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Research Article

FORMULATION AND EVALUATION OF FLOATING ORAL IN-SITU GEL OF RANITIDINE HYDROCHLORIDE

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ABSTRACT

Ranitidine is a H2 receptor antagonist used in the treatment of gastric and duodenal ulceration and gastro-esophageal reflux disease. It is absorbed from the gastrointestinal tract with the bioavailability of about 50% and an elimination half-life of 3 hours. The aim of the present investigation is to formulate floating in situ gel of Ranitidine Hydrochloride in order to achieve: Greater therapeutic efficacy, Exhibit expected viscosity and drug content, Sustained drug release by increased residence time resulting in controlled drug delivery in gastro intestinal tract. In this Sodium Alginate is used as Gelling agent, Pectin is used as rate retarding polymer, Calcium Chloride is used as cross linking agent, Sodium Bicarbonate is used as alkalizing agent and Sodium Citrate is used as buffering and neutralizing gastric acid. All the formulations were subjected for evaluation like physical appearance, pH, viscosity, and measurement of water uptake by the gel, in-vitro drug release, drug content, in-vitro floating study in order to assess the suitability of the formulations with respect to the dosage form and intended therapeutic purpose. FTIR showed no interaction between drug and polymers. The optimized formula consisted of 0.3g of Ranitidine HCl, 2g of Sodium Alginate, 1g of pectin, 1g of Sodium Bicarbonate, 1g of Calcium Chloride, 1g of Sodium Citrate and 100ml of distilled water considered to be the best among all 9 formulations since it exhibited a good dissolution profile, appearance, and drug content. From this study the Floating Oral In-Situ Gel of Ranitidine HCl appeared to be a novel alternative for effective management of Gastric Ulcers.

Keywords: Ranitidine HCl, Floating oral Insitu-gel, FTIR.

1. INTRODUCTION

The main aim of any drug delivery system is to provide correct therapeutic amount of drug at the appropriate site in the body to achieve and maintain the desired drug concentration. The drug delivery system should thus produce desired therapeutic output and clinical efficacy. Controlled drug delivery is one which delivers the drug at a predetermined rate, locally or systemically, for specified period of time. Continuous oral delivery of drugs at predictable and reproducible kinetics for predetermined period throughout the course of GIT. Gastro Retentive Drug Delivery Systems (GRDDS) can be defined as a system which retains in the stomach for a sufficient period of time and releasing active moiety in a controlled manner, and finally metabolized in the body. This system help in continuous release of drug before it reaches the absorption window, thus ensuring optimal boiavailability[6] Gastric retention time can be prolonged by various methods such as floating drug delivery system (hydro dynamically balanced system), swelling and expanding systems, polymeric boiadhesive system, modified- shape system, high density system, and other delayed gastric emptying devices[8].

Oral in situ gel forming system also known as stomach specific or raft forming systems have provided a suitable way of providing the controlled drug delivery within stomach with enhanced gastro-retention. The tablet/capsule floating dosage forms are stable as compare to liquids but the problem with them is that are needed to swallow as whole unit. In case of

dosage adjustment these cannot be broken in halves as these are also designed for controlled release and floating ability also depends on dimensions of tablets. Elderly patients, children some adult person and patient with certain conditions suffer from dysphasia, so it becomes difficult for them to swallow tablet/capsule dosage forms. Also in case of dosage adjustments these floating solid dosage forms are needed to be available in different strengths. Where an environment specific gel forming solution, on conversion to gel, floats on the surface of the gastric fluids (due to less density than gastric contents). In this technique, a solution of low viscosity is used which on coming in contact with the gastric fluids, undergo change in polymeric conformation and a viscous gel of density lower than the gastric fluids is the contact time, but also produce the continuous and produce. This low density gel formation called as raft not slow drug release.

1.1 Various Approach for in Situ Gel Formation

- Different approaches and mechanisms utilized or involved in producing the in situ gel formation are as follows
- Based on producing physical changes
- Based on producing chemical changes
- Based on physiological stimuli
- Dilution-sensitive.
- Electrical signal-sensitive.
- Light-sensitive.

2. MATERIALS AND METHODS

2.1 MATERIALS

Ranitidine Hydrochloride is obtained as a generous gift sample from KP Laboratories, Hyderabad. Sodium Alginate and Calcium Chloride from Sri Venkateshwara Scientifics. Pectin from SEZ Fine Chemicals. Sodium Citrate from Sd Fine Chem Ltd and Sodium Bicarbonate from Luzenac Pharma.

