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DESIGN AND CHARACTERISATION OF RANITIDINE HYDROCHLORIDE FLOATING TABLETS

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AIM OF WORK

Ranitidine is a histamine H_2-receptor antagonist; it is unstable in the intestinal or colonic environment.

1) To estimate the effect of concentration of polymers, gas generating agent on the floating and drug release from floating tablets.
2) To utilize the dissolution data and gain insight into the mechanism of drug release from polymer floating tablet.
3) To study the effect of,

- Tablet density on Floating lag time.

PLAN OF WORK

1) Construction of calibration curve of Ranitidine HCl,
2) Studies on compatibility of drug and excipients,
3) To prepare floating tablets by wet granulation process,
4) The floating tablets are to be characterized for the following parameters,

a. Preformulation studies,
b. Physico chemical parameters,

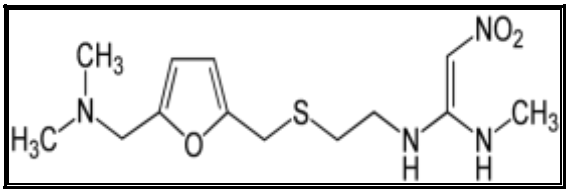
- Hardness Weight variation,
- Thickness,
- Friability,
- Drug content,
- Floating lag time,
- Swelling index.

c. In-vitro studies

- In-vitro bouncy,
- In-vitro drug release.

DRUG PROFILE

- **Generic name:** Ranitidine HCl.
- **Synonyms:** Ranitidine Base, Ranitidine HCl.
- **Chemical name:** N-(2-[(5-(dimethyl amino methyl) furan- 2-yl) methyl thio] ethyl) - N-methyl- 2-nitroethene- 1, 1-diamine.



Chemical Structure

- **Molecular formula:** $C_{13}H_{22}N_4O_3S$
- **Molecular weight:** 314.40
- **Description:** Ranitidine HCL is a white to pale yellow, granular substance that is soluble in water. It has a slightly bitter taste and sulfur like odour.
- **Melting point:** 69-70ºC.
- **Solubility:** Freely soluble in water, 0.1N HCL, methanol, slightly soluble in ethanol, acetone, and dichloro methane.
- **Pharmacological profile:** Ranitidine is a histamine H_2-receptor antagonist similar to cimetidine and Famotidine. H_2 RAs bind competitively to gastric H2 receptors to reversibly inhibit acid secretion. Blockade of parietal cell histamine receptors inhibit all phases of gastric acid secretion induced by histamine, gastrin and acetylcholine. The net effect is an increase in the pH of the stomach.
- **Mechanism of action:** The H_2 antagonists are competitive inhibitors of histamine at the parietal cell H_2 receptor. They suppress the normal secretion of acid by parietal cells and the meal-stimulated secretion of acid. They accomplish this by two mechanisms histamine released by ECL cells in the stomach is blocked from binding on parietal cell H_2 receptors which stimulate acid secretion, and other substances that promote acid secretion(Such as gastrin and acetylcholine) have a reduced effect on parietal cells when the H_2 receptors are blocked.

Table: 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 VITRO STUDIES

***In Vitro* Buoyancy:** In vitro buoyancy studies were performed for all the formulations. The randomly selected tablets from each formulation were kept in a 100ml beaker containing simulated gastric fluid, pH 1.2 as per USP. The time taken for the tablet to rise to the surface and float was taken as floating lag time (FLT). The duration of time the dosage form constantly remained on the surface of medium was determined as the total floating time (TFT).

Table: *In Vitro* buoyancy.

S. No	F. Code	*In vitro* buoyancy (h)
1	R1	>24
2	R2	>24
3	R3	>24
4	R4	>24
5	R5	>24
6	R6	>24
7	R7	<2
8	R8	>24
9	R9	>24
10	R10	>24
11	R11	>24
12	R12	>24
13	R13	>24

0 sec **60 sec** **120sec**

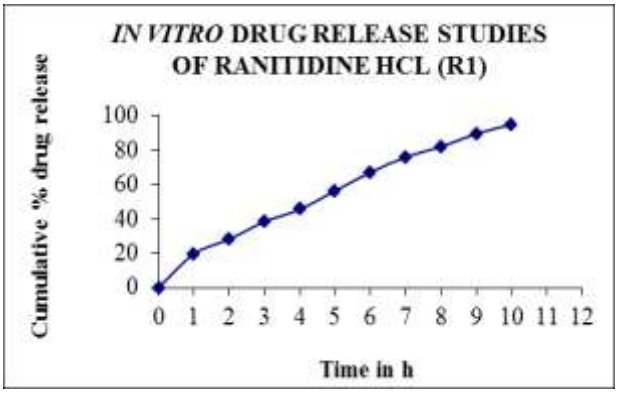
In Vitro Buoyancy Study of Ranitidine HCl Floating Tablets

