Indian Journal of Novel Drug Delivery

IJNDD

An Official Publication of Karnataka Education and Scientific Society

Research Article

Design and Development of Floating Gastro Retentive Tablets for Mosapride Citrate Dihydrate: *In vitro-in vivo* Evaluation

IGE PRADUM PUNDLIKRAO *, PATEL KALPESH MOHANBHAI

Department of Pharmaceutics and Quality Assurance, R C Patel Institute of Pharmaceutical Education & Research, Shirpur, Dist, Dhule, Maharashtra 425405, INDIA.

ARTICLE DETAILS

Article history:
Received on 30 July 2012
Modified on 10 October 2012
Accepted on 15 October 2012

Keywords:
Mosapride citrate dihydrate,
Floating matrix tablets,
HPMC K4M,
Eudragit RS,
Gas forming agent.

ABSTRACT

The aim of the current work is to develop stable formulation of mosapride citrate dihydrate in the form of floating matrix tablet, in combination with two different polymers hydroxy propyl methyl cellulose (HPMC K4M) and Eudragit RS. The Mosapride citrate dihydrate in a form of gastro retentive floating sustained release dosage forms, which provides enhanced bioavailability. In the present study mosapride citrate dihydrate controlled release tablet were prepared with the help of the direct compression method, using sodium bicarbonate and citric acid as the gas forming agent. It was characterized by FTIR spectroscopy, floating ability, swelling ability, *in vitro* drug release, *in vivo* x-ray imaging and stability studies. The physical characterization of the floating matrix tablets was examined by SEM and results showed that the shape and texture of the tablets were uniform. Percent drug content from the tablets was determined by UV spectrophotometer and exhibited about 99.32 ± 0.08. The *in vitro* drug release from the tablets was found to have 78.3 ± 0.2 to 99.04 ± 0.12 for 12 h. The optimized formulations F3 were kept for 90 days at 40°C / 75% RH. After 90 days of exposure the percent drug content was found to be 99.70 ± 0.04. In conclusion, the combination of eudragit RS and HPMC K4M at the 1.0:4.5 w/w ratios could be the effective carrier for the sustained release floating matrix tablets of mosapride citrate dihydrate.

INTRODUCTION

The oral route is considered as the most promising route of drug delivery. The high level of patient compliance in oral drug delivery systems is due to the ease of administration and handling of these systems. Most of the oral dosage forms possess several physiological limitations such as variable gastrointestinal transit, because of variable gastric emptying leading to non-uniform absorption profiles, incomplete drug release and shorter residence time of the dosage form in the stomach [1-4].

Dosage forms that can be retained in the stomach are called gastro retentive drug delivery systems (GRDDS). GRDDS can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs.

Author for Correspondence:
Email: pradyumna_1978@rediffmail.com

Prolonged gastric retention improves bioavailability, increases the duration of drug release, reduces drug waste, reduces undesirable effects and minimize the fluctuation of drug concentrations [5-7]. It improves the drug solubility that are less soluble in a high pH environment and also prolonged gastric retention time (GRT) in the stomach could be advantageous for local action in the upper part of the small intestine e.g. treatment of *H. pylori* infection. GRDDS can improve the controlled delivery of drugs that have a narrow absorption window in GIT by continuously releasing thedrug for a prolonged period of time [8-9]. GRDDS suffer from mainly two unfavorable conditions: the short gastric retention time (GRT) and unpredictable short gastric emptying time (GET), therefore incomplete drug releases from the dosage form at the absorption window (stomach or upper small intestine) leading to diminished efficacy of administered dose [10-12].

Floating drug delivery systems (FDDS) are retained in the stomach for a prolonged period of

time by virtue of their floating properties, which can be acquired by effervescent and non-effervescent systems. FDDS have a bulk density less than gastric fluids and remain buoyant in the stomach without affecting gastric emptying rate for a longer period of time. When the system is float on the gastric contents, the drug is released slowly in the desired controlled rate from the system. Hence, this will result in a better control of the fluctuations in plasma drug concentrations [13-16].

Drugs that are easily absorbed from gastric pH environment and have short half-lives are eliminated quickly from the systemic circulation. The more frequent dosing of these drugs is required to achieve suitable therapeutic activity [17]. To avoid this limitation, the development of oral floating sustained release formulations is an attempt to release the drug and maintain an effective drug concentration in the systemic circulation for a long time.

Mosapride citrate dihydrate is BCS II class drug having low solubility and high permeability. It is slightly soluble in water, soluble in dimethyl formamide [18-20]. Mosapride citrate diydrate is a gastro prokinetic agent that acts as a selective $5HT_4$ agonist which accelerates gastric emptying. Mosapride citrate dihydrate enhance upper gastro intestinal motor activity with minimal or no effect on lower gastrointestinal motor activity. It binds to 5-HT4 receptor in stomach and that stimulates acetylcholine release from cholinergic neurons in the gastro intestinal wall and enhances upper gastrointestinal motor activity and so, increases motility of bowel loops [21-25]. Mosapride citrate diydrate is used for the treatment of acid reflux, non-ulcer dyspepsia, gastroparesis, gastric stasis, irritable bowel syndrome and has beneficial effects on glycemic control in patients with type II diabetes mellitus [26-28]. Main problem of this drug is solubility, but it is better soluble in acidic environment, increase the pH decrease the solubility [29-31].

