PRODUCT DEVELOPMENT AND EVALUATION OF FLOATING PELLETS OF RANITIDINE HYDROCHLORIDE FOR THE TREATMENT OF GASTRIC ULCER

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ABSTRACT

The aim is to develop floating matrix pellets of Ranitidine Hydrochloride to achieve gastric retention for a period of 12 hour. Ranitidine HCL is a H2 - receptor antagonist widely prescribed in gastric ulcer, duodenal ulcers, Zollinger Ellison syndrome and gastro-oesophageal reflex. Ranitidine HCL has shorter half-life of 1-2 hours, in order to improve the oral sustained delivery there is a need for the design sustained release dosage. Since Ranitidine Hydrochloride is having a very short half life and also mostly absorbed (absorption window) in the stomach and upper part of small intestine. Hence ranitidine hydrochloride is suitable for gastro retentive drug delivery system (GRDD'S). The sustained release helps in continuous release of drug thus ensuring optimal bioavailability of the drug which favors development of floating matrix dosage form. The effervescent floating system helps in increasing stomach site bioavailability and efficacy of drug to reduce acid secretion

Keywords: pellets, buoyancy, ulcer, retention

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INTRODUCTION

DRUG DELIVERY OF FLOATING SYSTEMS [FDDS].

Floating systems or dynamically operated systems are low-density systems with sufficient buoyancy to float over gastric contents and remain buoyant in the stomach without interfering with the process of gastric emptying[1]. . The use of powders, granules, tablets, capsules, hollow microspheres, and laminated films to create buoyant structures has resulted in an increase in gastric retention time and a better understanding of plasma fluctuations. . The ability to prolong and control the time it takes for dosage forms to empty from the stomach is a valuable characteristic of dosage forms that remain in the stomach for longer durations than conventional dosage forms. The ability to restrict dosage in a specific location is one of these obstacles.[2] To circumvent this physiological issue, a number of drug delivery systems with prolonged stomach retention have been investigated. There are efforts to develop a controlled drug delivery system that can deliver a controlled and repeatable supply of medicinal products with a therapeutically effective plasma concentration for an extended period of time, while decreasing dosing frequency and minimising plasma drug concentration fluctuations at steady state. Gastro retentive is the capacity to retain food Systems can remain in the stomach for an extended period of time. Consequently, the duration of drug retention in the stomach is greatly increased. Longer gastric retention enhances bioavailability, reduces drug waste, and improves patient compliance. . The reduced solubility of a drug in an environment with a high pH.[3] Gastric retention has the potential to offer new therapies and substantial patient benefits. . To achieve controlled stomach retention of solid dosage forms, one can use the mechanisms of flotation, sedimentation, mucoadhesion, shape alteration, and expansion. systems, or the use of medications that postpone gastric emptying Considering these techniques, floating drug delivery devices seem like a good choice. The most promising

pharmaceutical delivery systems for releasing controlled doses.[4]

MATERIAL AND METHODS

The pure drug Ranitidine hydrochloride was obtained as a gift sample from **Max-Med Laboratories Pvt Ltd.** HPMC, Carbopol, Sodium bicarbonate and Citric acid were procured from S.D. Fine Chemicals Ltd. All of the chemicals used in the experiments were of analytical grade. Purified water that had been freshly prepared was used.

Precompression investigations

Preformulation studies are an integral part of the development of new drugs. It provides the scientific foundation for formulation creation.[5]

Study of drug-excipient compatibility:

The medication and excipients selected for formulation were evaluated for compatibility.[6]

FT-IR compatibility testing:

/It was possible to identify the drug-excipient interaction by contrasting the FT-IR spectra of pure Ranitidine with those of its physical mixture with excipients. FT-IR-8400S was utilised to obtain the IR spectra (Shimadzu Corporation, Tokyo, Japan). The potassium bromide (KBr) pellet technique was utilised in this investigation. The samples were completely mixed with dry KBr crystal powder. The mixture was compacted into a disc form. The spectrum was recorded after the disc was inserted into the spectrophotometer.[7]

Granules/pellets underwent all precompression experiments, including Bulk density, tapping, CI, and Hausners ratio.[8]

Bulk density:

The ratio of the mass of an untapped powder sample (W) to its volume (V0), which includes the contribution of the inter-particulate void volume, is the bulk density of a powder. Hence the bulk density depends on both density of powder particles and the spatial arrangement of particles in the powder bed.[9] The bulk density can be expressed in grams per millilitre (g/ml).

Bulk density is calculated using the equation

$$\textbf{Bulk density (BD)} = \frac{\textbf{weight of the powder}}{\textbf{Volume of powder}}$$

Tapped density:

The tapped density is obtained by tapping a measuring cylinder containing a powder sample and the volume is measured as initial volume. Measuring cylinder was fixed in the 'Tapped Densitometer' and tapped for 750-1250 times until the difference between succeeding measurements is less than 2%. The final reading was denoted by (V_f). The Tapped density can be expressed in grams per millilitre (g/ml)[10]

$$\textbf{Tapped density (TD)} = \frac{\mathbf{W}}{\mathbf{V_f}}$$

Preparation of Pellets:

Preparation and Evaluation of pellets by Extrusion-spheronization[11]

