



Received on 29 May, 2010; received in revised form 14 August, 2010; accepted 18 September, 2010

FORMULATION OF RANITIDINE HYDROCHLORIDE GASTRO RETENTIVE FLOATING TABLET BY USING DIFFERENT RATIO OF POLYMERS

A. K. Dave¹, V. Saklle¹, Sachin Jain*², Ankit Jain², and A. Pawar²

Department of Pharmacy, Technocrats Institute of Technology¹, Bhopal (MP), India
College of Pharmacy, I P S Academy², Indore (MP), India

ABSTRACT

The aim of the present investigation was to develop a novel gastro retentive dosage form of Ranitidine hydrochloride (RHCl) to achieve prolong gastric retention, increase drug bioavailability and to modulate the release of RHCl in the stomach, by using various ratios of HPMC E-15, a low-density grade polymer and it was cheaper and easily available along with Carbopol 934, as gel former. Sodium bicarbonate and citric acid were added as Effervescent agent. The tablets were prepared by wet granulation technique as 12 different formulation batches F1 to F12 depend on variable polymer ratios by using single punch hand operating machine, were evaluated for physical characteristics viz. hardness, swelling index, thickness, and weight variation. Further, tablets were evaluated for in vitro buoyancy time and in vitro release characteristics for 12 hr. Tablet achieved sufficient buoyancy due to the CO₂-gas formation and their entrapment by polymeric gel membrane. The increased amount of a gas forming agent did not affect time to float but increased the drug release from the floating tablets while increasing HPMC matrix content increased time to float and slightly retarded drug release. Formulation batch no. 8 was found to be the best formulation having maximum buoyancy 395 minute and a sustained drug release for 655 minutes. This study indicates that maximum buoyancy and sustained release of drug can be achieved using appropriate combination of gel forming agents and gas generating agents in the formulation of floating tablet. A higher proportion of gas generating agent to gel formatting agent found to be promising for achieving prolong gastric retention and sustained release. The floating tablet offers a simple and practical approach to achieve increased gastric residence time for the dosage form and sustained drug release.

Keywords:

Ranitidine
Hydrochloride,
Floating Tablet

Correspondence to Author:

Sachin Jain

College of Pharmacy, I P S
Academy, Indore (MP), India

INTRODUCTION: Gastroretentive dosage forms have potential for use as controlled-release drug delivery systems¹. The use of floating dosage forms (FDFs) is one method to achieve prolonged gastric residence times (GRTs), providing opportunity for both local and systemic drug action¹, they can be retained in the stomach and assist in improving the oral sustained delivery of drugs that have an absorption window in a particular region of the gastrointestinal tract¹. These systems help in continuously releasing the drug before it reaches the absorption window, thus ensuring optimal bioavailability².

Ranitidine HCL has short biological half-life of drug (~2.5-3 hours) and absorption window only in the initial part of the small intestine with 50% absolute bioavailability, thus why there is a strong need for development of their oral sustained release formulation. The conventional dose of 150 mg can inhibit gastric acid secretion up to 5 hours but not up to 10 hours. An alternative dose of 300 mg leads to plasma fluctuations; thus a sustained release dosage form of RHCl is desirable.

Objective: The objective of the present study was to develop floating tablet of Ranitidine hydrochloride (RHCl) to achieve prolong gastric

retention, enhance drug bioavailability and to sustained the release of RHCl in the stomach, by using various ratios of HPMC E-15, a low-density grade polymer, it was cheaper and easily available along with Carbopol 934, as gel former and Sodium bicarbonate, citric acid as Effervescent agent.

Experimental methods:

Preparation of floating tablet: Ranitidine floating tablet were prepared by Wet-granulation method. RHCl (336 mg equivalent to 300 mg of ranitidine) was mixed with the specified quantities of HPMC E-15, sodium bicarbonate, Carbopol and citric acid by continues mixing in a Mortar pestle. After complete mixing in this mixer binder 2% w/v solution of PVP K-30 in isopropyl alcohol was added and stirred until IPA was evaporated to form a wet mass. Granules were obtained by passing this through the sieve no 16. Then granules were dried in hot air oven. This dried granule was again passed through the sieve no. 22. Then lubricant magnesium stearate (1% w/w) and purified talc (1% w/w) added and mixed with granule prior to compression. Then granules were compressed to form floating tablet.

