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Research Paper

Formulation Development and Characterization of Floating Matrix Tablet of Ranitidine HCl

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The goal of the study was to formulation Development and Cherecterization of Floating Matrix Tablet of Ranitidine HCl by using a combination of HPMCK4M, HPMCK15M, HPMCK100M, Sodium Alginate, Psyllium, Sesbenia Gum, Gur Gum, Gum Acacia, Magnesium stearate, Talc. Ranitidine HCl is used in the treatment of Antiulcer. It has a short half life(2 hrs). Ranitidine HCl 100 mg matrics were prepared by direct compression method and evaluated for thickness, hardness, weight variation, friability, drug content and *in-vitro* release of drug. *In-vitro* drug release was carried out using USP type II apparatus at 50 rpm in 900ml of dissolution media for 12 hrs. Mean dissolution time is used to evaluate drug release rate from a dosage form and indicates the drug release retarding efficiency of polymer. Various kinetics model were applied to the dissolution profile to determine the drug release kinetics. All the physical characteristics evaluated for the tablets were obtained to be within the acceptable limits. The release profile of optimized formulation of Ranitidine HCl was close to zero order release pattern. Irrespective of the polymer type and its concentration, the prepared optimized matrix tablets showed non fickian (anomalous) release. Finally it was clear that HPMCK4M, HPMCK15M, HPMCK100M, Sodium Alginate, Psyllum, Sesbenia Gum, Gaur Gum, Gum Acacia, Magnesium stearate and Talc are good candidates for preparing Floating matrix tablets of Ranitidine HCl.

Key Words: Floating Matrix Tablet, Floating Lag Time, Gastro retentive, Ranitidine HCl.

INTRODUCTION

Different studies reported in the literature indicate that pharmaceutical dosage forms exhibiting good in vitro floating behavior show prolonged gastric residence in vivo [1,2,3,4]. The physical properties of the drug delivery system (e.g., density and size) as well as the presence of food in the stomach have been identified as the two most important parameters determining the in vivo performance of the dosage form[5].

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Under fasted conditions the stomach is cleared of undigested material every 1.5 to 2 h by housekeeper waves. To provide good floating behavior in the stomach, the density the density of the device should be less than that of the gastric contents (≅1.004 g/cm^3). However, it has to be pointed out that good in vitro floating behavior alone is not sufficient proof for efficient gastric retention in vivo. The effects of the simultaneous presence of food and of the complex motility of the stomach are difficult to

estimate. Obviously, only in vivo studies can provide definite proof that prolonged gastric residence is obtained.

Extended-release dosage forms with prolonged residence times in the stomach are highly desirable for drugs (i) that are locally active in the stomach, (ii) that have an absorption window in the stomach or in the upper small intestine, (iii) that are unstable in the intestinal or colonic environment, and/or (iv) have low solubility at high pH values. In addition, as the total gastrointestinal transit time of dosage forms is increased by prolonging the gastric residence time, these systems can also be used as sustained release devices with a reduced frequency of administration and, therefore, improved patient compliance. Recent approaches to increase the gastric residence time of drug delivery systems include (i) bioadhesive devices, (ii) systems that rapidly increase in size upon swallowing, and (iii) low density devices that float on the gastric contents. Floating tablets containing a mixture of drug and hydrocolloids that remain in the stomach for an extended period of time have been described[6,7]. Matrix tablets based on hydroxy-propyl methylcellulose (HPMC K4M) have been developed by Baumgartner et al.[12]. Upon contact with gastric fluid, the systems take up water and swell. As the increase in volume is greater than the increase in mass during swelling, the densities of these devices decrease and the systems start to float after a short lag time. The influence of different processing and formulation parameters on the floating properties of matrix tablets has been studied. [8,9]

Materials and Equipments:

Materials used in present Research work:

Ranitidine HCl was obtained as a gift sample from Elcon Drugs Formulation pvt. Ltd. Jaipur. All polymers and chemicals