2.2 Preparation of in-situ Gel of Ranitidine Hydrochloride

Sodium alginate solution was prepared in distilled water by heating at 60℃ under continuous stirring. After cooling below 40℃. Ingredients including drug, gelling agent and other excipients were weighed accurately. Then sodium alginate solutions of different concentrations were prepared by adding the sodium alginate to distilled water containing different concentrations of calcium chloride and different concentration of sodium citrate by heating to 60℃ under continuous stirring. Appropriate of amounts of ranitidine hydrochloride was then dissolved in resulting solution and formulations were prepared. (See table no.1)

3. Evaluation Tests

3.1 Fourier Transform Infrared (FTIR) Analysis

IR study was carried out to check compatibility between Ranitidine Hydrochloride and all other excipients. FTIR spectra of purified drug and excipients were recorded using an infrared spectrophotometer (Shimadzu-8400S). Spectrum was recorded over the wave number 400-4000 cm^{-1}.

3.2 Physical appearance and pH

Prepared sodium alginate in situ solutions of Ranitidine HCL are checked for their clarity and the time required for gel formation and type of gel formed. pH is measured using a calibrated digital pH meter at 27°C.(See table no.2).

3.3In Vitro Gelation Study And Viscosity Measurement

Viscosity of the samples is determined using a Brookfield digital viscosity using 2ml aliquot of the sample with spindle number 1rpm and sample temperature was maintained at 25℃ before each measurement. Ranitidine HCL in-situ solution (5ml) and artificial simulated gastric fluid (100 ml) are mixed and gelation is observed by visual examination.(See table no.3).

3.4 In-Vitro Floating Study

The in vitro floating study is determined using USP dissolution apparatus having 900ml of simulated gastric fluid. The petri dish containing 10ml of withdrawn in situ gelling solution was immersed into dissolution apparatus at 37℃. The time taken by the formulation to emerge on the medium surface and the time the formulation constantly floated on the dissolution medium surface are noted visually.(See table no.4).

3.5 Measurement of Water Uptake By The Gel

The water uptake by the gel is determined by following method. The in situ gels formed in 40ml of hydrochloric acid buffer (pH 1.2) are separated. The initial weight of the gel taken is weighed and to this gel 10ml of distilled water is added and after every 30 minutes the water is decanted and the weight of gel is recorded and difference in the weight is calculated.(See table no.5).

3.6 Determination of Drug Content

The amount of ranitidine HCL in each sample is determined by using UV spectrophotometer. The absorbance is determined at a wavelength of 225nm. The formulations which show good drug content, physical appearance and flow ability is selected as best formulations.(See table no.6)

3.7In-Vitro Drug Release Study

The in-vitro drug release of the in-situ floating gel were carried in 0.1N HCl from 0 to 12 hrs by USP type-II apparatus and the values are shown in table. The plot of % Cumulative drug release v/s time (hrs) was plotted and depicted

In vitro drug release study was conducted on the formulations for a period of 12 hours during which the highest drug release of 99.89 was observed in F4 and the least drug release of 94.56 in F6 during the 12 hour dissolution study. The influence of SA and pectin is found in in-vitro drug release, as the concentration of SA and pectin used in the formulation were increased from low to high, a decrease in the amount of drug release was observed. The drug release from the formulations with higher concentration of SA and pectin were slower compared to formulations with medium and low concentration of SA and pectin.(See table no.7)

Table 1: Formulation of Prepared in-situ Gel of Ranitidine Hydrochloride

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Ranitidine hydrochloride (g)	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
Sodium alginate (g)	1	2	3	1	2	3	1	2	3
Calcium chloride (g)	1	1	1	1	1	1	1	1	1
Sodium bicarbonate(g)	0.5	0.5	0.5	1	1	1	1.5	1.5	1.5
Sodium citrate (g)	1	1	1	1	1	1	1	1	1
Pectin (g)	1	1	1	1	1	1	1	1	1
Distilled Water(100ml)	100	100	100	100	100	100	100	100	100

Table 2: pH of prepared In situgel formulation

Formulation Code	pH
F1	6.84
F2	7.3
F3	6.96
F4	7.0
F5	7.1
F6	7.15
F7	7.23
F8	6.98
F9	6.85

Table 3:Viscosity of prepared In-situgel formulation

Formulation code	Viscosity (CP)
F1	260
F2	268
F3	280
F4	240
F5	248
F6	236
F7	240
F8	255
F9	273

