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Research Article

Design and Characterization of Ranitidine Hydrochloride Floating Tablets by Wet Granulation Method

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ABSTRACT

Currently there are a number of technologies available that have been used to provide sustained release dosage forms and some of these involve the use of a wide range of polymers. This present research describes an investigation of the effects of formulation and processing parameters on a floating matrix controlled drug delivery system consisting **Methods:** The tablets were prepared by Wet granulation process using Ranitidine hydrochloride, HPMC K-4M ,Carbopol ,sodium carboxy methyl cellulose ,Guar Gum ,Xanthan gum ,sodium bicarbonate ,citric acid ,Stearic acid ,Hydrochloric acid ,Talc ,Mag.Stearate. The physicochemical properties like thickness, hardness, Weight variations, Friability, Drug content, Floating log time, Swelling Index etc were determined. The In-Vitro drug release rate of floating tablets was determined using United States Pharmacopeia Dissolution Testing Apparatus 2 (paddle method). The dissolution test was performed using 900 ml of 0.1N HCL, at 37 ± 0.5°C and 50 rpm. A sample (5 mL) of the solution was withdrawn at 1,2,3,4, up to 12hrs from and the samples were replaced with fresh dissolution medium. The samples were filtered. Through a 0.45µ membrane filters and diluted to a suitable concentration with 0.1N HCL. Absorbance of these solutions was measured using a UV- spectrophotometer and the stability studies were conducted for a period of three months Conclusion: It was established that formulation R11 (360 minutes) has better *in vitro* release profiles in comparison to the commercial product. The result obtained is encouraging, because a longer gastric residence time is an important condition for higher bioavailability of the drugs included in the floating dosage forms. Hence Ranitidine HCL floating tablets could be promising one as they, minimizes the dose, and reduces the side effects.

Key words: Ranitidine, Hydrochloride, Wet Granulation Method.

INTRODUCTION

Oral administration is the most convenient and preferred means of any drug delivery. Oral controlled release drug delivery have recently been of increasing interest in pharmaceutical field to achieve improved therapeutic advantages, such as ease of dosing administration, patient compliance and flexibility in formulation.

Drugs that are easily absorbed from gastrointestinal tract (GIT) and have short half-lives are eliminated quickly from the systemic circulation. Frequent dosing of these drugs is required to achieve suitable therapeutic activity. To avoid this limitation, the development of oral sustained-controlled release formulations is an attempt to release the Drug slowly into the gastrointestinal tract and maintain an effective drug concentration in the systemic circulation for a long time. After oral administration, such a drug delivery would be retained in the stomach and release the drug in a controlled manner, so that the drug could be supplied continuously to its absorption sites in the gastrointestinal tract.

MATERIALS AND METHODS

Materials: The following chemicals like Ranitidine hydrochloride, HPMC K-4M ,Carbopol ,sodium carboxy methyl cellulose ,Guar Gum ,Xanthan gum ,sodium bicarbonate ,citric acid ,Stearic acid ,Hydrochloric acid

Table 1: Composition of Floating Tablets Containing Ranitidine HCL.

S. No	INGREDIENTS	R1 (mg)	R2 (mg)	R3 (mg)	R4 (mg)	R5 (mg)	R6 (mg)	R7 (mg)	R8 (mg)	R9 (mg)	R10 (mg)	R11 (mg)	R12 (mg)	R13 (mg)
1.	Drug	150	150	150	150	150	150	150	150	150	150	150	150	150
2	HPMC-K4M	150	100	75	50	100	75	50	100	75	50	100	75	50
3	Carbopol934	-	50	75	100	-	-	-	-	-	-	-	-	-
4	SCMC	-	-	-	-	100	75	50	-	-	-	-	-	-
5	Guar gum	-	-	-	-	-	-	-	100	75	50	-	-	-
6	Xanthan gum	-	-	-	-	-	-	-	-	-	-	100	75	50
7	$NaHCO_3$	50	50	50	50	50	50	50	50	50	50	50	50	50
8	Citric acid	20	20	20	20	20	20	20	20	20	20	20	20	20
9	Mag.Stearate	4	4	4	4	4	4	4	4	4	4	4	4	4
10	Talc	4	4	4	4	4	4	4	4	4	4	4	4	4
11	Stearic acid	5	5	5	5	5	5	5	5	5	5	5	5	5

In all formulations (2%) HPMC solution was used as granulating agent except CP.