TABLE 1: COMPOSITION OF THE DIFFERENT FORMULATION BATCHES (F1-F12)

Formulation Code	Ranitidine HCL (mg)	HPMC E-15 (mg)	Carbopol (mg)	NaHCO ₃ (mg)	Citric acid (mg)	PVP K-30 (w/v)
F-1	336	20	10	10	20	2
F-2	336	30	20	10	30	2
F-3	336	30	40	20	30	2
F-4	336	40	40	30	30	2
F-5	336	80	40	30	50	2
F-6	336	100	50	30	60	2
F-7	336	140	80	40	60	2
F-8	336	160	80	30	60	2
F-9	336	85	40	30	50	2
F-10	336	90	40	30	50	2
F-11	336	95	40	30	50	2
F-12	336	110	40	30	50	2

* Magnesium stearate (1% w/w) and purified talc (1% w/w) was added in each formulation

Evaluation of floating tablet:

A. Swelling Index of Formulation: The swelling behavior (fig. 1) of floating tablet was measured by studying its weight gain or water uptake. Water uptake was measured in terms of percent weight gain, as given by the equation;

$$WU = (W_1 - W_0) \times 100 / W_0$$

W_t = Weight of dosage form at time t.
 W_0 = Initial weight of dosage form

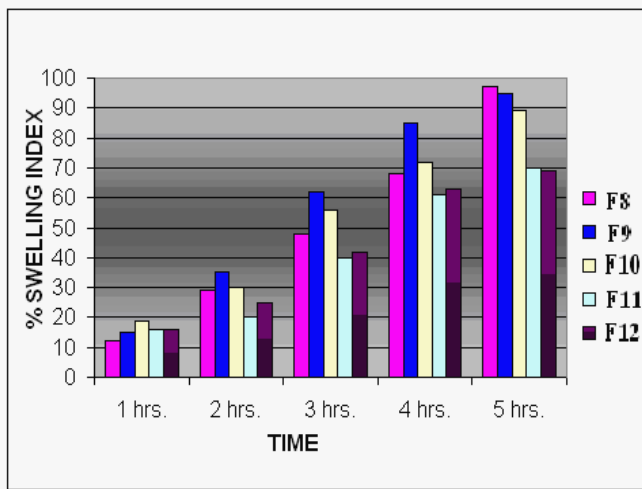


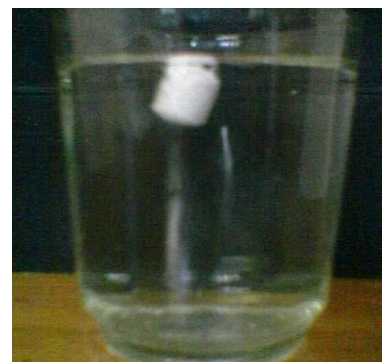
FIG. 1: SWELLING INDEX

The result indicates that quantity of HPMC E-15 incorporated in formulation has significant effect on % swelling index. Formulation F-8 poses 95 % swelling index for achieving greater buoyancy this values are agreeable.

B. In Vitro Buoyancy Studies: The in vitro buoyancy was determined as per the method described by Rosa et al. The tablets were placed in a 100-mL beaker containing 0.1N HCl. The time required for the tablet to rise to the surface and float was determined as floating lag time. The total time for the tablet remains buoyant reported as floating time.



(A) AT INITIAL TIME



(B) DURING FLOATING

TABLE 2: IN VITRO BUOYANCY OF DIFFERENT FORMULATION BATCHES

FORMULATION BATCH	BUOYANCY (MIN.)
F-1	0
F-2	0
F-3	0
F-4	20
F-5	150
F-6	325
F-7	450
F-8	655
F-9	390
F-10	370
F-11	310
F-12	410

Formulation batches from F8-F12 showed good in vitro buoyancy but the best one is from formulation F-8, this provides total buoyancy of

655 min. The floating ability of floating tablet is increased by increasing the HPMC content.