Table 4: Floating Behaviour of In situ Gel Formulation

Formulation Code	Floating Lag Time (sec)	Floating time(hr)
F1	56	>10
F2	43	>8
F3	60	>8
F4	48	>10
F5	26	>12
F6	55	>11
F7	48	>9
F8	40	>11
F9	50	>9

Table 5: In Vitro Gelling Capacity of In SituGel Formulation

Formulation Code	Gelling Capacity (hr)
F1	8
F2	9
F3	>12
F4	11
F5	12
F6	>12
F7	8
F8	10
F9	>12

Table 6: Results of Drug Content of All Formulation

Formulation Code	Drug Content
F1	97.21
F2	96.35
F3	98.41
F4	96.54
F5	99.75
F6	95.75
F7	98.47
F8	94.52
F9	95.41

Table 7: % Drug Release Of All Formulation of In Situ Floating Gel

%Drug Release									
Time (Hr)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	18.64	19.5	18.45	16.64	18.45	19.1	19.5	17.36	16.36
2	27.5	28.64	29.68	28.9	26.7	28.36	28.63	26.18	29.74
3	34.41	39.91	37.51	40.1	34.64	37.61	36.45	37.6	36.79
4	42.28	46.54	49.7	52.64	42.3	44.32	49.81	46.72	47.14
5	54.68	54.12	55.1	64.12	53.74	53.14	59.6	57.14	59.21
6	68.9	63.36	62.36	80.14	62.62	60.84	70.69	64.36	68.74
7	81.14	76.45	70.48	88.36	70.14	69.91	84.23	73.86	76.1
8	89.89	83.36	79.36	93.18	78.34	79.54	91.89	82.14	85.67
9	92.36	90.14	88.56	96.54	86.7	84.14	94.55	87.68	89.94
10	96.94	92.36	91.81	98.14	92.21	88.36	97.99	90.14	92.63
11	99.96	95.14	93.31	99.89	95.48	91.92	99.64	92.36	94.12
12		97.36	95.42		98.64	94.56		95.8	96.87