Preparation of Pellets: Extrusion-spheronization pellet preparation and evaluation 11I table number: formulation for pellet preparation was detailed. Extrusion-spheronization was evaluated as a granulation technique for preparing Ranitidine Hydrochloride pellets with the desired pellet characteristics. The initial step of this procedure was to investigate the effect of formulation and process variables on pelletized product characteristics in order to obtain pellets with the highest possible yield, good flowability, and desired particle size distribution. Ranitidine hydrochloride equivalent to 300 mg of ranitidine hydrochloride in addition to nine other medications. : All materials were mixed in a polybag according to the geometric dilution principle and kneaded into a wet mass of the required plasticity using distilled water. Extrudate is the result of dissolving PVP K30 in water, which acts as a binder and

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granulating agent in the motor, and extruding the cohesive mass through an extruder.[12] The extrudates were rotated in the spheronizer under optimal process conditions of 900 rpm spheronizer speed and 5 minutes of residence time. Magnesium stearate was used to lubricate the spheronizer for one minute in order to prevent pellets from sticking and to facilitate the smooth discharge of pellets from the spheronizer. The pellets were dried on paper-lined trays in a 450°C hot air oven for one hour.

Table No: 1 Formulation Table For The Preparation Of Ranitidine Hydrochloride Which Is Expressed In The Ratios (Drug: Hpmc: Carbopol: Sodium Bicarbonate: Citric Acid)

BATCH	DRUG	HPMC	CARBOPOL	SODIUM BICARBONATE	CITRIC ACID
F1	20	14	6	0.6	0.4
F2	20	14	6	0.8	0.2
F3	20	14	6	0.9	0.1
F4	20	16	4	0.6	0.4
F5	20	16	4	0.8	0.2
F	20	16	4	0.9	0.1
F7	20	18	2	0.6	0.4
F8	20	18	2	0.7	0.2
F9	20	18	2	0.9	0.1

*****All the values are expressed in ratios.

Evaluation parameters

Invitro buoyancy studies were conducted on all nine formulations, with 336 mg equivalent weight of ranitidine hydrochloride pellets from each formulation placed in a 100ml glass beaker containing 0.1N hydrochloric acid. The floating lag time (FLT) is the length of time it took for the tablet to rise to the surface and float, and the total floating time (TFT) is the amount of time the dosage form stayed there continuously (TFT). 12 In vitro Dissolution studies :Using a paddle and USP type II apparatus, the pellets of each batch were dissolved. A dissolution vessel was filled with 900 ml of 0.1 N Hydrochloric acid, and the temperature was set to 370.5°C. In each dissolution vessel, pellets were added and the paddle speed was set to 50 revolutions per minute. Every hour for 12 hours, 10 ml of sample was withdrawn from the dissolution apparatus and replaced with the same volume of fresh medium. This solution's absorbance was measured at 265.5 nm using an ultraviolet spetrophotometer.[13]

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Table No. 2: Dissolution Conditions

Dissolution conditions	
Medium	0.1 N Hydrochloric acid
Volume	900ml
Temperature	37^0C
Apparatus	USP type-II (paddle)
RPM	50
Time interval	1 hour

Stability study: For all pharmaceutical dosage forms, it is important to determine the stability of the dosage form. This will include storage at exaggerated temperature conditions, with the necessary extrapolations to ensure that the product will provide medication for absorption at the same rate over its designed shelf life as when it was initially formulated. In the ICH guidelines, the concept of different acceptable criteria for release and shelf life specifications is addressed.[14] The pellets of the optimal formulation are subjected to accelerated and long-term stability tests for three months. Three months are spent exposing the tablets to 400°F 20°C and 75% RH. The pellets' physical appearance, moisture content, assay values, impurities, and dissolution values are monitored at the end of the first, second, and third months. The stability of the optimal formulation was thus determined.[15] Dynamics of release: The release kinetics methods are founded on various mathematical functions that characterise the dissolution profile. After selecting an appropriate function, the resulting model parameters are used to evaluate the dissolution profiles. To determine the most appropriate drug release kinetic model describing the dissolution profile.[16] Zero-order model: Drug dissolution from dosage forms that do not disaggregate and slowly release the drug can be represented by the following equation:Q O- Q 1 = k O modification of the preceding equationQ t = Q O + K O t Where:Qt = quantity of drug dissolved at time tQ0 = the initial concentration of the drug in the solution (in most cases, Q0 = 0).K0 denotes the zero order release constant It is measured in concentration per time units. The release kinetics data from in vitro drug release studies were plotted as the cumulative amount of drug released versus time.[18] First order model.[19] This model has also been utilised to represent the absorption or elimination of several medications, despite the difficulty in theoretically conceptualising this mechanism. The equation that describes the drug's release according to first-order kinetics. dC/dt = -Kc Where K is the first-order rate constant in time units. . The aforementioned expression can also be written as logC=logC (O)-logC (t)/2.303. Where C0 is the starting drug concentration K is the first order rate constant with respect to time. The received data would result in a straight line with a slope of -K/2,303 when plotted as log cumulative percentage of medicine remaining vs time. Application: The drug dissolution in pharmaceutical dosage forms comprising water-soluble medicines in porous matrix, which follows this type of dissolution profile, can be described using this connection. The amount of drug released per unit of time diminishes over time because the amount of drug still inside the body determines how much is released.

