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Formulation and evaluation of ranitidine floating tablet

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Abstract

The aim of present investigation is to formulate floating tablet to increase duration of action of ranitidine. Floating tablet of ranitidine has long duration of action as compare to its sustained release formulation, Floating tablet has double duration of action than sustained release formulation.

Floating tablet is developed by using various polymers like HPMC (15000) and few grades of carbopol, citric acid and sodium bicarbonate were added for effervescence. Tablets were prepared by wet granulation technique by using single operation punch machine in different formulation with polymers, also included testing of some physical parameters like swelling index , hardness and weight variations.

In vitro buoyancy evaluation was carried-out and *in vitro* release of drug was also performed. Increase in quantity of effervescence did not affect buoyancy while facilitating the release of drug. In-Vitro drug release increased when increased quantity of polymers like HPMC and carbopol.

Keywords: Polymers; HPMC; Citric acid; Sodium bicarbonate; Effervescence; Buoyancy

1 Introduction

Oral delivery is the preferred method of drug delivery due to its easy handling, patient compliance and flexibility in formulation. From the immediate release to the site-specific delivery, the oral volume form has really improved. It is clear from recent scientific and patent literature that the growing interest in new and predictable new dosage forms exists today in academic and industrial research groups. Various efforts have been made to upgrade gastro delivery systems [1]. Over the past three decades, the pursuit and testing of machines designed to be maintained in the upper part of the Gastro Intestinal Tract (GIT) has developed steadily technologically and diversified, including a variety of systems and devices such as floating systems, scaling systems, growth systems, immunosuppressive systems, inflammatory systems and systems. This technology benefits drugs with a small suction window and a high GI tract. Gastrointestinal storage systems can remain in the abdominal area for a few hours and thus significantly increase the duration of drug overdose. Prolonged stomach retention improves bioavailability, reduces drug damage, and improves the solubility of soluble drugs at high pH. It also works for the delivery of the drug to the abdominal and small intestine nearby [2-3]. Gastro retention helps to provide better access to new products with new treatment opportunities and greater benefits for patients. This consideration has led to the development of a unique oral dose form with gastro preservative properties. One of the most possible ways to get long-term and predictable drug delivery to GIT is to control Gastric Duration (GRT), i.e. Gastro Retentive Dosage Form (GRDF) [4-6].

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Ranitidine is H2 antagonist which inhibits histamine 2 receptor, this inhibitory action decreases in volume and concentration of gastric acid secretion. Conventional ranitidine dose of 150 mg has half life of 2-3 hours only, so that frequent doses are required for maintaining the plasma level of ranitidine. Here, need of controlled release/sustained release formulation is required because conventional oral dose produce their action only for 5 hour. Enhancing the absorption window could result into increased duration of action up to 10 hour [7-9].

Formulation development of controlled release/sustained release tablets, dose retrieval is difficult due to high cost of formulation required to coat tablets with specific coating, while novel approach of development of floating tablet will produce cost effective and great gastro-retentive effect [10-11].

Concept of floating tablet involve buoyancy technique , according to which low density profile materials like polymers (HPMC, CARBOMERS) are capable to produce good quality of floating tablet , on the other hand it is required to add effervescent agent which will help active drug to release in required quantity within stipulated time [12-15].

Development of floating tablet composition involves different ratio of HPMC (15000MW) and Carbopol 934 as gel forming agents with sodium bicarbonate and citric acid for its effervescent agent. These floating tablet produce gastro retentive effect more than other sustained and controlled release form of ranitidine hydrochloride [16-17].

2 Material and Methods

Ranitidine Hydrochloride was obtained from J.P. Chemicals, HPMC, PVP & Carbopol 934 were obtained from Alpha Chemika, Sodium Bicarbonate, Citric acid, Magnesium Stearate, Isopropyl alcohol and Purified talc were obtained by Sugandha Chemicals. All Chemicals and reagent required for present work were of analytical grade.

2.1 Method

Formulation of floating tablet involved continuous mixing of ranitidine hydrochloride (300 mg), HPMC (15000), sodium bicarbonate and citric acid with carbopol 934 in pestle and mortar by wet granulation. After complete mixing, 2% w/v binder solution of PVP in isopropyl alcohol was added and it was stirred till isopropyl alcohol got evaporated. Wet granules were obtained by passing it through sieve no 16 and these wet granules were kept in hot air oven and then passed through sieve no 22. Then, lubricant magnesium stearate (1%w/w) and purified talc (1%w/w) with granules were added prior to compression and then finally compressed to form floating tablet [18-21].

2.2 *In-vitro* Characterization

2.2.1 Weight Loss Test

When a drug makes up a large portion of a tablet, any weight difference of the tablet clearly indicates the active ingredient variation. This test is similar to testing the weight similarity. 20 tablets were randomly selected and the median weight was calculated. Each tablet was then weighed and the individual's weight was measured in proportion.

Calculate the average weight of pills = Total weight of pills / number of pills

Medium weight of pills (X) = (X1 + X2 + X3 + …… + X20) / 20

2.2.2 Strength studies

Strength of the prepared structure was measured using a Monsanto Hardness tester. Six floating tablets were used in studies of similarity in strength. Consistency data was used to calculate variation and standard deviations.