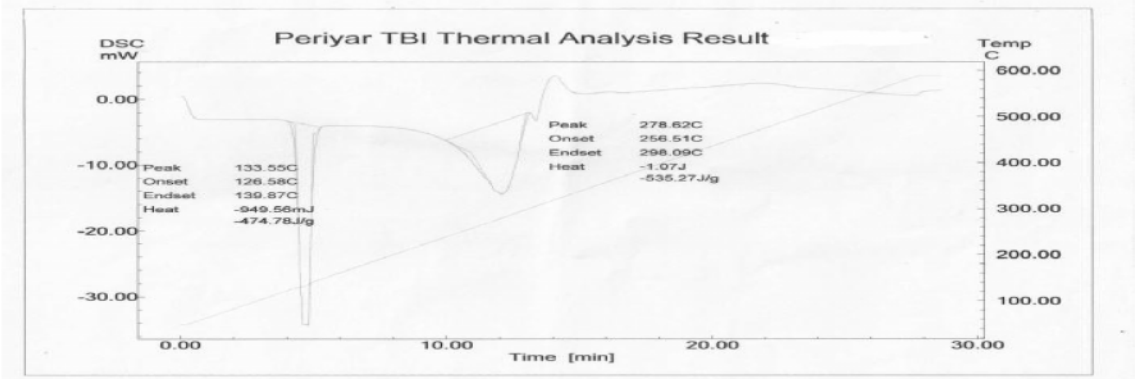

Fig.1 : DSC analysis of Ranitidine HCl

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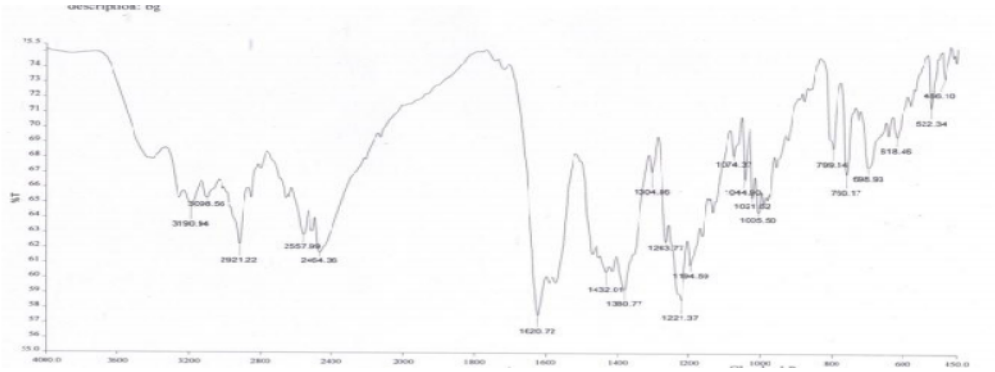

Fig. 2 : IR spectra of Ranitidine HCl

were of analytical grade and used.

Formulation of Floating matrix tablet:

The Floating matrix tablets containing Ranitidine HCl was prepared by a direct compression process. HPMC K100M, Sodium Alginate and Poly (Styrene-divinylbenzene), Magnesium stearate, Talc were Used. The Floating Matrix tablet formulations consisted of a drug and polymer were prepared in different ratios.. The drug, polymers and diluent were screened through 45 sieve and pre blended in a lab scale. The lubricant such as magnesium stearate in the concentration of 2 % was added and the blend was mixed again prior to compression. The drug blends were directly compressed by using rotary compression machine with a constant compression force. The excipients were taken according to drug weight. The different forms of tablets compressed together with their compositions. [8,10]

RESULT AND DISCUSSION:

Preformulation study:

Identification of drug:

Physical characteristics:

Ranitidine HCl is a white or Pale Yellow crystalline powder.

Table 1: Standard calibration curve of Ranitidine Hydrochloride in 0.1 N HCl

Sr. No.	Concentration (µg/ml)	Absorbance			Average Absorbance	Calculated Absorbance
		1	2	3		
1	0	0	0	0	0	0.003
2	10	0.041	0.041	0.041	0.041	0.039
3	20	0.079	0.080	0.077	0.078	0.075
4	40	0.151	0.150	0.151	0.151	0.147
5	60	0.215	0.213	0.212	0.213	0.219
6	80	0.275	0.278	0.277	0.277	0.291
7	100	1.127	1.129	1.127	1.127	1.127
Correlation Co-efficient : 0.9962 Absorbance= 0.0036x conc. + 0.0025						