Following Higuchi's classical diffusion equation, drug release from matrix devices has been characterised as diffusion.[22] Where

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:Q = the quantity of drug released at time t. D = drug diffusion coefficient A = quantity of drug per unit volume of matrix Cs = drug matrix solubility E = matrix permeability T = the time in hours at which q represents the amount of drug in release If D, Cs, and A are assumed to be constant, the above equation can be simplified. The equation is modifiable as follows. Q=K t^(1/2)Where data were plotted as cumulative percentage of drug release versus time's square root .Application: This relationship can be used to describe the drug dissolution form for a variety of modified release pharmaceutical dosage forms, such as certain transdermal system and matrix tablets with water solution drugs.[23] Korsmeyer Pappas model: To comprehend the mode of drug release from swellable matrices, the data were entered into the following equation.[24] M t M ∞= Kt^nMt /M equals the fraction of drug released at time t K = constant including the structural and geometrical properties of the drug/polymer system n = diffusion coefficient pertinent to the mechanism of release Applying log on both sides of the previous equation simplifies it to Log M t/M ∞ =Log K+n Log t Where data is plotted as a log of drug released versus log time, a straight line with slope equal to n is obtained, and the k can be derived from the y-intercept.> 0.45 and 0.89 for non-Fickian release, and 0.89 for case 2 type release.[25] RESULTS AND DISCUSSION:PREFORMULATION STUDIESA) Authentication checks IR Spectroscopy: The IR spectrum of the pure drug resembles that of Ranitidine Hydrochloride. The ranitidine hydrochloride spectrum revealed the following functional groups at their respective frequencies:[26]

RESULTS AND DISCUSSION

PREFORMULATION STUDIES:

A) Identification tests

IR Spectroscopy: The IR spectrum of the pure drug matched that of Ranitidine Hydrochloride. The spectrum of Ranitidine Hydrochloride revealed the frequencies of the following functional groups.[26]

Table 3: IR Spectroscopy

cm-1	Group
3441	N-H stretch
2964	C-H stretch (alkanes)
1391	NO2 stretch
1237	C-O stretch

B) Compatibility studies:

From the IR spectra of the pure drug and the combination spectra of the drug with the polymers, it was determined that all the characteristic peaks of Ranitidine Hydrochloride were also present in the combination spectra, indicating the drug's compatibility with the polymers employed.[27]

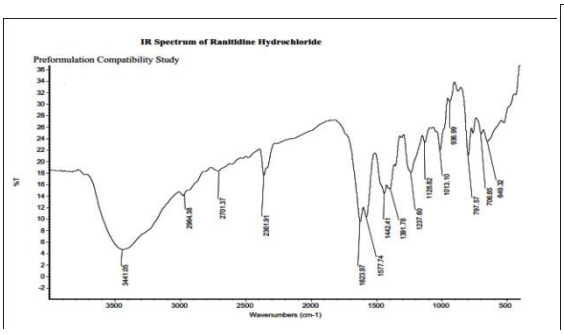

Fig no.1: FTIR pure drug of Ranitidine Hydrochloride

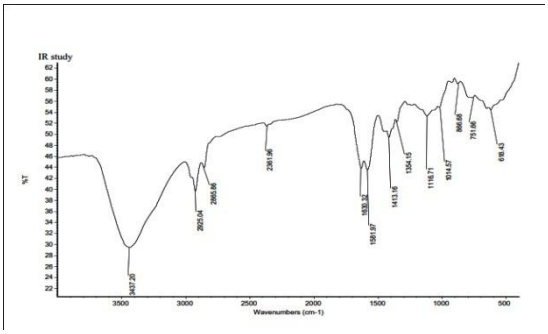

Fig no.2: FTIR pure drug of Ranitidine hydrochloride + HPMC + Carbopol

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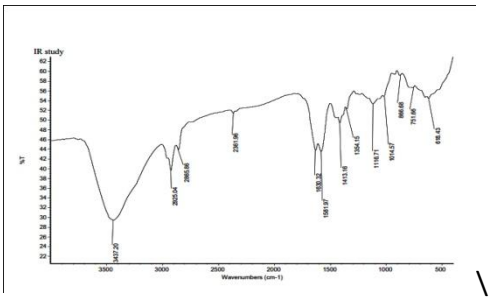

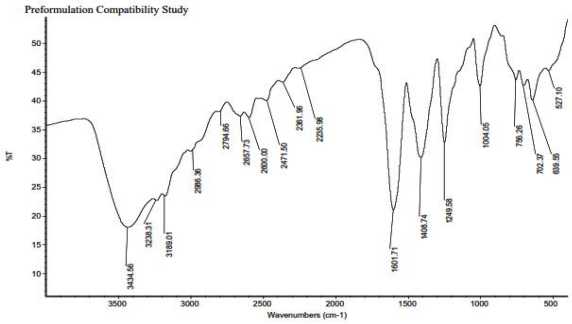

Fig no.3: FTIR pure drug of Ranitidine hydrochloride +HPMC +CABOPOL+ NaHCo3+citric acid

Fig no.4: FTIR pure drug of Ranitidine hydrochloride Pellets

Flow properties:

Table No.4 : Flow properties of pellets of Ranitidine hydrochloride

Formulation	Bulk density (gm/ml)	Tapped density (gm/ml)	Compressibility index (%)	Hausner's ratio	Floating lag time(min)	Total Floating time (hour)
F1	0.313±0.02	0.426±0.05	26.5±0.1	1.33±0.02	4.23±0.1	**6**
F2	0.363±0.01	0.507±0.009	28.4±0.2	1.35±0.01	5.12±0.02	**8**
F3	0.325±0.01	0.498±0.01	24.6±0.3	1.52±0.05	5.32±0.09	**8**
F4	0.360±0.03	0.470±0.01	23.4±0.3	1.32±0.02	5.48±0.01	**6**
F5	0.358±0.02	0.459±0.03	21.5±0.4	1.28±0.04	1.46±0.09	**8**
F6	0.330±0.03	0.450±0.04	26.6±0.1	1.34±0.01	5.43±0.08	**10**
F7	0.345±0.01	0.465±0.01	25.8±0.3	1.35±0.01	5.56±0.04	**10**
F8	0.325±0.04	0.430±0.03	24.4±0.2	1.30±0.02	6.81±0.04	**12**
F9	0.349±0.05	0.478±0.02	26.4±0.3	1.38±0.01	6.42±0.06	**≥12**

*Mean± SD, n = 3

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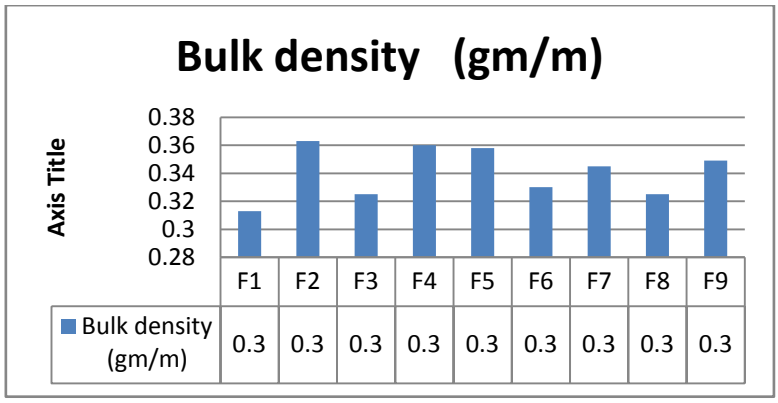

*All values are mean± SD, n = 3

Fig no. 5 Bulk density

Table No.5: % Drug Release of Ranitidine hydrochloride from F1 to F9

S.No	Time (hr)	% Drug Release								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	1	32.4 ±0.4	39.5 ±0.3	22.2 ±0.3	17.8 ±0.1	28.4 ±0.3	29.2 ±0.	24.9 ±0.	20.3 ±0.	15.7 ±0.3
2	2	43.5 ±0.2	45.3 ±0.5	40.6 ±0.3	27.7 ±0.2	40.8 ±0.1	37.7 ±0.2	32.5 ±0.4	29.6 ±0.1	23.2 ±0..2
3	3	61.2 ±0.5	56.1 ±0.8	61.1 ±0.8	49.8 ±0.1	53.7 ±0.2	48.2 ±0.7	43.6 ±0.2	41.9 ±0.1	36.7 ±0.2
4	4	88.3 ±0.2	69.9 ±0.1	75.6 ±0.3	68.7 ±0.2	61.4 ±0.5	63.8 ±0.1	57.7 ±0.1	54.8 ±0.2	48.8 ±0.1
5	6	96.4 ±0.4	88.6 ±0.4	87.4 ±0.5	74.6 ±0.3	72.7 ±0.2	75.4 ±0.4	70.4 ±0.4	62.6 ±0.3	57.9 ±0.1
6	8		93.7 ±0.2	96.7 ±0.2	80.2 ±0..7	91.4 ±0.3	87.3 ±0.6	82.6 ±0.2	73.2 ±0.8	65.3 ±0.3
7	10				89.3 ±0.6		99.3 ±0.2	91.8 ±0.1	86.6 ±0.3	72.5 ±0.2
8	12				93.99± 0.1			96.5 ±0.3	98.2 ±0.7	81.9 ±0.2

*All values are expressed as mean± SD, n = 3

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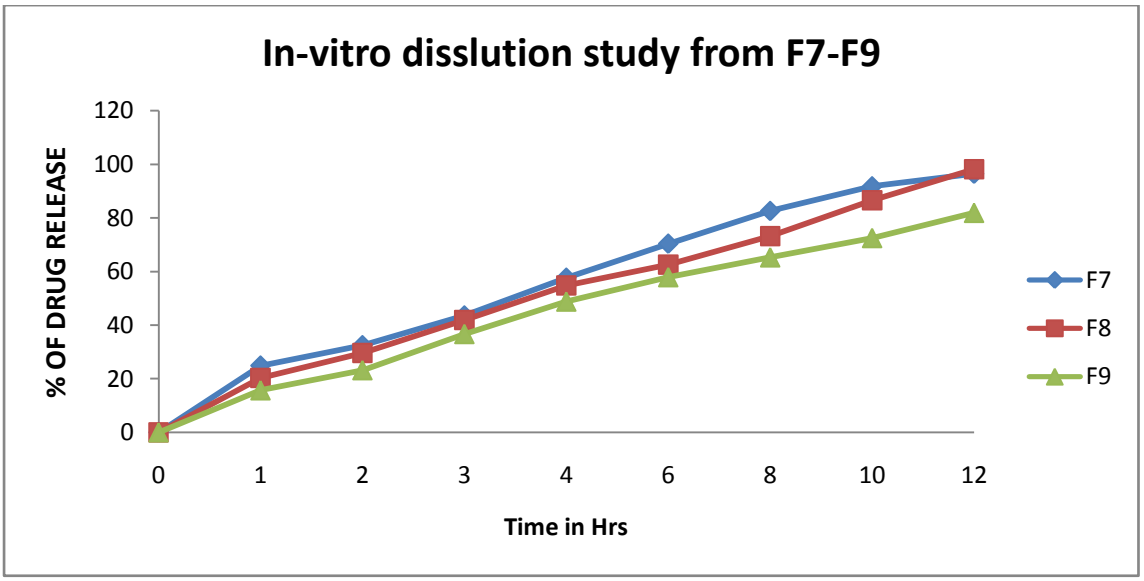