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Table 2: Flow property of the Blend

F.CODE	DERIVED PROPERTIES		FLOW PROPERTIES		
	Bulk density (mean±SD)	Tapped density (mean±SD)	Angle of repose (mean±SD)	Carr's index (mean±SD)	Hausner's ratio (mean±SD)
R1	0.294±0.01	0.357±0.04	29.73±0.01	17.65±0.01	1.21±0.01
R2	0.4545±0.03	0.666±0.03	40.6±0.03	31.73±0.01	1.47±0.02
R3	0.385±0.01	0.555±0.01	39.47±0.04	30.63±0.02	1.44±0.03
R4	0.4±0.02	0.476±0.03	34.18±0.01	15.97±0.01	1.19±0.01
R5	0.313±0.01	0.370±0.01	29.36±0.05	15.4±0.01	1.18±0.02
R6	0.334±0.04	0.41±0.02	28.21±0.02	16.81±0.01	1.22±0.01
R7	0.3125±0.03	0.385±0.02	27.26±0.04	18.73±0.01	1.23±0.04
R8	0.476±0.01	0.666±0.01	34.11±0.01	28.63±0.03	1.4±0.01
R9	0.364±0.02	0.409±0.04	30.69±0.03	11.01±0.02	1.123±0.02
R10	0.357±0.01	0.4±0.03	24.51±0.01	10.75±0.01	1.12±0.01
R11	0.567±0.04	0.66±0.01	27.9±0.05	14.86±0.01	1.174±0.01
R12	0.333±0.01	0.4±0.04	29.74±0.01	16.75±0.02	1.2±0.02
R13	0.458±0.02	0.581±0.03	30.91±0.02	21.17±0.01	1.26±0.01

Table 3; Physiochemical properties of the tablet

F.CODE	Thickness (mean±SD) (mm)	Hardness (mean±SD) (kg)	Friability (mean±SD)	Weight variation (mean±SD) (mg)	Floating Lag Time (mean±SD) (sec)	Swelling index (mean±SD)	Drug content (mean±SD)
R1	3.97±0.05	5.25±0.15	0.45±0.10	398.19±2.94	260±10	175±0.15	98.33±0.92
R2	3.92±0.1	5.66±0.24	0.51±0.08	391.18±3.77	310 ±5.7	207.5±0.15	99.20±0.34
R3	4.03±0.05	5.9±0.32	0.34±0.12	402.33±1.50	370±10	192.5±0.18	98.19±0.55
R4	3.95±0.05	6.3± 0.18	0.26±0.10	398.30±3.30	410±10	184±0.11	97.60±0.39
R5	3.93±0.1	5.4±0.25	0.36±0.04	394.13±3.10	290±10	279±0.17	98.21±0.07
R6	4.12±0.06	5.6 ± 0.26	0.31±0.07	403.16±2.33	280±5.7	262.5±0.13	98.14±0.69
R7	4.05±0.05	5.8±0.36	0.21±0.05	404.18±1.11	330±10	-	99.52±0.81
R8	3.98±0.05	5.6±0.22	0.28±0.08	397.04±2.56	280±6.8	300±0.16	98.34±0.65
R9	4.06±0.05	5.9±0.12	0.38±0.15	401.39±1.14	310±10	289±0.14	97.71±0.92
R10	4.01±0.05	6.7 ± 0.35	0.31±0.14	398. 43±2.70	290±5.7	265 ±0.19	97.34±0.37
R11	4.03±0.03	5.5±0.2	0.29±0.12	400.63±1.29	290±10	345±0.11	99.25±0.1
R12	3.96±0.04	5.8±0.45	0.36±0.09	397.21±2.56	260±5.7	341±0.17	98.34±0.2