2.2.3 Friability (F)

The durability of the tablet was determined using the Roche Friabilator. It is expressed as a percentage (%) of 20 tablets those weights were first measured and transferred to a friabilator. The friabilator was operated at 25 rpm per minute for 4 minutes (100 revolutions). Tablets were again weighed (W final) [22].

2.3 Size and Width

Tablet thickness is important for tablet installation; very thick pills that affect the packaging of blisters or plastic containers. The size of the tablet is determined by the width of the die, the amount of filling allowed to enter the die and the force or pressure applied during compression. Tablet size can be measured manually or by default. The size and width of the tablets was measured by Vernier Calipers. It is expressed in mm.

2.4 Content Similarity

Twenty tablets were taken and the amount of medication available with each tablet was determined. The tablets were crushed and a powder equal to 100 mg of the drug was transferred to 100 ml of normal flask. The powder was dissolved in a suitable solvent and made the final dose with a suitable solution (0.1N HCl). The sample was thoroughly mixed and filtered through a 0.45µ membrane filter. The filtered solution was thoroughly purified and analyzed for drug content with a UV spectrophotometer, using a 0.1N HCl solution as a solvent.

2.5 *In vitro* Buoyancy

In vitro buoyancy studies were performed on all formulations. Randomly selected tablets from each formulation were stored in a 100 ml beaker containing imitated stomach fluid, pH 1.2 as per USP. The time taken for the tablet to rise and float was considered Floating Lag Time (FLT). The duration of the permanent dose form over the central area was determined as Total Floating Time (TFT).

2.6 Drug release kinetics

The effectiveness of HPMC in controlling drug release was studied to understand the order and potential mechanism involved in the release pattern. To analyze the drug release mechanism in the formulation, the data was obtained from the *in vitro* studies. Release form are sub-order of the first zero order model, Higuchi model, Korsemeyer model and Hixson's Crowell kinetics [23].

3 Results and Discussion

3.1 Evaluation Studies

3.1.1 Swelling index of formulations

Swelling index of floating tablets was measured by studying its weight gain or water uptake. It was measured in percent weight gain as given by the equation:

$$Wu = (Wt- W_{o)} * 100/ W_o$$

Where,

Wt = weight of dosage form at time
Wo = initial weight of dosage form

Results of swelling index are best shown in F.8, F.9. Large amount of HPMC (15000MW) in F.8 shows, large quantity of polymer. HPMC enhanced its swelling index.

3.2 *In-Vitro* Buoyancy Test

In-vitro drug release study for all the formulations was conducted and tabulated in Table no. 6. Formulation with both the polymers (F8) showed sustained release. It was observed that formulations F.8, F.9, F.10, F.11 and F.12 were showing good floating ability among all the formulations. F.8 had shown best floating ability in which quantity of polymer HPMC (15000MW) is highest, which shows quantity of polymers is directly proportional to its floating ability. The HPMC solubilized less which retards the drug release to a greater extent. Thus the HPMC with the combination of Carbopol-934 provides the optimum drug release. *In vitro* testing involved preparation of 0.1 N HCl in which prepared floating tablets were added so as to notice the floating time. According to concept more it float more will be its duration of action.

Table 1 Material Required

S.no.	Ingredient	Source
1	Ranitidine Hydrochloride	JB Chemicals pvt ltd.
2	HPMC (15000MW)	Alpha chemika
3	Carbopol 934	Alpha chemika
4	Sodium Bicarbonate	Shugandha chemical
5	Citric acid	Shugandha chemical
6	Magnesium Stearate	Shugandha chemical
7	PVP	Alpha chemika
8	Isopropyl alcohol	Shugandha chemical
9	Purified talc	Shugandha chemical

Table2 Table of Floating Time

S.NO	Formulations	Floating Time
1	F.1	0 MIN
2	F.2	05 MIN
3	F.3	10 MIN
4	F.4	25 MIN
5	F.5	160 MIN
6	F.6	330 MIN
7	F.7	450 MIN
8	F.8	660 MIN
9	F.9	390 MIN
10	F.10	395 MIN
11	F.11	345 MIN
12	F.12	420 MIN

3.3 *In – Vitro* Drug Release

In vitro drug release of ranitidine hydrochloride was determined by using dissolution test as per Indian pharmacopeia according to which dissolution was carried out with dissolution apparatus 2 (paddle type) using 900 ml of 0.1 N HCl at 37 +- 0.5 C on 100 rpm.

A Sample of 10 ml of solution was taken from dissolution apparatus, in 1 hour interval, and maintained the sink condition by adding same amount of 10 ml of dissolution medium to dissolution apparatus.

Sample was filtered through membrane filter of 0.5 micro grams and diluted to suitable concentration with 0.1 N HCl.

Absorbance of sample solutions was measured at 315 nm using SHIMADZU UV–1700.