Fig no.6 Invitro drug release study of F1-F3

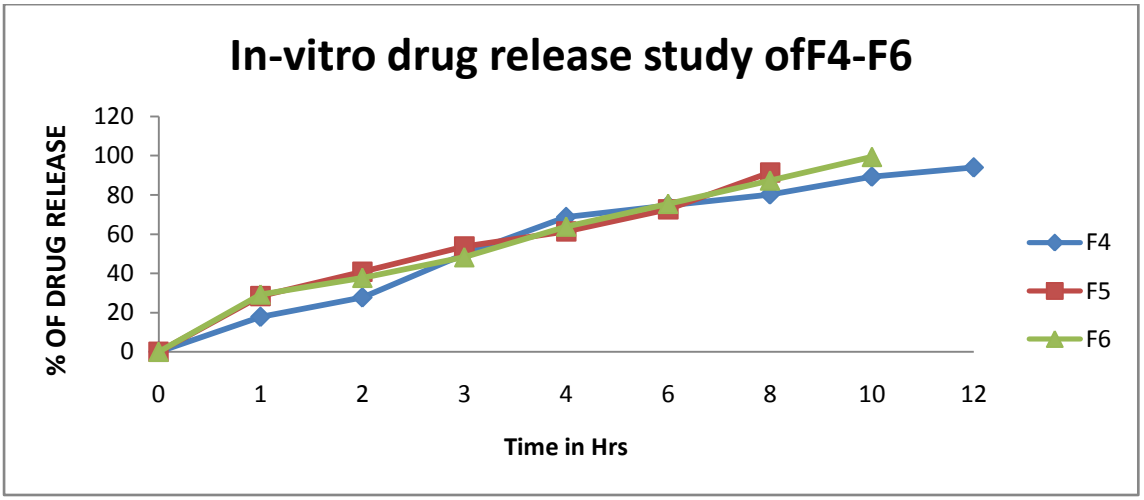

Fig no.7 In-vitro drug release study ofF4-F6

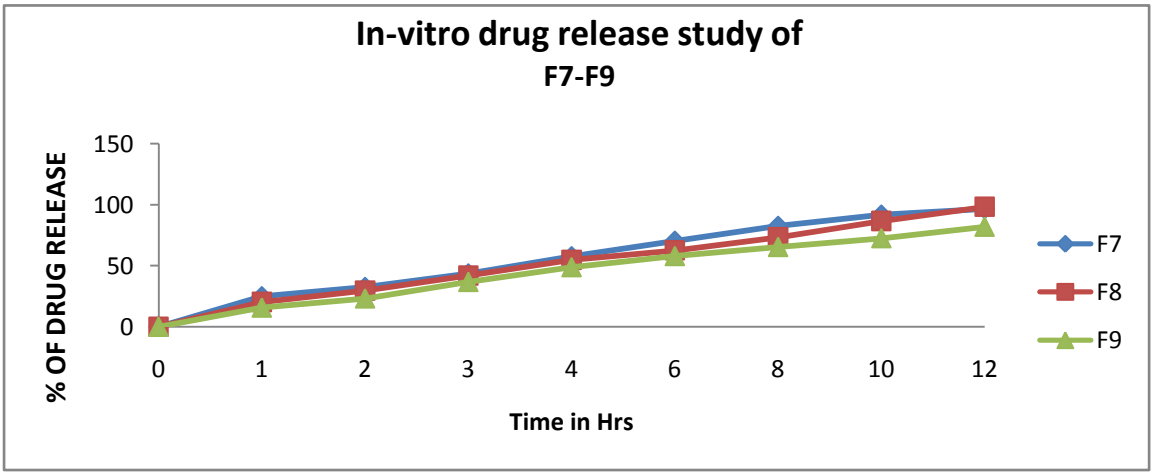

Fig no.8: Invitro dissolution study from F7-F9

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Table No.6: Determination of release kinetics

S.No	Time (hour)	Square root of time	Log time	Cum %drug release	Log cum % drug release	Cum % drug remaining	Log cum % drug remaining
1	**1**	1.000	0.000	20.3	1.255	82	1.914
2	**2**	1.414	0.301	29.6	1.490	69.1	1.839
3	**3**	1.732	0.477	41.9	1.640	56.3	1.751
4	**4**	2.000	0.602	54.8	1.711	48.6	1.687
5	**6**	2.449	0.778	62.6	1.797	37.3	1.572
6	**8**	2.828	0.903	73.2	1.866	26.6	1.425
7	**10**	3.162	1.000	86.6	1.927	15.4	1.188
8	**12**	3.464	1.079	98.2	1.996	1	0.000

