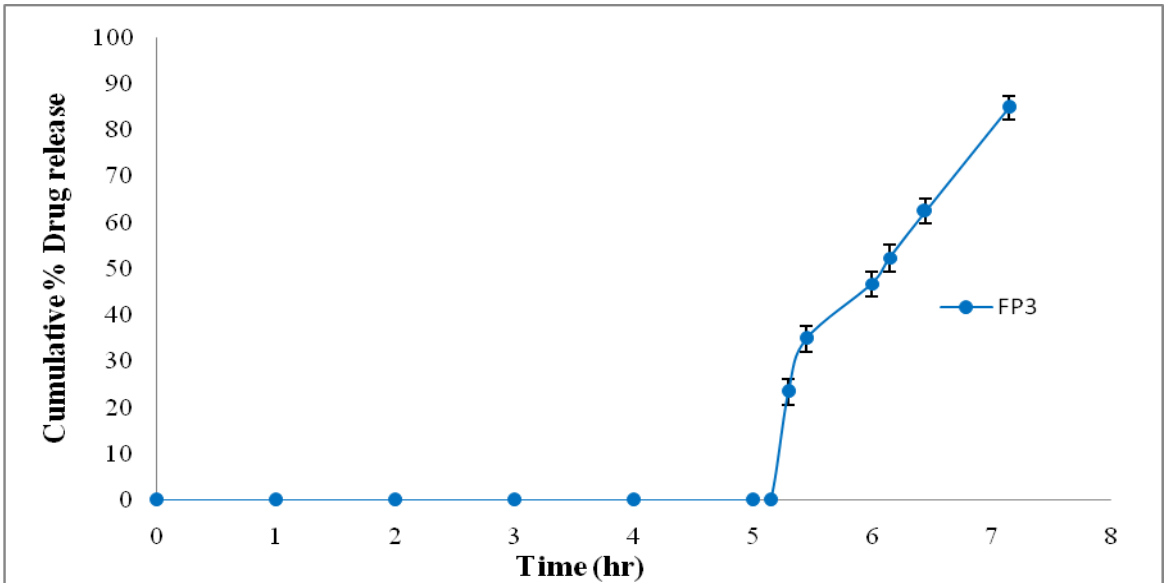

Figure 10: In vitro drug release profile of floating pulsatile release tablets (FPRT).

Figure 1. Meloxicam alone showed two carbonyl absorption bands at 1734 and 1603 cm−1, assigned to the carboxyl carbonyl and amide carbonyl stretching, respectively. These bands are of indicative value to elucidate drug–polymer interactions. No interaction was seen as the spectra remained have.

Physicochemical characterization of tablets

Design of rapid release tablets (RRT)

Different tablet formulations of meloxicam were prepared by direct compression (C1-C3, P1-P5, FP1-FP5). The tablet powder blend was studied for angle of repose, Carr's index and Hausner ratio. The tablets of different batches showed uniform thickness (2.0±0.25 to 2.5±0.14mm). Tablets are studied for hardness, disintegration, friability and weight variation. The hardness was found to be 2.5±0.7 to 3.0±0.4 kg/cm^2.The friability was within the official limits (<1.0%). The