On the basis of these literatures, it can be attempted to formulate floating matrix tablets of mosapride citrate dihydrate using different polymer combinations. In combination, HPMC K4M and Eudragit RS, investigate the combined effect of these polymers on the floating behavior and *in vitro* release pattern of the drug. Hydrophilic polymer (HPMC K4M) slowly forms thick gel, which retains integrity of the formulation, which promotes drug release through thick gel and hydrophobic polymer (Eudragit RS) resist the water penetration in matrix which controls the burst release [32]. Citric acid and sodium bicarbonate can be explored as a gas generating agent to achieve enhanced gastric resident time.

In the current work, we developed floating matrix tablets containing mosapride citrate dihydrate to get the sustained release for 12 h. The tablets were designed using design expert software 8.0.1.0 and prepared by mini rotary machine. Floating matrix tablets were characterized by flow properties, physical properties, swelling ability, *in vitro* lag time, *in vitro* floating ability, drug content, *in vitro* drug release, *in vivo* x-ray imaging and stability studies. In this work we have focused on floating drug delivery system that are expected to remain lastingly buoyant on the gastric contents, without affecting the intrinsic rate of gastric emptying as their bulk densities are lower than that of gastric fluids.

MATERIALS AND METHODS

Materials

Mosapride citrate dihydrate were supplied as gift sample by DPB Antibiotic Ltd., Bombay, India. Eudragit RS and HPMC K4M were supplied as gift sample by Rohm pharma polymer Ltd. and Ideal cure Pvt. Ltd., Goa, India respectively. All other materials were of reagent grade and obtained from Central Drug House Pvt Ltd., New Delhi, India and used without further purification.

Design expert software

Floating matrix tablets containing mosapride citrate dihydrate was designed using software (two factors with three level-optimal) *Design Expert version 8.0.1.0* (Stat-Ease Inc Minneapolis, MN) and manufactured by direct compression method and their compositions are reported in Table 1.

Equipment and process of tablleting

The mosapride citrate dihydrate floating matrix tablets were prepared by direct compression method. Lactose was used as diluent. Citric acid and Sodium bicarbonate were used as a gas generating agent. Talc and magnesium stearate were used as lubricants. Drug, polymers and lubricants were blended and sifted through different sieves. Then mixed and blended the ingredients to form a dry mixture. Compression of formulation blend were done using tablet Mini rotary machine (Dynamic machine, Aurangabad, India) with 7 mm diameter tooling.

Table1: Different formulations of mosapride citrate dihydrate floating matrix tablets

Compositions in mg	F1	F2	F3	F4	F5	F6	F7	F8	F9
Mosapride citrate dihydrate	15	15	15	15	15	15	15	15	15
HPMC K4M	35	40	45	35	40	45	35	40	45
Eudragit RS	10	10	10	15	15	15	20	20	20
Sodium bicarbonate	6	6	6	6	6	6	6	6	6
Citric acid (anhydrous)	3	3	3	3	3	3	3	3	3
Talc	1	1	1	1	1	1	1	1	1
Magnesium stearate	2	2	2	2	2	2	2	2	2
Lactose	28	23	18	23	18	13	18	13	8
Total	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**

Characterization of floating matrix tablets
Fourier Transform Infrared Spectroscopy (FTIR)
The physical mixtures were prepared by blending the samples with potassium bromide (1:100) and scanned over range of 4000-400cm^{-1}. The infrared absorption spectra of pure mosapride citrate dihydrate and formulation blend F3 containing mosapride citrate dihydrate, HPMC K4M and eudragit RS (Ratio 1.5:4.5:1) were analyzed using FTIR spectrophotometer (8400 S Shimadzu, Japan).

Flow properties
The flow properties of the formulation blend of respective batch were determined by angle of repose, Carr's index and Hausner's ratio [33, 34].

$$\text{Carr's Index} = \frac{\text{TBD - LBD}}{\text{TBD}} \times 100 \quad \text{.....Eq(1)}$$

$$\text{Hausner's Ratio} = \frac{\text{TBD}}{\text{LBD}} \quad \text{.....Eq(2)}$$

TBD and LBD are tapped and loose bulk density, respectively.

Physical properties of floating matrix tablets
Weight variation
Twenty tablets were selected randomly from the respective batch and weighed individually. Average weight was calculated and compared the individual tablet weight to an average. The tablet pass the USP test if no more than two tablets are outside the percentage limit and if no tablet differs by more than two times the percentage limit.

Hardness
Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Pfizer hardness tester. It was expressed in kg/cm^2. Three tablets were randomly picked and hardness of the tablets was measured.

Friability
The friability of tablets was determined using Roche friabilator. It was expressed in percent (%). Twenty tablets were initially weighed (W) and transferred into friabilator. The friabilator was operated at 25 rpm for 4 minutes (100 revolutions). The tablets were weighed again (W_0). The percent friability was calculated using equation

$$\%F = 1 - \frac{W_0}{W} \times 100 \quad \text{.....Eq(3)}$$

% friability of tablets less than 1% are considered acceptable.

