Journal of Advanced Pharmacy Education & Research
2 (1) 18-24 (2012) ISSN 2249-3379

Meloxicam Loaded Floating Sustained Release Matrix Tablet

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ABSTRACT

The objective of this present research is to formulate floating sustained release matrix tablets using hydroxyl propyl methyl cellulose (HPMC) K15M as matrix forming polymer and sodium bicarbonate as a gas generator. Meloxicam was used as model drug. The directly compressed tablets were evaluated for physical parameters such as weight uniformity, hardness, friability, drug content, *in-vitro* buoyancy, and swelling index. It was observed that the buoyancy lasted for up to 24 h and supported by *in-vitro* dissolution studies. The dissolution data was subjected to various release kinetic models.

Keywords: Floating tablet, HPMC K15M, Meloxicam, sodium bicarbonate

INTRODUCTION

Floating drug delivery system (FDDS) shows buoyancy in stomach for extended time period thus offers extended gastric residence time for the dosage form ensuring optimal bioavailability (BA). [1] The residence time of the dosage form in the stomach depends upon various factors like pH, size of the dosage form, food intake, and biological factors which include age, body mass index, gender, posture, and diseased states (hepatic failure, diabetes, chrons disease). Other techniques for gastro retentive dosage forms involve swelling, mucoadhesion, sedimentation, microballoons[2],[3] and low density systems. Out of all systems available, the floating beads, floating tablets and floating microspheres have gained major importance. FDDS possess lower bulk density than the gastric fluid exerting buoyancy in the stomach leading to slow drug release in an extended manner before it reaches absorption window. [4] In this present formulation, dual benefits of buoyancy as well as sustained action is achieved with an intention to maintain the steady state of drug release.[5] Hydrophilic matrix system is one of the easiest approaches for developing modified and sustained release dosage forms. A polymer like hydroxyl propyl methyl cellulose (HPMC) function as a pH independent

gelling agent and drug release is shown by swelling and erosion mechanism occurring simultaneously contributing to overall drug release. [6]

Matrix system is the commonly used method for modulating the drug release. [7] The manufacture of matrix tablets by direct compression is cheaper, simpler process, broad regulatory acceptance, and allows flexibility in obtaining desirable release profiles. [8] In spite of the poor flow property of controlled release polymers, by admixture of directly compressible microcrystalline cellulose (MCC) and other excipients, excellent flow property is being achieved. This investigation is restricted to floating tablets of meloxicam with sustained release by employing various concentrations of release retarding polymers, HPMC K15M, and gas generators. [9]

MATERIALS AND METHODS

Materials:

Meloxicam was obtained as gift sample from (Micro Labs, India). HPMC K15M, talc, magnesium stearate, microcrystalline cellulose, lactose and sodium bicarbonate were procured from SD Fine chemicals, India. All the materials used were analytical grade, purchased from India.

Methodology:

Formulation of floating matrix tablet

Sustained release floating matrix tablets were prepared by direct compression method. All the excipients were weighed accurately and sifted through 40# mesh screen. Drug was geometrically mixed with excipients followed by addition of the matrix forming polymer and gas generating agent. Mixing was done and final sifting was carried through 22# mesh screen. Pre-lubrication and lubrication was done for 5 and 2 minutes, respectively. Compression was carried out by manual single punching machine. The formulated tablets were further evaluated of the tablet parameters. In all the formulations, polymers concentration was varied from 10 to 50% of the total weight. The composition of various formulations is shown in the Table 1.

Characterization of floating matrix tablet

Thickness and weight variation test

Six tablets were selected randomly for thickness measurements by using vernier calliper. Average values were calculated and tabulated. To study the weight variation,

10 tablets of each formulation were weighed individually using an electronic balance (Shimadzu, Japan) and the test was performed. [10]

Table 1: Formulation Table of Meloxicam loaded Floating Matrix Tablet

Ingredients	F1	F2	F3	F4	F5
	Quantity in mg/tab				
Meloxicam	10	10	10	10	10
HPMC K15M	15	30	45	60	75
sodium bicarbonate	20	20	20	20	20
Microcrystalline Cellulose	40	35	30	25	20
Lactose	62	52	42	32	22
Talc	3	3	3	3	3

Drug content

10 tablets of same weight were selected and crushed using mortar and pestle. Powder equivalent to the average weight of the tablet was weighed and dissolved in 0.1 M HCl and diluted suitably. The concentration of drug in the samples was detected using ultra violet (UV)-visible spectrophotometer. [11]

Hardness and friability

Six tablets from each formulation were subjected for crushing strength and friability by using the Monsanto hardness tester (Cadmach, Ahmedabad, India) and the Roche friabilator (Veego, Mumbai, India), respectively. [12]

***In-vitro* buoyancy study**

The *in-vitro* buoyancy was determined by observing the floating lag time and the total floating duration (floating capacity). For determining the floating lag time, 0.1 N HCl was taken as the media and three tablets were placed in it. The time required for the matrix tablet to rise from the bottom to the surface of the media for floating was determined. The time was observed visually and recorded using stop watch. For observing the total floating duration, three individual tablets from each formulation were put in a beaker containing 900 ml of 0.1N HCl media. Then the time taken for each tablet to constantly float on the media was measured. The sample mean and standard deviation were calculated for the observed data. [13]