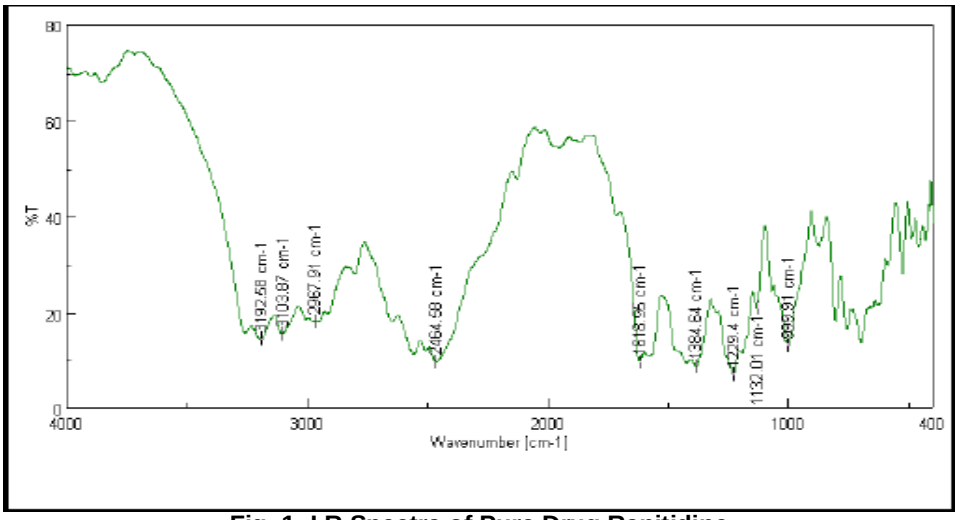

Fig. 1: I.R Spectra of Pure Drug Ranitidine

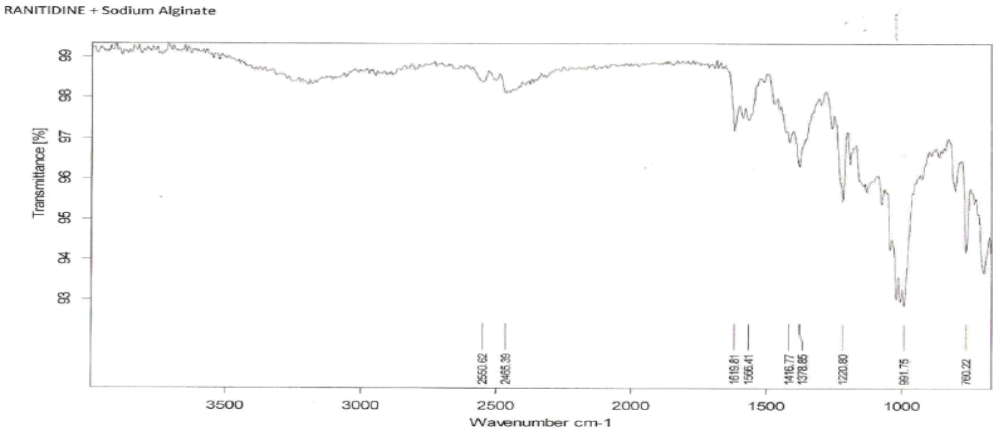

Fig. 2: FTIR Spectra of Ranitidine Hydrochloride and Sodium Alginate

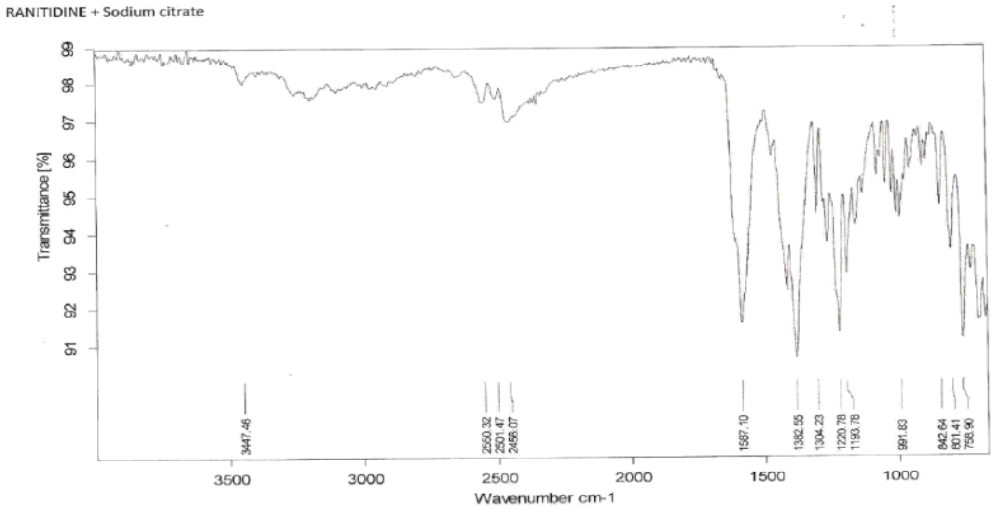

Fig. 3: FTIR Spectra of Ranitidine Hydrochloride and Sodium Citrate

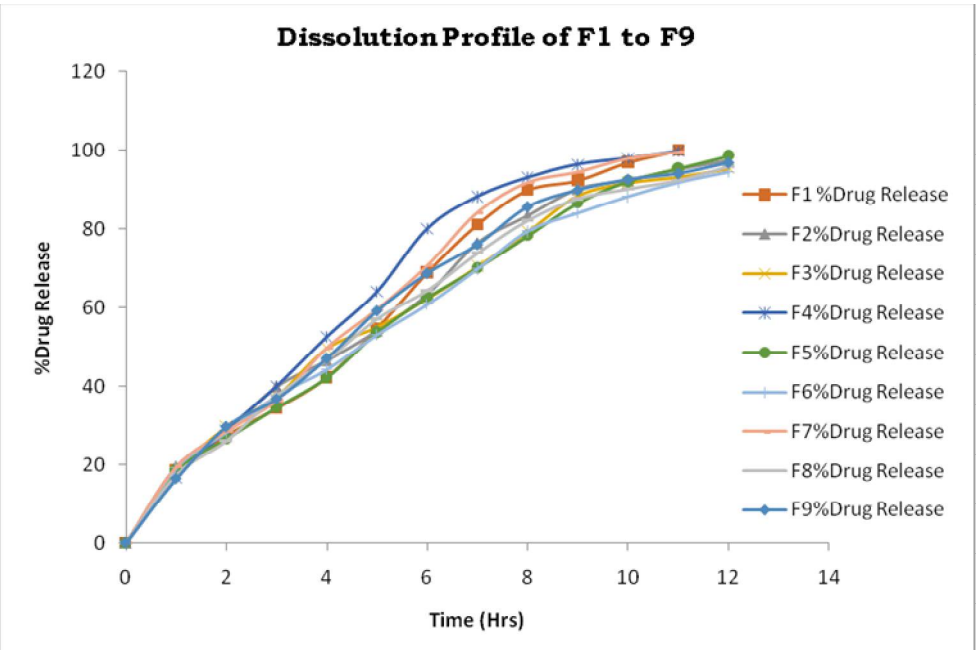

Fig. 4: Graph Showing Cumulative % Drug Release

RESULTS AND DISCUSSION

The present work is an attempt to formulate and evaluate floating oral in-situ gel of Ranitidine HCl. This dosage form is associated with many advantages like sustained delivery of drug release which helps in continuous release of drug before it reaches the absorption window, thus ensures optimum bioavailability.