IN VITRO DRUG RELEASE STUDIES

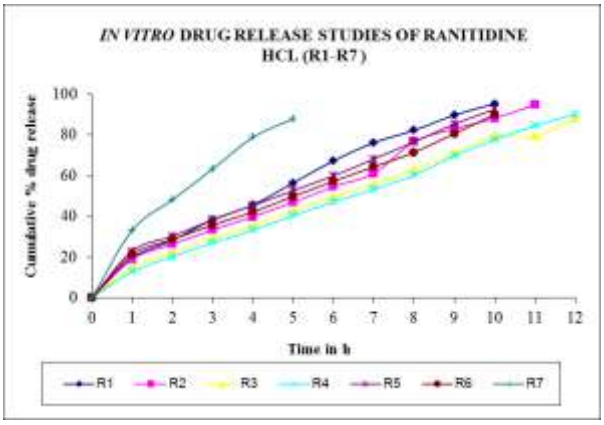
The release rate of floating tablets was determined using United States Pharmacopeia Dissolution Testing Apparatus 2 (paddle method). The dissolution test was performed using 900 ml of 0.1N HCL, at 37 ± 0.5°C and 50 rpm. A sample (5 mL) of the solution was withdrawn at 1,2,3,4, up to 12hrs from and the 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.

***In Vitro* Drug Release Data for R1 Formulation.**

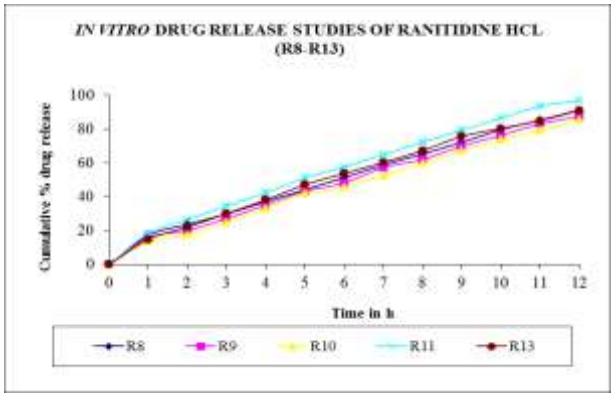
S. No	1	2	3	4	5	6	7	8	9	10
Time (hrs)	1	2	3	4	5	6	7	8	9	10
CDR	19.6	28.2	38.4	45.6	56.4	67.2	76.1	82.1	89.6	95.2



In vitro Release profile of Formulation.



Comparative Studies for R1-R7 Formulations.



Comparative Studies for R7-R13 Formulations.

RESULTS AND DISCUSSION

In Vitro Studies

***In vitro* Buoyancy:** *In* vitro Buoyancy of all the formulations showed better *in vitro* buoyancy which was greater than 24 h except formulation R7. *In vitro* Buoyancy of all the formulations R7 is decreased (2h) which may be due to less concentration of HPMC. The values of In vitro Buoyancy for All formulations were given in table no 24.

In Vitro Drug Release Studies

In vitro drug release studies were performed for all the prepared formulation by using 0.1 N HCL buffer (pH 1.2) as dissolution medium and measuring drug concentration UV- Spectrophotometrically at 314 nm.

Formulations R1, R2, R3 and R4 containing HPMC alone and Combination of HPMC and Carbopol. The Formulations R1 has shown release 95.2% at the end of 10^{th} h, Formulations R2 has shown release 94.6% at the end of 11^{th} h, Formulations R3 has shown release 95.2% at the end of 12^{th} h, Formulations R4 has shown release 90.1% at the end of 12^{th} h.

Formulations R5, R6, and R7 containing Combination of HPMC and SCMC. The Formulations R5 has shown release 92.5% at the end of 10^{th} h, Formulations R6 has shown release 89.9% at the end of 10^{th} h, Formulations R7 has shown release 87.7% at the end of 5^{th} h. Formulations R8, R9, and R10 containing Combination of HPMC and Guar gum. The Formulations R8, R9, and R10 have shown release 89.3%, 87.4 and 85.3 respectively at the end of 12^{th} h.

Formulations R11, R12, and R13 containing Combination of HPMC and Xanthan gum. The Formulations R11, R12, and R13 have shown release 96.7%, 95.8 and 91.2 respectively at the end of 12^{th} h.

CONCLUSION

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, improve bioavailability, minimize the dose, and reduces the side effects.

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