Swelling studies
The ability of floating matrix tablets to swell in 0.1N HCl (pH 1.2) medium was determined by swelling them up to their equilibrium [35]. The measurement of swelling rates of tablet were carried out after immersion of weighed tablets in the test medium to relate the observed phenomena of drug release with rate of polymer hydration. Weighed tablet (W_0) was placed in the closed plastic containers and rotated at 100 rpm using environmental orbital shaking incubator (Remi Instruments Ltd, Bombay, India) with a medium of 0.1N HCl (pH=1.2) at 37±0.5°C. After 1, 2, 3, 4, 5 and 6 h each swollen tablet was withdrawn from the medium and blotted to remove the surface water and then weighed (W_1) on an single pan balance.

$$\% \text{ Swelling} = \frac{W_1 - W_0}{W_0} \times 100 \quad \text{.....Eq(4)}$$

W_0 indicates weight of the dry tablet before immersion into the test medium. W_1 indicates weight of the swollen tablet after immersion into the test medium.

In vitro buoyancy studies

The in vitro buoyancy was determined by floating lag time method described as the tablets were placed in 250 ml beaker containing 0.1 N HCl using environmental orbital shaking incubator (Remi Instruments Ltd, Bombay, India). The time required for the tablets to rise to the surface and float was determined as floating lag time. The time between introduction of dosage form and its buoyancy in 0.1 N HCl and the time during which the dosage form remain buoyant were measured. The time taken for dosage form to emerge on surface of medium called floating lag time (FLT) and total duration of time by which dosage form remain buoyant is called total floating time (TFT).

$$f_2=50 \log\{[1+ \frac{1}{n} \sum_{t=1}^{n} W_t(R_t - T_t)^2]^{-0.5} \times 100\} \quad \text{.....Eq(6)}$$

Scanning electron microscopy (SEM)

To prepare specimens for the SEM, they are first fixed with Karnovsky's fixative and had taken through graded alcohol dehydration series. Once dehydrated, the specimens are placed in a critical point dryer, mounted and placed in a gold coater. Once gold coating is complete, specimens are ready to be viewed on the SEM. Images may be scanned on a digital imaging system by computer enhancement or Polaroid pictures may be taken using an attached camera (JEOL, JSM-5800LV, Tokyo, Japan) .

Drug content

Ten tablets were randomly selected, weighed and powdered. The powder equivalent to average weight of drug in one tablet was taken and transferred in dry 100 mL volumetric flask to it add 20 mL of 0.1 N HCl and make the volume by 0.1 N HCl and shake and sonicated for 15 min. the solution was filtered. Pipetted out 5 mL and diluted the with respect to the standard using 0.1 N HCl. The absorbance was measured at about 272 nm using 0.1 N HCl (pH 1.2) as a blank.

In vitro dissolution studies

An in vitro dissolution study of the prepared floating tablets of mosapride citrate dihydrate was carried out on USP-I dissolution apparatus. The dissolution study of different tablets was carried under the temperature 37°C ± 2 in 0.1 N HCl (pH 1.2) medium at 100 RPM. The absorbance was measured at 272 nm. Absorbance for the sample withdrawn was recorded and percent drug release at different time intervals. Cumulative percent of drug release were calculated using the equation obtained from a standard curve [36-37].

To confirm the similarity of drug release profiles before and after stability studies, a model-independent statistical tool for comparison of dissolution profile dissimilarity factor (f1) and similarity factor (f2) was calculated.

$$f_1 = \{ [\sum_{t=1}^{n} (R_t - T_t)] \times 100 \} \quad \text{.....Eq(5)}$$

Where, f1 indicates dissimilarity factor and f2 indicates similarity factor, n is the number of observations, w_t is optional weight, R_t is percentage drug dissolved from reference formulation (before stability studies) and T_t is percentage drug dissolved from test formulation at (after completion of 90 days in stability chamber). In general, f_2 values higher than 50 (50 – 100) show similarities of the dissolution profiles [39, 40]. The results were expressed as mean values of three determinations ±S.D.

In vivo x-ray imaging studies

The protocol (RCPIPER/IAEC/2011-12/20) for *in vivo* study was approved by the institutional animal ethical Committee (IAEC) of R. C. Patel Institute of Pharmaceutical Education and Research, Shirpur and is in accordance with guidance of committee for the purpose of control and supervision of experiments on animals (CPCSEA), Ministry of Social Justice and Empowerment, Government of India. In order to evaluate the *in vivo* residence time of the floating matrix tablets the formulation batch F3 was selected for *in vivo* x-ray imaging [38]. Six adult male New Zealand white strain rabbits of three months age and weighing approximately 2.5–30. kg were used for this study. The rabbits were fasted overnight before the start of the study. The floating matrix tablets (115 mg) containing 30 mg of $BaSo_4$ without drug compressed using Minipress rotary machine with 5 mm tooling. The tablets were administered through plastic tubing followed by flushing of 25–30 ml of water. During the entire study, the rabbits had free access to water only. Photomicrographs (Wipro Ge Dx300 with horizontal x-ray system, Wipro GE medical system, Pune-04, India) were taken at 0, 2, 4, 6 and 8 h.