C. In Vitro Drug Release from formulation: The drug release of Ranitidine from floating tablets was determined using United States Pharmacopoeia (USP) 24. Dissolution Testing Apparatus 2 (paddle method). The dissolution test was performed using 900 mL of 0.1N HCl, at $37 \pm 0.5^\circ\text{C}$ and 75 rpm. A sample (10 mL) of the solution was withdrawn from the dissolution apparatus hourly for 12 hours, and the samples were replaced with fresh dissolution medium. The samples were filtered through a $0.45\text{-}\mu$ membrane filter and diluted to a suitable concentration with 0.1N HCl. Absorbance of these solutions was measured at 315 nm using a Shimadzu UV-1601, a double-beam spectrophotometer. The formulation F-8 showed 92 % drug release in 0.1 N HCL and phosphate buffer pH 6.8 respectively at 12 hours (fig. 2).

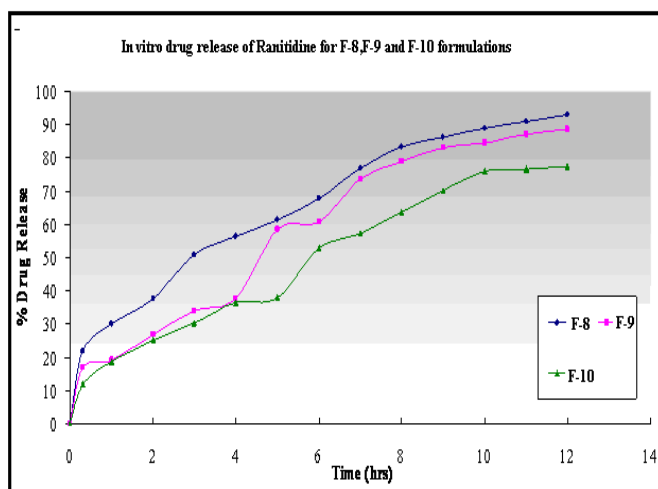


FIG. 2: IN VITRO DRUG RELEASE FROM F-8, F-9 AND F-10

CONCLUSION: This work discusses the preparation of floating tablets of Ranitidine by using HPMC E-15 was exhibit combined excellent buoyant ability and sustained drug release pattern could possibly be advantageous in terms of enhanced pharmacokinetic profile and increased bioavailability. HPMC E-15, a low density grade polymer was found to be a better alternative to their higher density grade HPMC polymer because of their cost effectiveness as well as their good gel forming ability and for achieving in vitro buoyancy of nearly 11 hours sustained drug release profile satisfactorily.

REFERENCES:

1. Li S, Lin S, Daggy BP, Mirchandani HL, Chien YW. Effect of HPMC and Carbopol on the release and floating properties of Gastric Floating Drug Delivery System using factorial design. *Int J Pharm.* 2003; 253:13-22.
2. Velasco MV, Ford JL, Rowe P, Rajabi-Siahboomi AR. Influence of drug: hydroxyl propyl methylcellulose ratio, drug and polymer particle size and compression force on the release of diclofenac sodium from HPMC tablets. *J Control Release.* 1999;57:75-85
3. Baumgartner S, Kristl J, Vrečer F, Vodopivec P, Zorko B. Optimization of floating matrix tablets and evaluation of their gastric residence time. *Int J Pharm.* 2000; 195: 125-135.
4. Coffin M, Parr A. Ranitidine solid dosage form. US Patent 5 407 687. April 18, 1995.
5. Singh B, Kim K. Floating drug delivery systems: an approach to oral controlled drug delivery via gastric retention. *J Control Release.* 2000; 63: 235-259.
6. Singh BN, Kim KH. Floating drug delivery systems: an approach to oral controlled drug delivery via gastric retention. *J Control Release.* 2000;63: 235-259.
7. Rosa M, Zia H, Rhodes T. Dosing and testing in-vitro of a bioadhesive and floating drug delivery system for oral application. *Int J Pharm.* 1994; 105: 65-70.
8. Chueh HR, Zia H, Rhodes CT. Optimization of sotalol floating and bioadhesive extended release tablet formulations. *Drug Dev Ind Pharm.* 1995; 21:1725-1747