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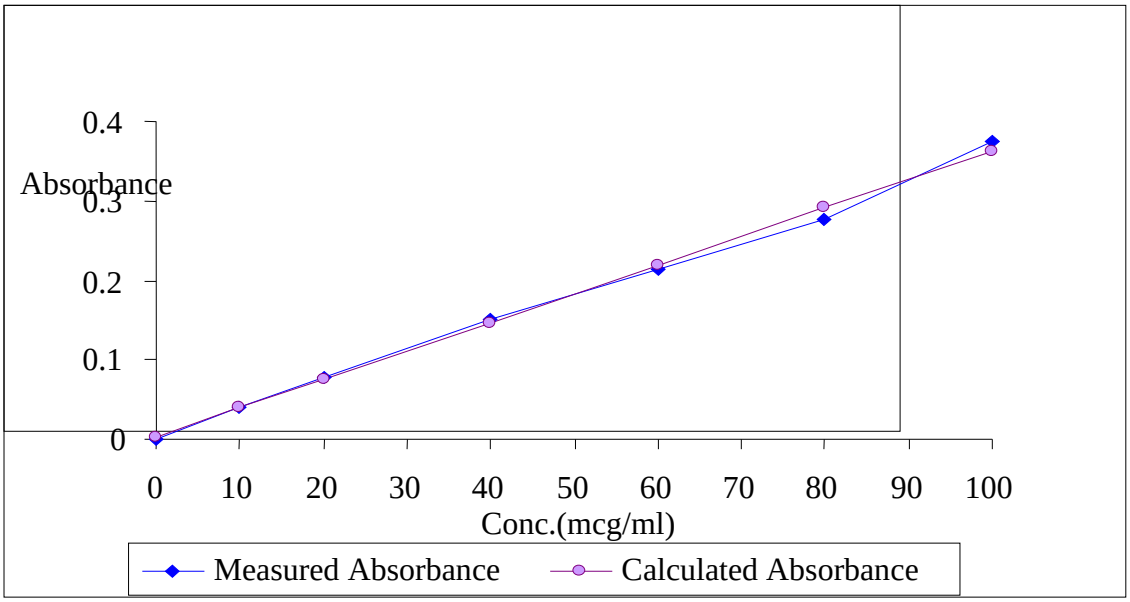

Fig. 3: Calculation of theoretical release profile of Ranitidine Hydrochloride from floating matrix tablets

Table:2 Pre compression characterization

Form.	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's Index	Hausner's ratio	Angle of repose
F1	0.66±0.020	0.80±0.035	17.5±1.63	1.21±0.035	30.11±1.11
F2.	0.68±0.030	0.80±0.035	15±1.90	1.17±0.025	27.47±1.76
F3.	0.68±0.030	0.83±0.030	18.07±1.56	1.22±0.040	30.54±1.13
F4.	0.68±0.030	0.80±0.020	15±1.63	1.17±0.025	29.68±1.60
F5.	0.68±0.030	0.83±0.030	18.07±1.58	1.22±0.035	30.54±1.61
F6.	0.66±0.035	0.81±0.030	18.51±2.24	1.22±0.050	30.96±2.00
F7.	0.71±0.020	0.81±0.015	12.34±1.87	1.14±0.026	23.74±1.50
F8.	0.70±0.015	0.78±0.025	10.25±2.30	1.11±0.040	23.74±0.72
F9.	0.68±0.015	0.76±0.036	10.52±2.17	1.11±0.040	22.29±1.46
F10.	0.69±0.026	0.80±0.035	13.75±1.61	1.15±0.030	25.17±1.42
F11.	0.68±0.030	0.81±0.026	16.04±1.86	1.19±0.025	25.64±1.17
F12.	0.71±0.015	0.83±0.015	14.85±1.14	1.16±0.041	26.56±1.41
F13.	0.71±0.015	0.86±0.035	17.44±1.89	1.21±0.036	25.17±1.88
F14.	0.68±0.026	0.81±0.035	16±1.85	1.19±0.036	27.02±1.64
F15.	0.66±0.035	0.78±0.026	15.38±1.16	1.18±0.026	29.24±2.02
F16.	0.68±0.036	0.78±0.026	12.82±1.68	1.14±0.035	29.24±2.02

Values are Expressed as Mean ± S.D.

On the basis of DSC analysis the melting point of Ranitidine HCl was found to be 268.6^{0}C.