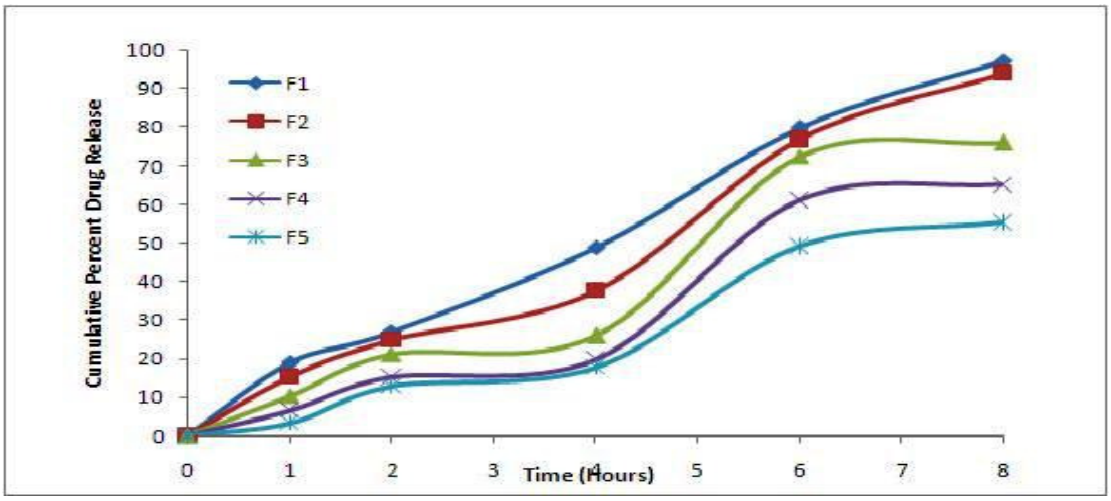
Hydration response

The swelling properties of matrices containing drug were determined by placing the tablet in the dissolution test apparatus containing 900 ml of 0.1 N HCl and maintained at 37 ± 0.5°C. At periodic time intervals, the tablets were taken out of the medium and the weight gain in each tablet was checked using electronic weighing balance (Model: BL-220H, Shimadzu Corporation, Japan). The swelling characteristics were expressed in terms of the percentage water uptake (WU %) according to the equation. [14]

$$WU = \frac{\text{Weight of swollen tablet-initial weight of tablet}}{\text{Initial weight of tablet}} \times 100$$

***In-vitro* dissolution studies**

Dissolution studies were performed using 900 ml 0.1M HCl with pH 1.2 using paddle method at 100 rotations per minute (rpm) and 37°C. Samples of 10 ml were withdrawn from each basket at periodic time intervals. Equal amount of fresh dissolution media was replaced to maintain the sink condition. [15] The amount of meloxicam release in each sample was determined at wavelength of 339 nm using UV-Visible spectrophotometer (Shimadzu). Release data is shown in Figure 1.



RESULT AND DISCUSSION

Tablet Characterization

The average weight of the tablet ranges from 143 to 149 mg for all the formulations which complied with the monograph specification limit of ±7.5%. As a measure of

mechanical strength, these formulations exhibited satisfactory hardness of 1.5 to 2.5 kg/cm ^{2} and the same fact was further supported by friability of less than 1%. Drug content of all the formulations ranged between 98.94 to 99.34 %, which was within the standard limits of 90.00 - 110.00 %. The average wetting time for the formulation F-1 to F-5 was in the range of 8-10 minutes and buoyancy lag time showed less than one minute, and the buoyancy duration showed more than 24 h [Table 2]. The tablets showed elegant appearance and excellent floating property

***In-vitro* Dissolution Studies**

As shown by *in-vitro* dissolution data, the increase in the polymer concentration of HPMC K15M progressively retarded the drug release. The lowest polymer concentration (F-1) showed faster release 97.8% in 8 hrs and the highest polymer concentration (F-5) released only 55.32% drug after 8 h as shown in Table 3. When the concentration of the hydrophilic polymer was increased, the time taken for its swelling and erosion in the media was increased due to high viscous gel strength. Therefore, the diffusion of the water insoluble drug from the matrix was retarded to its maximum and the drug release was slowed down.

Table 2: Physical Evaluation of Compressed Matrix tablet

Physical Parameters	F1	F2	F3	F4	F5
Hardness (kg/cm²)	1.5±0.35	1.5 ± 0.15	2.0 ± 0.17	2.5 ± 0.28	1.5 ± 0.93
Thickness (mm)	3.4±0.03	3.3 ± 0.55	3.4± 0.82	3.4 ± 0.19	3.4 ± 0.05
Friability (%)	5 ± 0.5	3.2 ± 0.74	0.78±0.03	0.63 ± 0.39	0.54 ± 0.2
Weight Uniformity (mg)	144.8±0.77	143.9±0.84	146.4±0.37	147.67±0.07	149.65±0.66
% Drug Content	99.78	98.45	98.92	99.65	99.13
Buoyancy lag time (sec)	<1	<1	<1	<1	<1
Buoyancy duration (h)	>24	>24	>24	>24	>24
Wetting time (min)	8.5	8	9	8	10

Table 3: *In Vitro* Drug Release Data for All Formulations

S. No.	Time (h)	F1	F2	F3	F4	F5
1	1	18.97	15.46	10.33	6.55	3.21
2	2	26.97	24.97	21.09	15.09	12.76
3	4	48.96	37.67	25.93	19.85	17.83
4	6	79.83	76.83	72.39	61.08	49.07
5	8	97.48	94.08	76.03	65.18	55.32

CONCLUSION

Floating drug delivery system can be successfully formulated by direct compression technique and combination of polymers. The present investigation proved that a hydrophobic drug can be designed as modified release dosage form with desired qualities, using a hydrophilic polymer HPMC K15M and sodium bicarbonate as a buoyancy initiator.

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