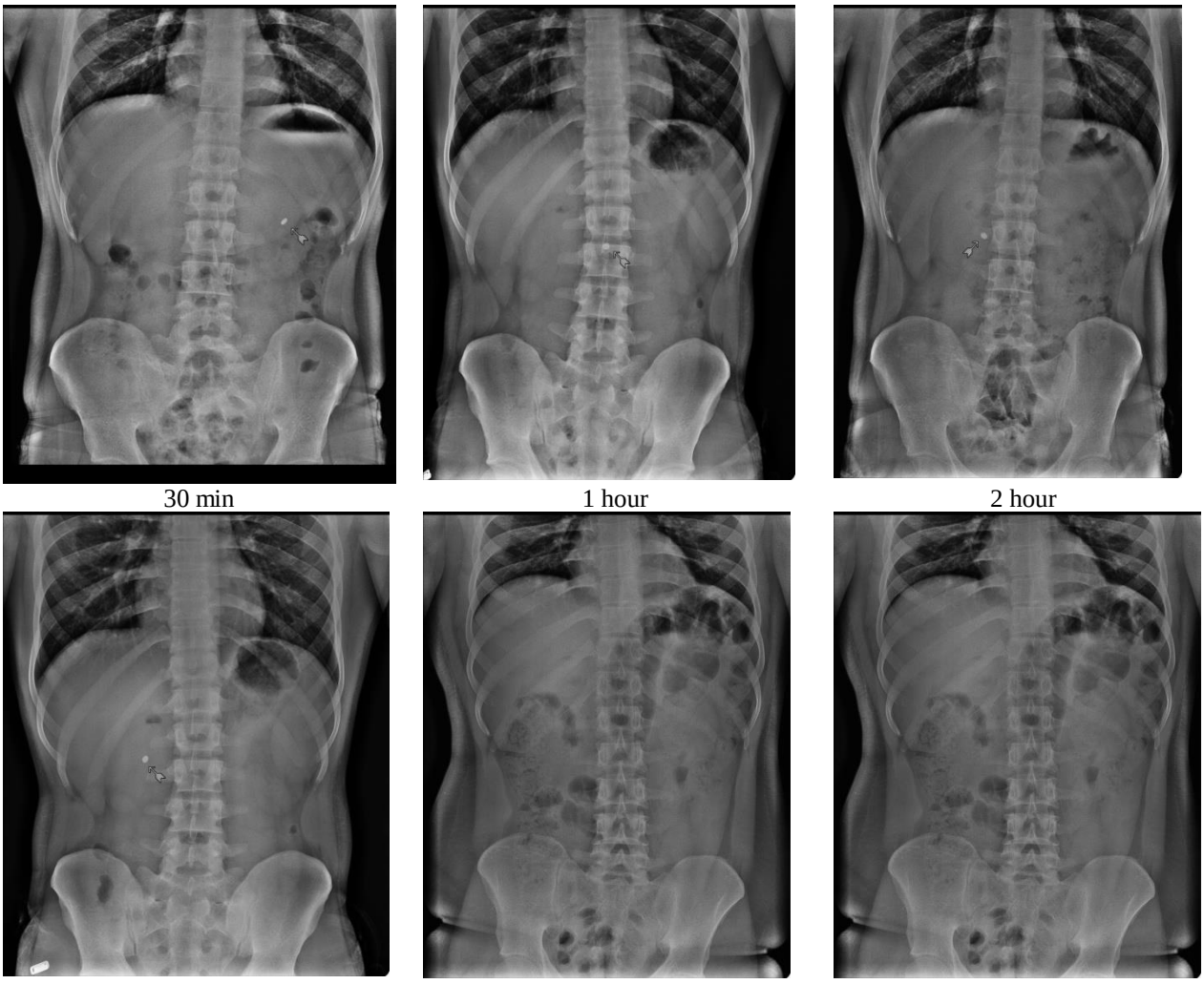

Figure 11: The localization of the tablet in the gastrointestinal tract in subject.

disintegration time taken by tablets without superdisintegrant was more than 10 min. The drug release was too slow and only 35.25±1.26% drug released in 120 min. Hence in order to get rapid release, super disintegrant was added in the formulation. Super disintegrants are generally used at a low level in the solid dosage form, typically 1–10% by weight relative to the total weight of the dosage unit. Examples of super disintegrants are crosscarmelose, crosspovidone (CPVP), sodium starch glycolate etc. CPVP is a water insoluble type tablet disintegrant exhibiting high capillary activity and prominent hydration capacity with little tendency to gel. The formulation C1 containing 5% CPVP disintegrated in 6 min, C2 (7.5% CPVP) in 3 min and C3 (10% CPVP) within <1 min. The drug release was rapid in all formulations compared to tablets without superdisintegrant. The formulation C3 as optimized and showed 99.35±1.26% release in 120 min and found to be suitable to use in pulsatile delivery system (Figure 2).

Formulation erodible tablets

Different erodible tablet formulations were prepared by direct compression. For this study, core tablets were compression coated with different low viscosity HPMC grades (E5, E15 and E50) at 250 level coat. The tablets of different formulations showed uniform thickness (4±0.37 to 4.2±0.23mm) and diameter (10mm±0.1). Tablets are studied for hardness, friability and weight variation. The hardness was found to be 5.1±0.5 kg/cm^2. The friability was within the official limits (<1.0%). The *in vitro* dissolution was carried in 0.1 N HCl solution and the release profile was shown in figure.3.