Table No.7: Coefficient of Correlation for kinetic drug release

	Zero order	First order	Higuchi modal	Peppas modal
Slope	6.8137	0.1381	28.495	0.6626
r2	0.9769	0.7722	0.9631	0.9922

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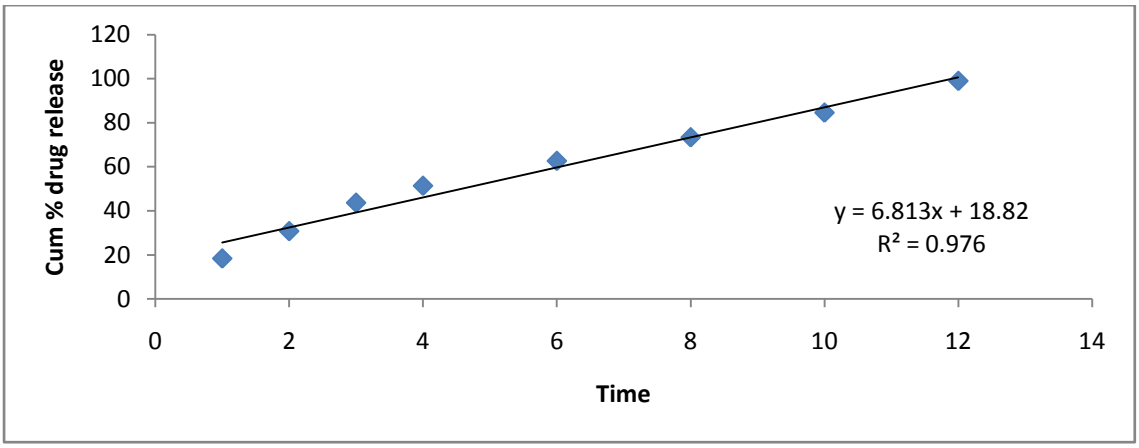