Stability studies

The ICH guidelines have established that long term stability testing should have done at 25°C ± 2°C and 60% RH ± 5% RH. Stress testing should have done at 40°C ± 2°C and 75% RH ± 5% RH. If

significant change occurs at these stress condition, then the formulation should be tested at an intermediate condition i.e. 30°C±2°C and 65% RH±5% RH. Hence, attempt has made for the stress testing stability studies.

RESULT AND DISCUSSION

According to two factors and three levels, we have designed the nine formulations. On the basis of desired floating, swelling, drug release pattern (Figure 2, 3 and 4) formulation batch code F3 was selected as the optimized formulation for developing a floating gastro retentive drug delivery system.

Fourier transforms infrared spectroscopy

The FTIR spectrum of the pure drug was found to be similar to the standard spectrum of mosapride citrate dihydrate. It was observed that characteristic peaks of mosapride citrate dihydrate were present in the combination spectra in the similar fashion with little differences. Hence, it is revealed that, drug and polymers are compatible with each other (Fig. 1).

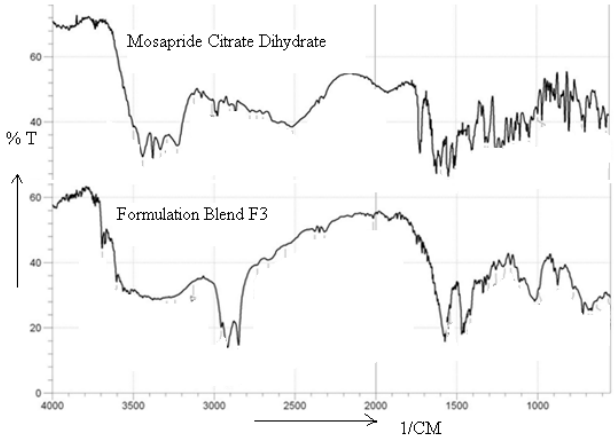

Figure1: FTIR spectra of pure mosapride citrate dihydrate and formulation blend F3

Flow properties

The flow properties of different the formulation blends were found by measuring the angle of repose, carr's index, haussner's ratio and bulk density and results are shown in table 2. The values of angle of repose were of the range 27.02º to 44.10º, which is indicated a good flow ability. The percent compressibility of powder mixture was found to have about 7.50 to 16.00, indicating that all the formulations showed good compressibility. The bulk density was found to have about 0.428-0.441 gm/cm^3. The Hausner ratio was calculated by using bulk density and tapped density data and was found to have 1.08-1.41.

Physical properties of floating matrix tablets

Floating matrix tablets were prepared using direct compression method. Since the material was free flowing, tablets were obtained of uniform weight due to uniform die fill. Tablets were obtained in the range with acceptable weight variations as per USP specifications, less than 10 percent difference. The thickness of the tablets was found to have 2.5 mm to 2.7 mm. Hardness of the tablets was not less than 4kg/cm^2 and friability of tablets was observed in acceptable range 0.24-0.45 (Table 3).

Swelling studies

The percent water uptake of the different floating matrix tablets exhibited about 27.55 to 62.74. Swelling increases as the time passes because the polymers gradually absorb water due to hydrophilicity of HPMC K4M (Figure 2). The HPMC K4M hydrates and swells and a gel barrier are formed at the outer surface. Drug diffusion depends significantly on the water content of the tablet. As the gelatinous layer progressively dissolves and/or is dispersed, the hydration or swelling release process is continuous towards new exposed surfaces. Eudragit RS can retard the release of drug from tablet, thus maintaining the integrity of the dosage form.

In vitro buoyancy studies

After immersion in 0.1N HCl (pH 1.2) media at 37ºC ± 0.5ºC, the tablets floats and remained buoyant without disintegration (Figure 2). This may be due to the nature of polymer and gas generating agent, which were kept constant in the present study. The gas generated is trapped and protected within the gel formedby hydration of polymer, thus decreasing the density of tablet. As the density of tablet falls below 1 the tablet becomes buoyant. The buoyancy lag times of the tablets are in between 37 to 84 min and total floating time is equal/ more than 10 h.

Scanning electron microscopy

The surface topography of sustained release matrix tablet can be studied through SEM study, by which we can revealed the surface texture for both optimized and unoptimized batch (Figure 5). It was revealed that batch F3 shows smoother texture and batch F7 has rough texture from which we can concluded that the release rate of the drug can be sustained for prolong time in optimized batch.