In the *in vitro* study, the three formulations were designed by changing weight (150, 200 and 250 mg) of coating layers with HPMC E50. The thickness of these formulations is found to be 3.0±0.85mm, 3.6±1.2mm and 4±0.37mm respectively. Tablets are studied for hardness, friability and weight variation. The hardness was found to be 5.1±0.5 kg/cm^2. The friability was within the official limits (<1.0%). The in-vitro dissolution was carried in 0.1 N HCl solution and the release profile was shown in Figure 4. As the erodible tablets were placed in the aqueous medium it was observed that the hydrophilic cellulosic barrier starts the progressive hydration, dissolution and erosion phenomena, thus preventing the drug from being delivered.During the dissolution phase procedure, the coating layer gradually starts to erode up to a limiting thickness. After this stage, a rapture of the outer layer was observed under the pressure applied by

the swelling of the core tablet due to the presence of superdisintegrant (crospovidone) and the drug is released. All of this process was responsible to lag time capable of exhibiting a pulsatile release of the drug (Figure 5).The lag time of pulsatile release tablet was clearly depended on the viscosity grade and amount of hydrophilic polymer which was applied on the core. The lag time *in vitro* of the tablet coated with 200 mg HPMC E50 was 5.15±0.1 h.

Water uptake and erosion studies

Since the rate of swelling and erosion is related and may affect the mechanism and kinetics of drug release, the penetration of the dissolution medium and the erosion of the hydrated tablets were determined. Simultaneously with the water uptake study, the percentage erosion of polymer was determined. The percentage water uptake and erosion of all formulations were shown in Figures 5, 6, and 7. Results showed that higher % water uptake was observed with HPMC E50 with 250 mg weight of the coat than HPMC E15 and HPMC E5. This may be due to the increasing the viscosity of HPMC E50 polymer and also increasing the thickness also effect the % water uptake. % Erosion was also depends on the thickness and viscosity grade of the polymer. Increasing thickness and viscosity of the polymer produced there is delaying polymer erosion.

Formulation of floating pulsatile release tablets

The compositions of the floating layer of the FPRT for floating testing were shown in Table 4. All powdered excipients were mixed for 5 min using a mortar and pestle to form a homogenous directly compressible powder mix. When the system was immersed in a 0.1 N HCl solution at 37^0C, it sank at once in the solution and formed swollen tablet with a density much lower than 1 g/mL. The reaction was due to carbon dioxide generated by neutralization in the floating layer with the 0.1 N HCl solutions. These systems (Table 5. F1, F2, F3, F4) were found to float completely within 1 min and remained floating over a period of 12 h. The onset time of F5 floating was about 2–3 min because there was no sodium bicarbonate in the buoyant layers.The duration time of F1 remaining floating was no more than 3 h because of too large amount of sodium bicarbonate in the buoyant layers.

The mechanism of floatation here is that the sodium bicarbonate, in addition to imparting buoyancy to the novel formulation, provides the initial alkaline microenvironment for polymers to gel. Moreover, the release of CO_2 helps to accelerate the hydration of the floating layer, which is essential for the formation of a bio adhesive hydrogel.

In vivo radiographic studies:

The radiographic images were taken at different periods post administration of barium sulphate- loaded tablets in three human volunteers (Figure11). It is the simplest and cheapest compared to other methods for studying the gastro-retentive behaviour of dosage forms *in vivo*. The analysis of *in vivo* radiology images for the volunteers showed that *in vivo* lag time values (5.0±0.1 h on average) of FPRT were found to be the relatively low variability and be consistent with the corresponding *in vitro* lag time (5.15±0.1 h).

CONCLUSION

The floating pulsatile release tablets containing the floating material, such as HPMC K4M and sodium bi carbonate (80:20), achieved a satisfactory buoyant force in-vitro, whereas the floating lag time was less than 1minute and the floating time were more than 12 hours. Drug releasing mechanism of FPRT is based on the exploitation of interaction between hydrophilic polymeric coating and the aqueous gastrointestinal fluids. The *in vitro* release profile of meloxicam from FPRT prepared using HPMC E50(200mg) as retarding polymer are characterized by pre-determined lag phase, the lag time which depends on the kind and amount of the polymeric layer applied on the cores. Overall the developed system provided a lag phase while showing the gastroretension followed by pulsatile drug release that would be beneficial for chronotherapy of rheumatoid arthritis and osteoarthritis. Future bioavailability studies may be required to prove the clinical effectiveness of such dosage forms.

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