The work done is summarized as follows:

The drug and excipient compatibility study were conducted to determine and select excipients for formulations. The formulations were developed by varying concentration of sodium alginate and pectin. But by varying concentration of sodium alginate and pectin the expected dissolution profile was obtained. The nine formulations were designed and evaluated for drug content, in-vitro floating study, measurement of water uptake by the gel.

Dissolution profiles were found to be well within the specifications of literature. The formulation F5 produced upto 50% drug release in 6hrs, but complete dissolution was achieved in 12hrs for F5 formulation, increasing the concentration of sodium alginate and pectin was favourable but optimum drug release is seen for F5 formulation. Hence F5 is considered as the best formulation among all the 9 formulations.Hence, it can be summarized from the present study that floating in-situ gel of Ranitidine HCl offers a novel approach for effective management of gastric ulcers and serves as good alternative to the oral floating in-situ gel.

CONCLUSION

In the present research work all formulations met the compendia limits in terms of physico-chemical parameters, dissolution. It was concluded that the rate of dissolution was found to be increased by increasing the concentration of sodium alginate and pectin and rate of dissolution was also influenced by them in the formulation. Floating oral in-situ gel of Ranitidine HCl provides several advantages especially sustained delivery of drug. The floating oral in-situ gel of Ranitidine HCl formulation of F5 batch containing 0.3g of Ranitidine HCl, 2g of Sodium Alginate, 1g of pectin, 1g of Sodium Bicarbonate, 1g of Calcium Chloride, 1g of Sodium Citrate and 100ml of distilled water considered to be the best among all 9 formulations since it exhibited a good dissolution profile, appearance, drug content.

From this study the Floating Oral In-Situ Gel of Ranitidine HCl appeared to be a novel alternative for effective management of Gastric Ulcers.

REFERENCES

1. Aukunurujithan. Oral Drug Delivery Technology. 176.

2. St Louis. Histamine H2 antagonists In: Drugs Facts And Comparisons. 16th edition; Wolters Kluwer Co; 1996;1862-1876.
3. Lauritsen K. Clinical Pharmacokinetics of Drugs Used In the Treatment of Gastrointestinal Diseases. Clinical Pharmacokinetic. 1990;19:94-125.
4. Grant S. Ranitidine; an Updated Review of Its Pharmacodynamic and Pharmacokinetic Properties and Therapeutic Use in Peptic Ulcer and Other Allied Diseases. 1987;37:801-807.
5. Basit A and Lacey L. Coloni Metabolism of Ranitidine Implications for Its Delivery and Absorption. International journal Pharm. 2001;227(1-2):157-167.
6. Singh BN and Kim KH. Floating Drug Delivery Systems: An Approach to Oral Controlled Drug Delivery via Gastric Retention. J Control Release. 2000;63:235-259.
7. Coffin M, Parr A. Ranitidine Solid Dosage Form. US Patent 407-687. April 18, 1995.
8. Arora S, Ali J, Ahuja A, Khar R and Baboota S. Floating Drug Delivery Systems: A Review. AAPS Pharma Sci Tech. 2005;6:E372-390.
9. Streubel A, Siepmann J and Bodmeier R. Floating Micro Particles Based On Low Density Foam Powder. Int J Pharm. 2002;241:279-292.
10. Singh BN and Kim KH. Floating Drug Delivery Systems: An Approach to Oral Controlled Drug Delivery via Gastric Retention. J. Control Release. 2000;63:235-259.
11. Coffin M, Parr A. Ranitidine Solid Dosage Form. US Patent 407-687. April 18, 1995.
12. Arora S, Ali J, Ahuja A, Khar R and Baboota S. Floating Drug Delivery Systems: A Review. AAPS Pharma Sci Tech. 2005;6:E372-390.
13. Streubel A, Siepmann J and Bodmeier R. Floating Micro Particles Based On Low Density Foam Powder. Int J Pharm. 2002;241:279-292.