Formulation F.7 showed 90 % of drug release in 0.1 N HCl

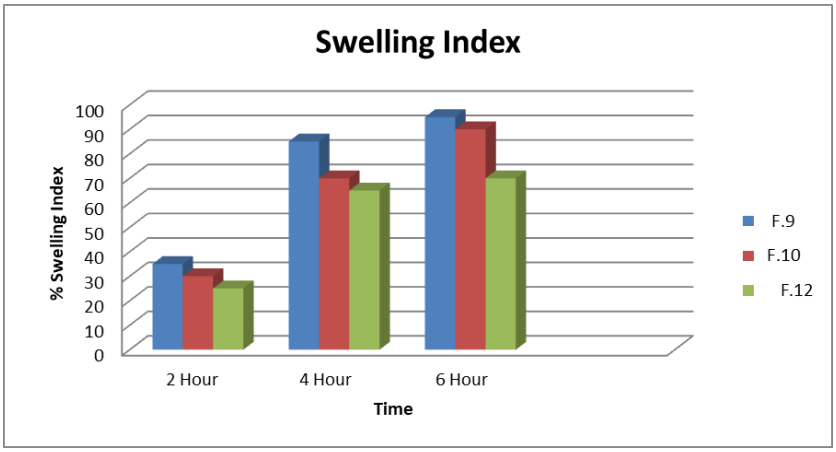

Figure 1 Graphical representation of Swelling Index of Ranitidine Hydrochloride Floating Time

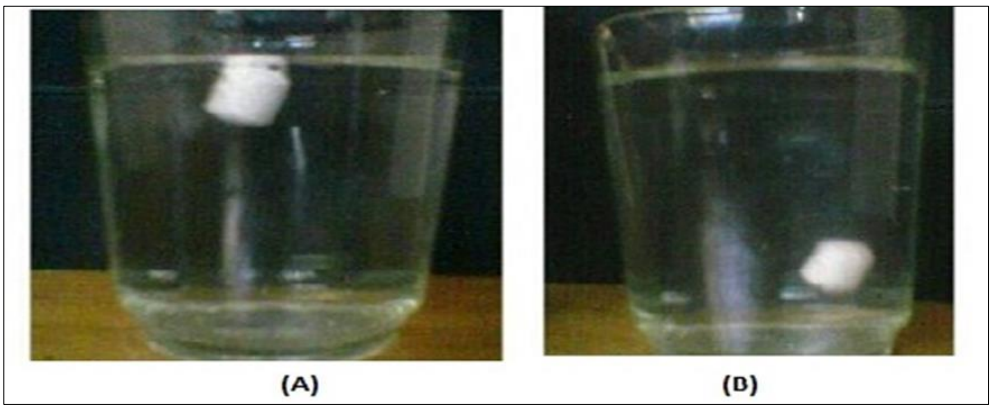

Figure 2 Floating Time of Ranitidine Hydrochloride floating Tablet

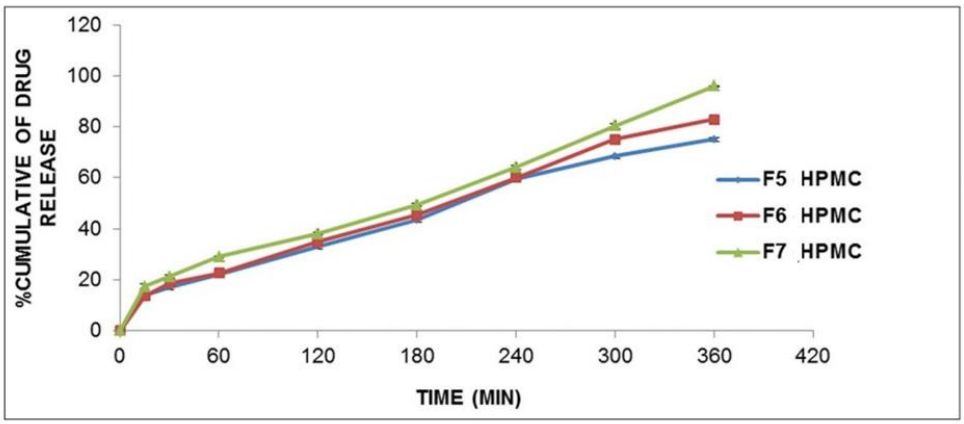

Figure 3 Drug Release Profile (F7, F8, F9)

4 Conclusion

The research was undertaken with the aim to formulate and evaluate the sustained release floating tablets of Ranitidine Hydrochloride using HPMC and Carbopol-934 as polymers. From results obtained, it was concluded that the formulation

of sustained release tablet of Ranitidine Hydrochloride containing a combination of polymers (HPMCCarbopol-934) was taken as ideal or optimized formulation for 24 hours release as it fulfills all the requirement of sustained release dosage form. This Novel approach of floating tablet will provide longer time of retention in stomach so that it can release ranitidine up to 12 hour and as a result frequent dosing of ranitidine can be minimized. Low density polymers HPMC (15000MW) are cheaper & better for forming floating tablet. Floating tablets provide better approach for the formulation development of sustained release formulation of Ranitidine Hydrochloride.

Compliance with ethical standards

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Disclosure of conflict of interest

It is declared that authors have no conflict of interest.

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