Table2: Flow properties of mosapride citrate dihydrate formulation blends

Formulation Code	Bulk Density	Tapped Density	Carr's Index	Hausner's Ratio	Angle of Repose
F1	0.43	0.506	12.5	1.14	34.21
F2	0.433	0.481	10	1.11	35.75
F3	0.439	0.518	12.5	1.14	44.1
F4	0.441	0.477	7.5	1.08	39.35
F5	0.428	0.505	15	1.41	27.02
F6	0.436	0.502	13	1.15	29.68
F7	0.431	0.502	14	1.16	32.98
F8	0.432	0.496	13	1.15	39.3
F9	0.434	0.516	16	1.19	30.96

Table3: Physical properties of floating matrix tablets of mosapride citrate dihydrate

Formulation Code	Percent Weight Variation	Thickness (mm) ± S.D.	Hardness (Kg/Cm^2) ± S.D.	Percent Friability S.D.	Percent Drug Content
F1	2.50	2.65±0.03	5.6±1.2	0.37±0.05	100.08
F2	1.25	2.58±0.02	4.5±1.1	0.28±0.06	100.24
F3	1.25	2.53±0.04	6.4±1.3	0.24±0.04	100.23
F4	2.50	2.66±0.02	5.1±1.4	0.39±0.05	97.84
F5	1.25	2.62±0.03	4.3±1.8	0.26±0.04	99.9
F6	5.00	2.56±0.03	5.1±1.5	0.34±0.03	98.38
F7	2.50	2.64±0.03	4.3±1.2	0.45±0.04	99.48
F8	1.25	2.67±0.02	6.4±1.3	0.25±0.03	101.64
F9	1.25	2.69±0.04	5.1±1.4	0.35±0.04	100.49

Table4: Similarity (f_2) and Dissimilarity (f_1) calculations of mosapride citrate dihydrate floating matrix tablets in 0.1 N HCl (pH 1.2)

Time in Hours	Reference	Test (T)	Rt-Tt	$(Rt-Tt)^2$	|Rt-Tt|
	Mosacon tablet	Floating matrix tablet			
0	0	0	0.00	0.00	0.00
1	19.91	26.04	-6.13	37.58	6.13
2	26.49	31.04	-4.55	20.70	4.55
3	34.67	35.74	-1.07	1.14	1.07
4	40.66	43.17	-2.51	6.28	2.51
6	48.04	52.58	-4.54	20.60	4.54
8	65.95	61.24	4.71	22.23	4.71
10	72.10	71.44	0.66	0.43	0.66
12	77.92	83.75	-5.17	26.68	5.17
Sum	385.75			135.63	29.33
Number of time points or intervals (Excluding zero)					8
Difference factor - f_1 [Acceptance criteria 0 - 15]					7.60
Similarity factor – f_2 [Acceptance criteria50 - 100]					68.65