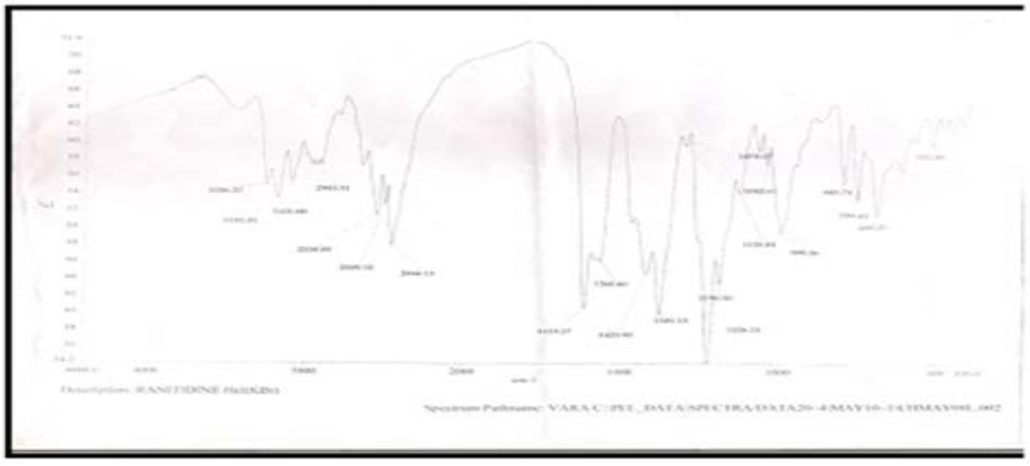

Fig 1 FT-IR of the drug and exiecpients

,Talc ,Mag.Stearate were used.

Method: Granules were prepared by using wet granulation technique. All the ingredients were weighed (Stearic acid, citric acid, sodium bicarbonate and Polymer) and taken in to motor. Finally the active ingredient was mixed homogeneously according to geometric proportions. (2%) HPMC solution acts as

Table 4; percentage drug release

FORMULATION	%DRUG RELEASE
R1	92.5
R2	94.6
R3	95.2
R4	90.1
R5	92.5
R6	89.9
R7	87.7
R8	89.3
R9	87.4
R10	85.3
R11	91.2
R12	96.7

Comparative Studies for R1-R7 Formulations

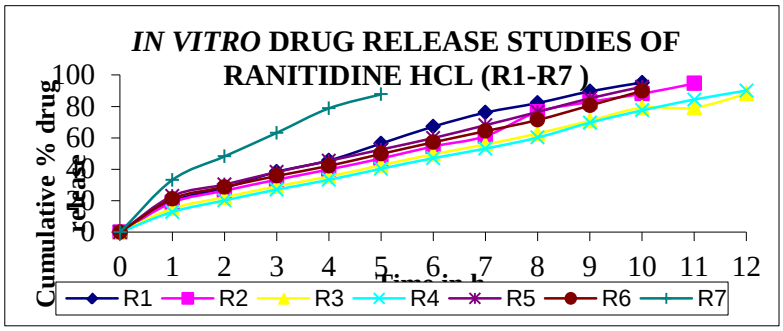

Fig 2; percentage drug release of batch 1-7

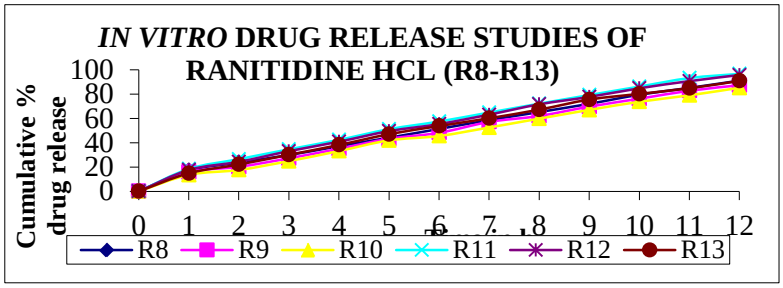

Fig 3:Comparative Studies for R7-R13 Formulations

Table No 5: Stability study (25°C, 40°C and 60°C) of best Formulation (R11).

S.No	Parameters	Initial	3rd Month		
			25°C 60%RH (mean±SD)	40°C 75% RH (mean±SD)	60°C 85%RH (mean±SD)
1	Hardness (kg/cm2)	5.5±0.2	5.2±0.1	5.7±0.3	5.8±0.1
2	Drug content (%)	99.25±0.1	98.5±0.3	97.3±0.5	96.7±0.7
3	floating lag time (sec)	290±5.7	300±10	310±5.7	310±10
4	Invitro Buoyancy	>24 h	>24 h	>24 h	>24 h

granulating agent. The coherent mass was thoroughly sieved through 16 meshes and then dried in hot air oven at 50ºC for 45 min. The dried granules were passed through sieve no 20 to get uniform granules. To this calculated amount of Magnesium Stearate (1%) and Talc (1%) were added as a lubricant. Citric acid and sodium bicarbonate were incorporated as a gas-generating agent. The addition of Stearic acid reduces the drug dissolution due to its hydrophobic nature. Then the prepared granules were evaluated in the following parameters bulk density, tapped density, angle of repose, compressibility index and Hauser's ratio.