Characterization of controlled release matrix tablet:

Pre compression characterization of controlled release matrix tablet:

The bulk density, tapped density, carr's index, hausner's ratio and angle of repose is the pre compression characterization of controlled release matrix tablet.

For each fabricated formulation, mixtures of drug and excipients were prepared and

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Table 3: Post compression characterization

Form.	Thickness (mm)	Avg.wt (mg)	Friability (%)	Hardness (kg/cm^2)
F1	4.15±0.010	197.8±1.70	0.96±0.098	4.2
F2	4.15±0.005	194.4±1.00	0.82±0.150	4.2
F3	4.15±0.010	195.9±1.47	0.81±0.150	4.4
F4	4.16±0.010	194.8±1.51	0.77±0.100	4.6
F5	4.15±0.005	195.5±1.56	0.66±0.077	4.6
F6	4.15±0.010	195.4±1.58	0.71±0.076	3.6
F7	4.17±0.005	195.6±1.55	1.12±0.213	4.4
F8	4.15±0.005	195.4±1.58	0.66±0.076	4.2
F9	4.16±0.005	194.8±1.50	0.77±0.077	4.4
F10	4.16±0.010	197.1±1.16	0.65±0.083	4.4
F11	4.17±0.005	198.2±1.70	0.70±0.055	4.4
F12	4.16±0.010	198.4±1.15	0.60±0.111	4.6
F13	4.16±0.010	196.3±0.98	0.61±0.105	4
F14	4.17±0.010	197.7±0.94	0.60±0.111	4.2
F15	4.17±0.010	196.2±1.60	0.66±0.104	4.2
F16	4.17±0.005	193.4±2.23	0.56±0.076	4.4

Values are Expressed as Mean ± S.D.

characterized for micromeritic properties and were tabulated in table no 7.12. These parameters show that the prepared mixture of all formulation have passable to excellent flow property range. The angle of repose is identifying to be determining of flow ability and the angle of repose of all formulation was shows excellent to passable flow.

Post compression characterization of controlled release matrix tablet:

The thickness, weight, friability and hardness are the post compression characterization of controlled release matrix tablet. All batches of formulation were evaluated for various physical parameters and tabulated in table no 7.13. According to IP the weight variation of each formulation was found in range. According to thickness of all formulation it was found in uniform size. The hardness of tablet was within range of 3.6 to 4.8 kg/cm^2 and friability is not more than 1%. These all parameters were satisfactory as specified in the pharmacopoeia except F7 and F34, because the friability of these formulations (F7 & F34) was not satisfactory.

Determination of Floating lag time and floating time:

In vitro buoyancy was determined by measuring floating lag time and period of

Table 4:Batch Floating Time

Batch	Time (Sec.)	Time (hrs.)
F1	142 Sec.	>12
F2	125 Sec.	>12
F3	105 Sec.	>12
F4	102 Sec.	>12
F5	98 Sec.	>12
F6	80 Sec.	>12
F7	78 Sec.	>12
F8	68 Sec.	>12
F9	58 Sec.	>12
F10	48 Sec.	>12
F11	44 Sec.	>12
F12	38 Sec.	>12
F13	28 Sec.	>12
F14	26 Sec.	>12
F15	24 Sec.	>12
F16	20 Sec.	>12

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Floating. The tablets were place in a 250 ml glass beaker containing 0.1 N Hydrochloric Acid. The time Need for the tablet to rise to the surface and float was determined as floating lag time. The duration during which the tablet remains floating was determined as floating time.

In-Vitro drug release:

The in- vitro drug release data are mention in following table 5

Table 5: Drug release and drug content data (F1 to F16)

Form.	%CDR (12hr)	Drug content
F1	78.08±1.68	93.3±1.35
F2	83.54±1.03	96±1.41
F3	72.56±1.42	94.5±0.75
F4	78.10±1.59	95.4±1.53
F5	90.81±1.20	93.9±1.80
F6	67.12±1.41	93.5±1.41
F7	61.56±1.39	94.8±1.08
F8	56.16±1.25	95.4±2.01
F9	50.74±1.18	97.5±1.41
F10	61.56±1.11	96.3±1.35
F11	61.6±1.12	95.7±1.83
F12	45.28±1.03	94.8±1.87
F13	67±1.15	95.4±1.41
F14	61.56±1.39	96±1.08
F15	56.12±1.25	94.8±1.35
F16	67.16±1.30	93.9±1.80

Values are Expressed as Mean ± S.D.