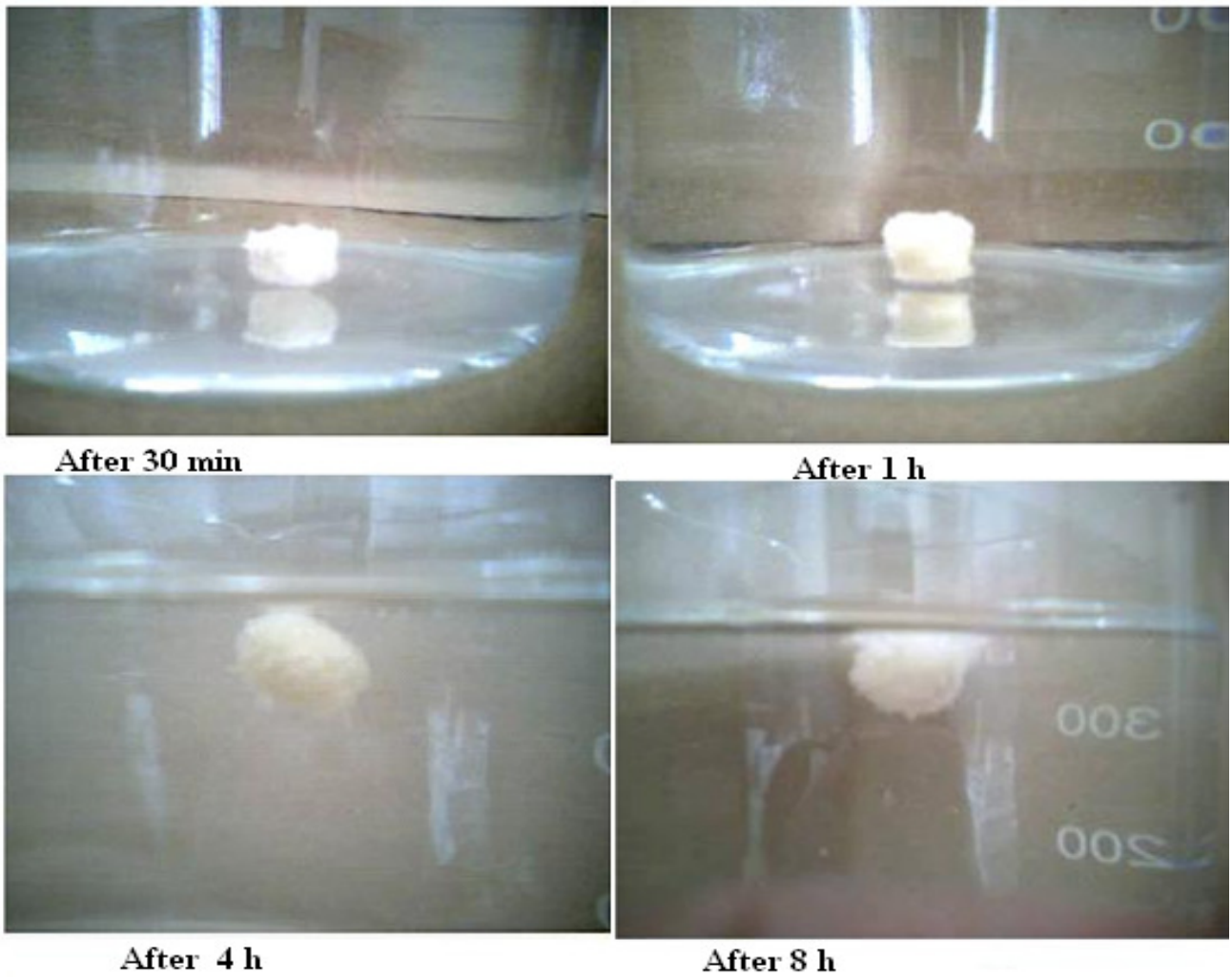

Figure2: Swelling photographs of floating matrix tablets at 30 min, 1 h, 4 h and 8 h

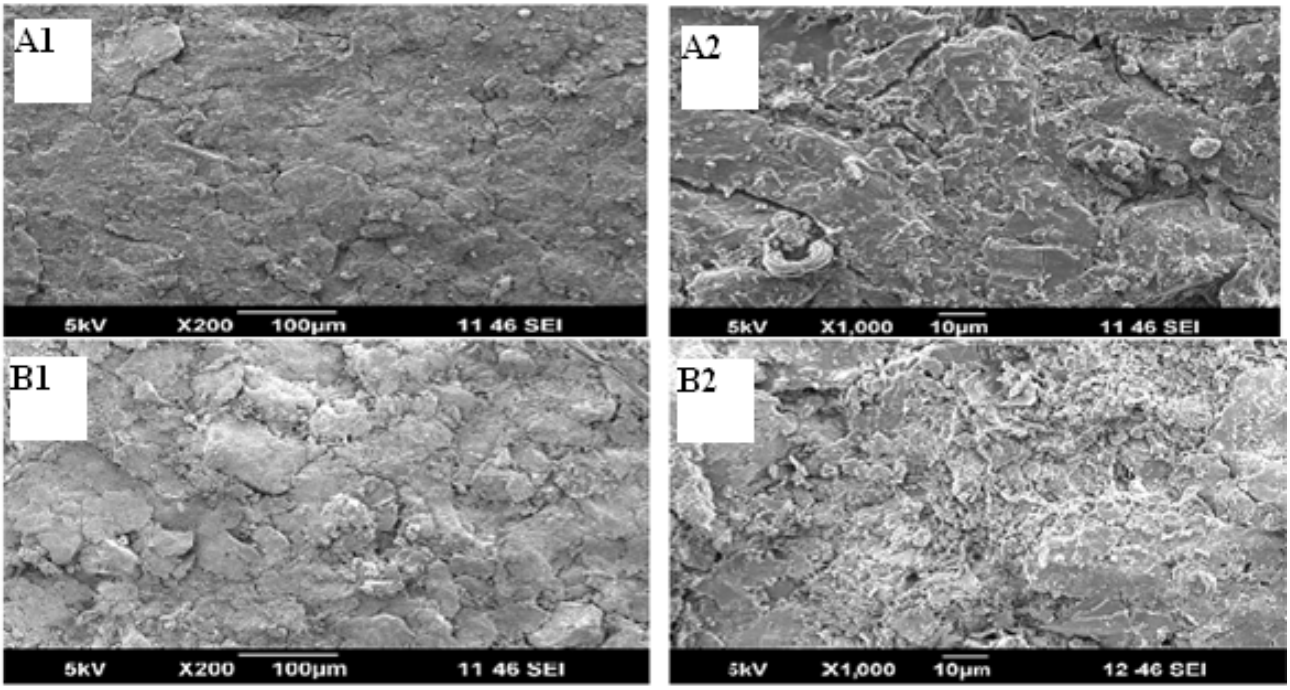

Figure5: SEM images of floating matrix tablet, A1 and A2 for unoptimized batch F7 and B1 and B2 for optimized batch F3

Drug content

The percent drug content was found to have about 97.84 to 101.6 which reflect good uniformity in drug among different formulations (Tablet 3).

***In vitro* dissolution studies**

The *in vitro* release of different batches of floating tablets showed the release without an initial burst effect. The prepared floating matrix tablets showed sustained the drug release for a period of 12 h (Figure 3). The two different types of polymers HPMC K4M and Eudragit RS are provided well sustained release characteristics. It was observed that the concentration of polymer maintain the drug release pattern (Figure 4). *In vitro* dissolution kinetic study of formulation code F3 by Korsemeyer- Peppas equation shows regression coefficient, R^2 = 0.9948 with release exponent, n = 2.0993, that means it follows super case-II transport mechanism, that indicates the polymer relaxation mechanism. Similarly, the formulation F3 showed good linearity (R^2 = 0.9889) with slope (n = 0.7501) respectively that appears to indicate that the drug release mechanism is anomalous transport, which reveals that both drug diffusion and polymer relaxation mechanism. The release pattern of the drug was studied by dissolution studies in same way as done earlier.