Evaluation of tablet: Thickness, Hardness, Weight variation, Friability, Drug content Floating log time, Swelling index etc dissolution as per USP has been evaluated and the results has been tabulated in table in table 2.

RESULT AND DISCUSSION

Thickness: The floating tablets showed thickness in the range of 3.91±0.02 - 4.12±0.06 mm and no significance difference in the weight of individual formulations. From the average value was observed and variations within the limits and are given in table 3

Hardness: The difference in the hardness did not affect the release of the drug from hydrophilic matrices which is 5.25±0.15 - 6.7 ± 0.35 kg/cm^2 released by diffusion through the gel layer and/or erosion of this layer and is independent of the dry state of the tablet the values are given in table 3

Weight variation: The floating tablets Weight variation showed in the range of 391.18±3.77 - 404.18±1.11mg and no significance difference in the weight of individual formulations. From the average value was observed and variations within the limits and are tabulated in table 3

Friability: Tablet strength was tested by Roche Friabilator. The friability of all formulations in limits (below 1%). The friability of all formulations were observed within the range of 0.21±0.05 - 0.51±0.08 and the results are tabulated in table 3

Drug content: The drug content of all formulations was observed within the range of 97.34±0.37 - 99.52±0.81 % the values are given in table 3

Floating log time: The floating log time among all formulations were observed in the range of 260±5.7 - 410±10 sec and the values are given in table 3

Swelling index: Swelling index of floating tablets showed significant differences in their swelling index. The swelling indexes of all formulations were observed within the range of175±0.15-345±0.11 the values are given in table 3

Drug –Polymer Compatibility Studies By Ftir: Drug polymer compatibility studies were performed by FTIR (Fourier transform infrared spectroscopy). FTIR absorption spectra of Ranitidine, HPMC, CP, SCMC, Guar gum, Xanthan gum and the combination of drug and polymers were shows no significant interaction between Ranitidine and polymer .which is given in figure 1

In- vitro drug release studies: The release rate of floating tablets was determined using United States Pharmacopeia Dissolution Testing Apparatus 2 (paddle method). The dissolution test was performed using 900 ml of 0.1N HCL, at 37 ± 0.5°C and 50 rpm. A sample (5 mL) of the solution was withdrawn at 1,2,3,4, up to 12hrs from and the samples were replaced with fresh dissolution medium. The samples were filtered. Through a 0.45µ membrane filters and diluted to a suitable concentration with 0.1N HCL. Absorbance of these solutions was measured using a UV- spectrophotometer.

The percentage drug release is given in table no 4

Stability studies: The stability study was carried out using the best batch. The stability of the tablets were characterized for hardness, drug content, floating lag time, and *In vitro* Buoyancy. Formulation was kept at various temperatures that are 25°C, 40°C and 60°C for three months. The amount of drug was detected UV-Spectrophotometrically at 314 nm.

CONCLUSIONS

The present study was aimed at developing an oral floating system for Ranitidine HCL using combination of polymers like HPMC, CP, SCMC, Guar gum and Xanthan gum the floating tablets were prepared by using wet granulation technique. The floating tablets of Ranitidine HCL were evaluated for physicochemical characteristics like thickness, hardness, weight variation, friability, drug content, floating lag time and swelling index. The *in-vitro* buoyancy studies, *in-vitro* drug release studies.

The optimized formulation R11 was compared with marketed product and the results were found that the optimized formulation R11 (360 minutes) has better *in vitro* release profiles in comparison to the commercial product. The result obtained is encouraging, because a longer gastric residence time is an important condition for higher bioavailability of the drugs included in the floating dosage forms. Hence Ranitidine HCL floating tablets could be promising one as they, minimize the dose, and reduces the side effects.

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