Fig no. 9 Formulation of F8 – Zero order kinetics

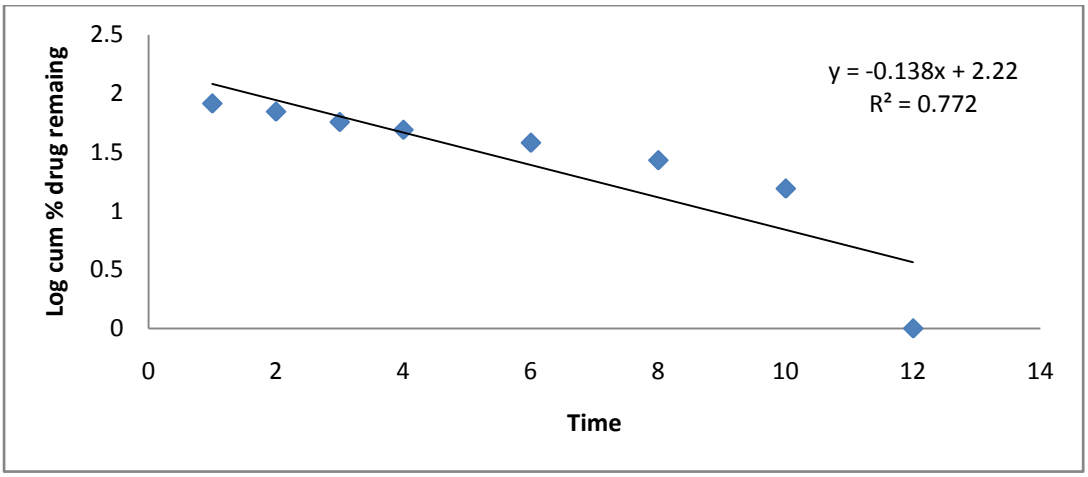

Fig No. 10 Formulation of F8 –First order kinetics

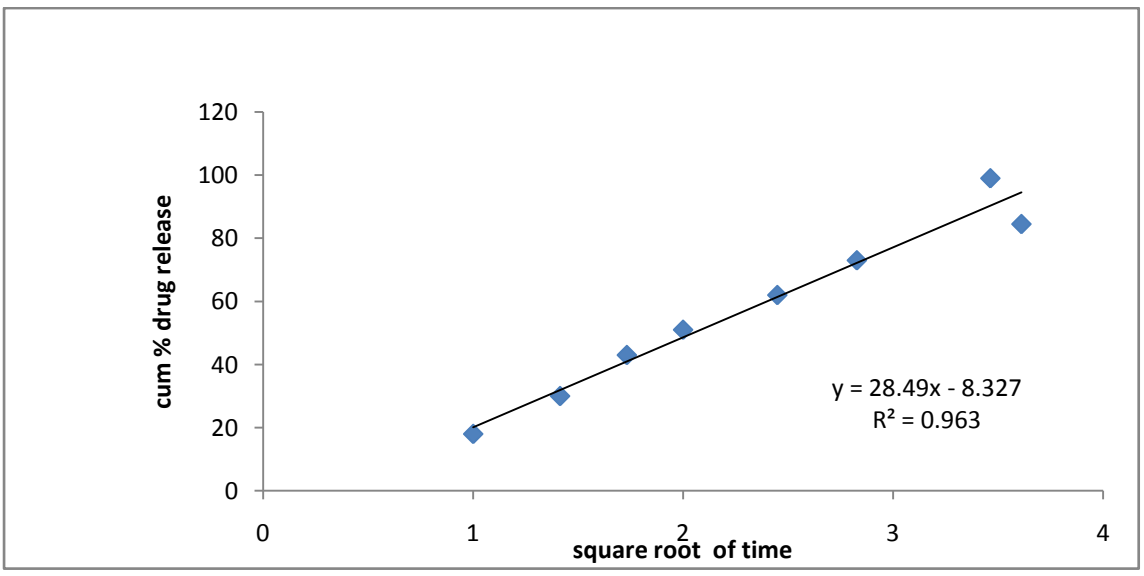

Fig No. 11 Formulation of F8 – Higuchi model

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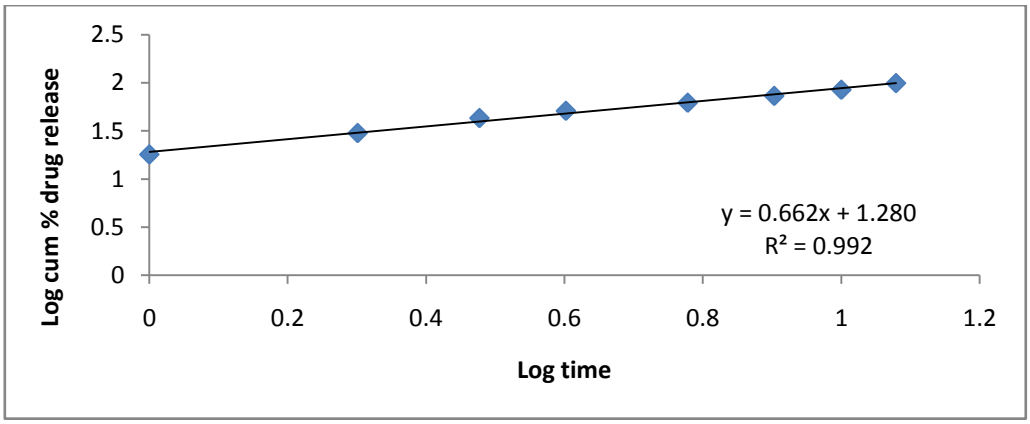

Fig No.12 Formulation of F8 –Koresmeyer Peppas model

Discussion:

Extrusion-spheronization was evaluated as a granulation technique to obtain desired pellet characteristics for preparation of Ranitidine hydrochloride pellets. The first step in this process was to study the effect of the formulation and process variables on pelletized product characteristics, so as to get pellets with best possible yield, good flowability and desired particle size distribution. Ranitidine hydrochloride equivalent to 300 mg of ranitidine and 9 different drug: utilised polymer:gas-generating agent ratios

For formulations F1-F3, three different gas generating agent ratios were used: drug:polymers (HPMC:CABOPOL):gas generating agents (sodium bicarbonate:citric acid) 20: (14:6): (0.6:0.4) for F1 formulation, 20: (14:6): (0.8:0.2) for F2 formulation, and 20: (14:6): (0.9:0.1) for F3 formulation. Here the ratios of HPMC:CARBOPOL were kept constant and the ratios of the sodiumbicarbonate:citric acid was varied

From F4-F6 formulations the drug:polymers(HPMC:CABOPOL):gas generating agents(sodium bicarbonate:citric acid) were used in the concentrations of 20: (16:4) : (0.6:0.4) for F4 , 20: (16:4) : (0.8:0.2) for F5 and for F6 20: (16:4) : (0.9:0.1). (0.9:0.1). The ratios of HPMC:CARBOPOL(16:4) were kept constant and the ratios of the sodium bicarbonate: citric acid was varied

Finally in case of formulations from F7-F8 the drug:polymers(HPMC:CABOPOL):gas generating agents(sodium bicarbonate:citric acid) were used in the ratios of 20: (18:2) : (0.6:0.4)for F7 formulation, 20: (18:2) : (0.8:0.2) for F8 formulation, and for F9 formulation were used in the ratios of 20: (18:2) : (0.9:0.1). (0.9:0.1). here also the ratios of HPMC:CARBOPOL(18:2) were kept constant and the ratios of the sodium bicarbonate: citric acid was varied

Sodium bicarbonate is the most frequently utilised bicarbonate in effervescent formulations.

The prepared pellets of all the 9 formulation are taken for evaluation studies like percent of entrapment efficiency, percent of drug content, floating lag time and total floating time and finally dissolution studies. The floating pellets are evaluated for percent of entrapment efficiency, percent of drug content, floating lag time, total floating time and assay. The results were shown in the Table No. Total floating time in all the formulations varies for the each batch ranges from 6-12 h and and floating lag time varies from 1.46 to 6.81mins.