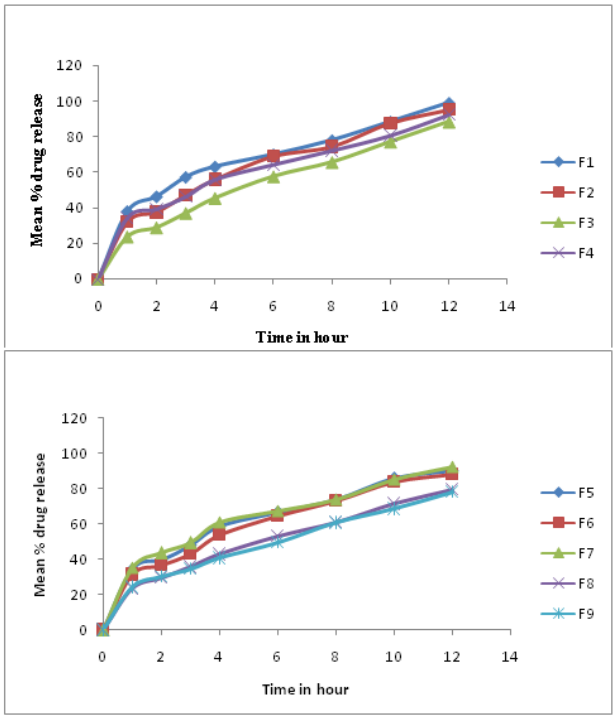

Figure3: Mean percent drug release of floating matrix tablets (Formulation cod F1 to F9)

Conventionally, test batch is considered similar to that of reference if the f2 value of the two profiles is in between 50 and 100. The f1 and f2 value (n =3; Mean±SD) was found to have 7.60 and 68.65, respectively. Therefore, it is revealed that the drug release pattern (Table 4) after stability studies was nearly same as before studies with very little difference**.**

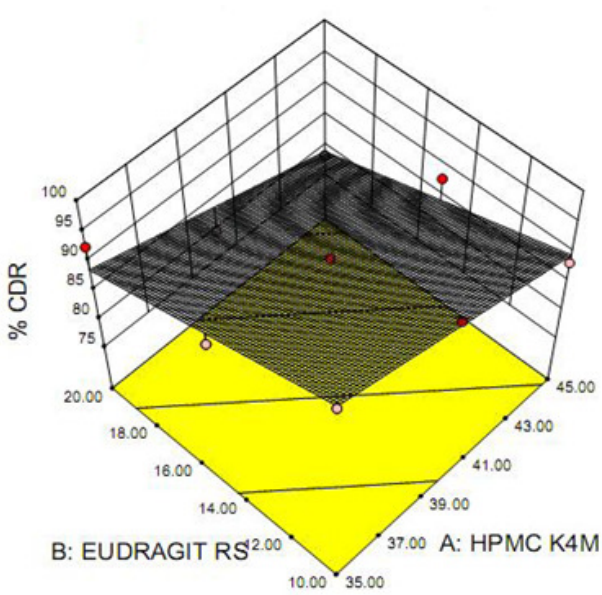

Figure4: Interpretation of percent cumulative drug release in 3D graph (Formulation code F1 to F9)

***In vivo* x-ray imaging studies**

Formulations of floating matrix tablets batch F3 have shown the good *in vitro* floating ability in these studies. Hence it was selected for *in vivo* x-ray imaging study to establish the product performance (residence time in stomach) in rabbits. Photomicrographs were taken immediately after 0, 2, 4, 6 and 8 h and are shown in figure 6. The presence of hydrogel of tablet in the upper small intestine can be clearly noticed and it remains in the stomach not being subjected to the drug release in rabbits. *In vivo* x-ray imaging study clearly indicated that the prepared floating matrix tablets of mosapride citrate dihydrate were remained float in gastric fluid up to 8 h in upper part of small intestine of the rabbit and hence they had good *in vivo* residence time in the stomach of rabbit. Photomicrographs was taken immediately after administration of the tablets with $BaSo_4$ tracer and revealed the nature and position of the microspheres up to 8 h in the upper small intestine of rabbit.