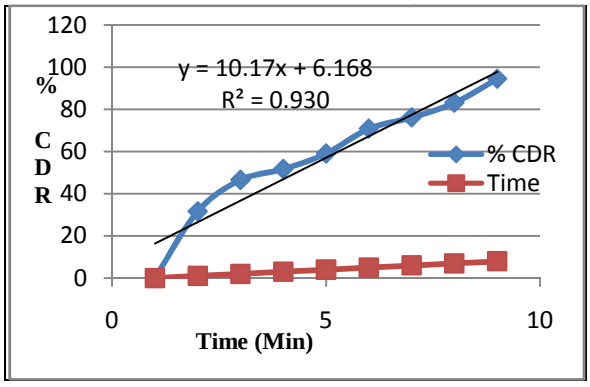

Fig.4: Drug release curve (F1)

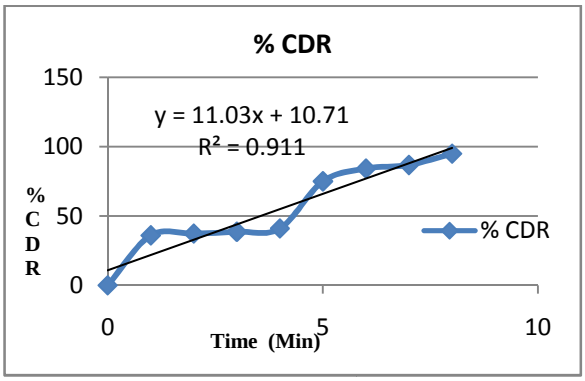

Fig. 5: Drug release curve (F2)

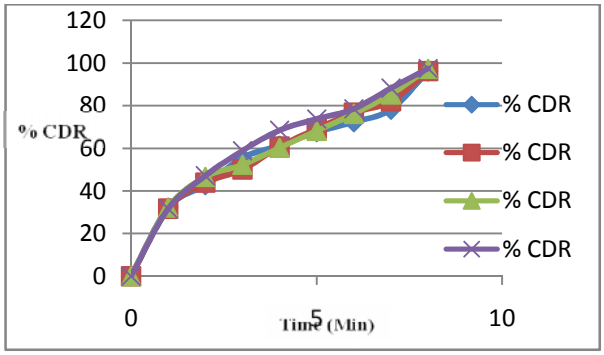

Fig. 6: Drug release curve (F9-F12)

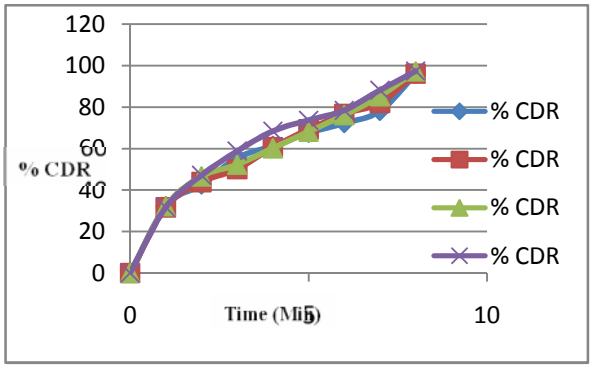

Fig. 7: Drug release curve (F13-F16)

CONCLUSION

Different types of matrix forming polymers were studied: chitosan, carbopol 940, HPMC K4 M, HPMC K15 M, HPMC K100 M, sodium alginate, psyllum, sesbania gum, guar gum, gum acacia for the study. Gastro retentive (low density) tablets of ranitidine

hydrochloride were prepared using Poly (Styrene Di vinyl Benzene) copolymer which not only imparted buoyancy to the formulations but also reduced floating lag times to a great extend. The use of PSDVB copolymer in matrix tablets as density reducing agent has given a different look. During the study with the copolymer various characteristics of the material were observed with drug and other copolymers, no significant effect on drug release and compatibility with drug and other polymers. it is concluded that chitosan-carbopol 940 and HPMC K100 M can be successfully used in formulation of ranitidine hydrochloride sustained release gastro retentive floating drug delivery system using low density copolymer.

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