Floating lag time and total floating time

This study involved the formulation of Ranitidine Hydrochloride floating matrix pellets. HPMC and carbopol are suitable for use in formulations of floating matrices, according to research**.** Here In all

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formulations, PVP K30 is used as one of the binders at a concentration of 1:0.001 by weight (Drug:PVPK30). As gas-generating agents, sodium bicarbonate and citric acid were used in all nine formulations.The entrapment efficiency was found to be between 93.5 and 99.5%, ensuring that at least 93% of the drug is completely entrapped in the pellets. The floating lag time ranges between 1.46 and 6.81 seconds for F1-F9 formulations. When it comes to the floating time, there is a significant range from F1 to F9 It was observed that the floating concentration increases as the sodium bicarbonate concentration increases in relation to the drug concentration.The dissolution study was conducted in simulated gastric fluid with a pH of 1.2 and paddles of USP Type II. Dissolution was performed on a total of nine formulations, and it was observed that the release profiles of each formulation differ. It was also observed that as the concentration of polymers, i.e., the drug-to-polymer ratio, increased, drug release was sustained for 12 hours. In F1-F3 where the drug:polymer ratio is constant, i.e. 20:(14:6), there is a difference in the gas generating agent, which is 20:(0.6:.04) in F1 formulation, 20:(0.8:0.2) in F2 formulation, and 20:(0.9:0.1) in F3 formulation. It was observed that as the concentrations of sodium bicarbonate and citric acid increased, so did the floating time of the pellets, whereas the drug concentration at the end of the sixth and eighth hour for formulations F1, F2, and F3 was only 86.4%, 93.7%, and 96.7%. In the first three formulations, the 12-hour release was therefore not met. From F4-F5 formulation, where the drug:polymer ratio is held constant at 20:(16:4), and by varying the sodium bicarbonate, citric acid ratios, i.e., 0.6:0.4 in F4 formulation, 0.8:0.2 in F5 formulation, and 0.9:0.1 in F6 formulation, the drug:polymer ratio can be optimised. The release rate was determined to be satisfactory for the F4 formulation, with a value of 93.99 at the end of the 12th hour, but the floating time was only limited to 6 hours; 12 hours was not achieved. At the conclusion of the eighth and tenth hour, the F5 and F6 Formulations released 91.4% and 99.3%, respectively. Finally, the drug from F7-F9 Formulations: polymer ratio was estimated to be 20:(18:2) which is kept constant by varying the drug: sodium bicarbonate citric acid ratio in range of 0.6:0.4 for F7 formulation and 0.8:0.2 for F8 formulation and finally 0.9:0.1 for F9 formulation, the drug release of F8 formulation was found to be satisfactory, which is 98.2% at the end of 12th hour and floating time was found to be upto 12 hours. Thus, the F8 formulation was deemed superior to F7 and F9 formulations.From the above graphs of kinetic release, namely zero order, first order, second order, and the higuchi plot, the date of drug release for formulation F8 can be determined. F8 was selected based on the release parameters, which aid in the investigation of release mechanisms and kinetics. Coefficient of correlation obtained for the different kinetic models. The release of ranitidine was found to be very close to zero-order kinetics, indicating that drug release was independent of concentration. The best explanation of the in vitro release mechanism was provided by Korsmeyer. Good linearity was indicated by Peppa's equation (r2 = 0.992). The release exponent n, which represents the diffusion constant, the typical operating release mechanism, was 0.6626 for the F8 formulation. It is common knowledge that the Peppas model is used to determine whether the release mechanism is Fickian or Non-Fickian diffusion. The value of 'n' (the release exponent of the Korsmeyer Peppas model) could be used to characterise various release mechanisms. The interpretation of n values was performed as follows:• n<0.5 (0.45) - quasi-Fickian Diffusion• n=0.5 (0.45)

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- Diffusion mechanism• 0.5<n<1 - Anomalous (non-Fickian) Diffusion - both relaxation and diffusion (erosion)• n=1 (0.89) - Case 2 transport (zero order release)• n>1 (0.89) - Super Case 2 transport (relaxation)The mechanism of release is atypical, as it involves both diffusion and erosion.

CONCLUSION

Floating drug delivery systems for the stomach have several advantages over other gastric retention methods. Ranitidine HCL's matrix-type gastric floating drug delivery system has been investigated. It is commonly used to treat duodenal ulcer, gastric ulcers, Zollinger – Ellison syndrome, and gastroesophageal reflux disease. For effective treatment, multiple doses of Ranitidine HCL are required, resulting in therapeutic fluctuations. Furthermore, the bioavailability of Ranitidine hcl is very low, found to be 35% due to site-specific absorption, and it is primarily absorbed from the stomach and upper parts of the small intestine with a short half-life; therefore, a sustained release dosage form of Ranitidine HCL is appropriate. Therefore, the design of a gastroretentive drug delivery system for Ranitidine HCL to enhance its bioavailability is required due to the aforementioned factors**.**

This study involved the formulation of Floating matrix pellets by Extrusion-spheronization using HPMC and Cabopol as matrix formers in varying ratios to the drug, as well as the use of sodium bicarbonate and citric acid as gas-generating agents in varying ratios to the drug. On increasing the ratio of the concentrations of the two gas-generating agents, the floating time increases, and on increasing the concentration of HPMC and decreasing the concentration of carbopol in the rations, the release of the drug appears to be prolonged up to 12 hours.

The results of percent of Drug Entrapment, floating lag time, floating time, and percent assay studies for all nine formulations were deemed satisfactory.

In vitro dissolution was used to conduct drug release studies, and based on the dissolution data, the optimal formulation was chosen. In addition, according to ICH guidelines, three-month accelerated stability studies were conducted on the optimal formulation, which was found to be stable.

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AUTHORS CONTRIBUTIONS

All the authors contributed equally.

CONFLICT OF INTERESTS

Declared none

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