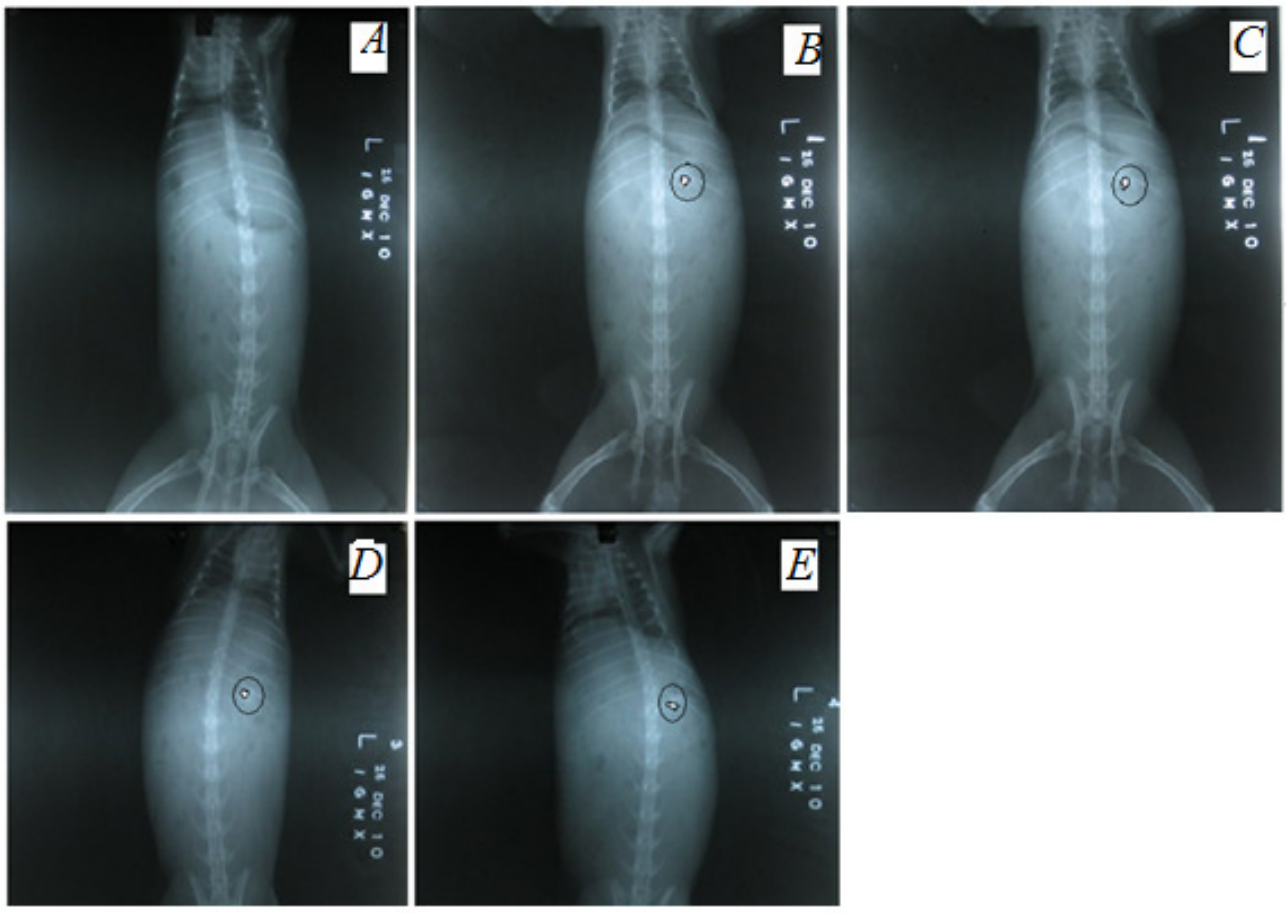

Figure 6: Photo micrographic images of floating matrix tablets of batch code F3 after 0 h (A), 2 h (B), 4 h (C), 6 h (D) and 8 h (E) in the upper small intestinal region of the rabbits

Stability studies

The optimized floating tablet (F3) was selected for stability study on the basis of *in vitro* dissolution studies. The tablets were stored as per stress testing studies for 3 months. However there was slight variation *in vitro* release when it is stored at accelerated condition (40°C ± 2°C and 75% RH ± 5%) and there was no change in floating lag time, drug content, hardness and release pattern when it is stored at controlled condition (25°C ± 2°C and 60% RH ± 5%). Hence, it is revealed the floating matrix tablets of batch F3 was found to be stable under the conditions mentioned before since there was no significant change in appearance, floating lag time, drug content, hardness, and in-vitro release.

CONCLUSION

Floating matrix tablets showed acceptable weight variation, friability, hardness, and drug content. A lesser floating lag time and a prolonged total floating time could be achieved by the effervescent system (Sodium bicarbonate and citric acid) and using two different polymer combination. Optimized formulation F3 containing HPMC K4M and Eudragit RS at the optimum proportion gave the desired swelling, floating and *in vitro* sustained drug release for 12 h. The combination of eudragit RS and HPMC K4M at the 1.0:4.5 w/w ratios could be the effective carrier for the sustained release floating matrix tablets of mosapride citrate dihydrate with improved bioavailability and site-specific action.

ACKNOWLEDGEMENT

The authors are grateful to DPB Antibiotic Ltd., Bombay, India and Ideal cure Pvt Ltd., Goa, India and Rohm Pharma polymer, Germany for the gift samples of mosapride citrate dihydrate, HPMC K4M and Eudragit RS. The authors would like to thank Principal, Dr. S. J. Surana (R C Patel Institute of Pharmaceutical Education & Research, Shripur) for providing necessary facilities to carry out research work.

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