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FORMULATION AND EVALUATION OF FLOATING EFFERVESCENT TABLETS OF CIMETIDINE

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Abstract:
The Floating Sustained released tablets using effervescent agent containing Cimetidine SR tablets were successfully prepared by wet granulation method. The physiochemical evaluation results for the granules of all trials pass the official limits in angle of repose, compressibility index. The prepared granules were also maintained the physiochemical properties of tablets such as thickness, hardness, weight variation, friability. The optimized formulation contains the average thickness of 3.11±0.02, average hardness of 4.94±0.05, average weight of 300±0.05, friability of 0.45. The optimized formulation F7 which releases the Cimetidine in sustained manner in 1st hour it releases 11.3% but the remaining drug release was sustained up to 8 hours. From the kinetics drug releases the optimized formulation, F7 have displayed zero order release. Hence it may be summarized that the F7 tablets prepared by wet granulation method for sustained release tablets might be a perfect and effective formulation to treat the Peptic ulcer.

Keywords: *SR tablets, effervescent, wet granulation, compressibility.*

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INTRODUCTION:

The study aimed to develop and assess effervescent floating tablets of Cimetidine by utilizing natural polymers such as Guar gum and Xanthan gum, chosen for their ability to prolong drug release and reduce dosing frequency. Key objectives included performing drug-excipient compatibility studies as per ICH guidelines, optimizing the polymer concentration for sustained release tablets, and evaluating formulation parameters like weight variation, hardness, friability, and assay. Additionally, in-vitro studies were conducted to examine the sustained-release behavior, and accelerated stability tests were performed to ensure the formulation's stability under various conditions Oral administration remains the most common and preferred route for drug delivery due to its convenience and design flexibility. However, oral controlled drug delivery faces challenges, particularly with drugs that have a narrow absorption window along the gastrointestinal tract (GIT). The major obstacle is modifying the GI transit time, as gastric emptying varies widely and depends on factors such as dosage form and fasted state. Typical gastric residence times range from a few minutes to two hours, which may limit the efficacy of drugs requiring longer absorption times. To overcome this, gastroretentive systems are designed to prolong gastric retention, enhancing absorption for drugs absorbed mainly in the stomach and upper intestine, and providing stable therapeutic levels. Gastroretentive forms are particularly beneficial for treating local conditions, such as H. Pylori infections that cause peptic ulcers, by ensuring the drug remains localized in the stomach.[1]

These buoyant drug delivery systems, prepared with natural polymers like xanthan gum and guar gum along with effervescent agents like sodium bicarbonate and citric acid, achieve prolonged gastric retention by floating on gastric fluids. On entering the stomach, the system releases carbon dioxide, allowing the tablet to float and gradually release the drug. Various other formulations, such as sodium alginate-based mixtures, floating minicapsules, and ion exchange resins, have also been explored for gastroretentive delivery.[2] These formulations enhance bioavailability, reduce drug waste, and improve solubility for drugs less soluble in the high-pH environment of the intestines, providing patients with more consistent therapeutic effects and potentially lower required doses, especially for drugs like Furosemide and Ofloxacin.[3]

MATERIALS AND METHODS:

PREFORMULATION STUDIES:

Preformulation may be described as a phase of the research & development process where the formulation scientist characterizes the physical, chemical properties of API, in order to develop stable, safe and effective dosage forms. During this evaluation possible interaction with various inert ingredients intended for use in final dosage.

A) Organoleptic properties

The color, odor and taste of the drug were evaluated using descriptive terminology.

B) Solubility

Solubility is defined as the number of gram substance which will dissolve in 100 grams of solvent at a stated temperature. The solubility of drug was studied in different solvents such as Organic and inorganic solvents by measuring how many parts of solvent is required for one part of solid.

C) Melting Point

Melting point of Model drug was determined by capillary method. Fine powder of Model drug was filled in glass capillary tube (previously sealed on one end). The capillary tube is inserted into the melting point apparatus and observed the temperature at which drug started to melt. Melting point of the drug was determined by using Scientec digital melting point apparatus.[4]

COMPATIBILITY STUDIES:

FT-IR studies for drug and excipients compatibilities

Prior to the development of the dosage forms the preformulation study was carried out. IR spectral studies lies more in the qualitative identification of substances either in pure form or in combination with polymers and excipients and acts as a tool in establishment of chemical interaction. Since I.R. is related to covalent bonds, the spectra can provide detailed information about the structure of molecular compounds. In order to establish this point, comparisons were made between the spectrum of the substances and the pure compound. The above discussions imply that infrared data is helpful to confirm the identity of the drug and to detect the interaction of the drug with the carriers. FTIR spectra

were recorded with a PERKIN ELMER spectrum two. In the range 400–4000 cm−1 using a resolution of 4 cm−1 and 16 scans. Samples were diluted with KBr mixing Powder, and pressed to obtain self-supporting disks. Liquid samples formulations were analyzed to form a thin liquid film between two KBr disks. . Then it was compared with original spectra. FTIR spectra was compared and checked for any shifting in functional peaks and non-involvement of functional group. From the spectra it is clear that here is no interaction between the selected carriers, drug and mixtures. Hence the selected carrier was found to be compatible in entrapping the selected Cimetidine with carriers without any mutual interactions.[5]

ANALYTICAL METHODS

SCANNING OF CIMETIDINE

10 mg pure drug was dissolved in methanol and was diluted to give concentration of 100 µg/ml and was scanned between 200 nm and 400 nm for the determination of λ_{max}. The wavelength of 224 nm was selected as for λ_{max}. The same was used for further analysis of drug solution and absorbance of final standard solution was measured at 224 nm.[6]

PREPARATION OF THE STANDARD CALIBRATION CURVES OF CIMETIDINE:

Standard calibration linearity curve of Cimetidine in 0.1N HCl pH 1.2

Cimetidine (100mg) was dissolved in 10ml of methanol and volume was made up to 100 ml in volumetric flask using 0.1N HCl pH 1.2. From this stock solution 10 ml was withdrawn and is diluted to 100ml in volumetric flask which gives the concentration of 100 µg/ml.

From this stock solution aliquots were withdrawn in volumetric flask to give concentrations 10µg/ml, 20µg/ml, 30µg/ml, 40µg/ml, 50µg/ml. Absorbance of each solution was measured at 230 nm using Shimadzu UV- 1700 UV-Vis double beam spectrophotometer with 0.1N HCl pH 1.2 as a reference standard.[7]

FORMULATION DEVELOPMENT

The pharmaceutical development studies have to be carried out with the purpose of selecting right dosage form and a stable formulation. These studies give detailed description of all the steps involved in the process of formulation development. Such details are intended towards identifying critical parameters involved in the process, which have to be controlled in order to give reliable and reproducible quality product.[8]

Formulation of effervescent floating tablets:

This sustained release tablets was prepared by wet granulation method.

- **Sieving**
  The active ingredient was passed through the sieve#40 followed by the other ingredients were passed the same sieve.

- **Dry mixing**
  Cimetidine, Micro Crystalline Cellulose, natural polymers and sodium bicarbonate were taken in a poly bag and mixed for 5minutes to ensure uniform mixing of the ingredients with the drug.[9]
- Preparation of binder solution
  - PVP-K_{30}
  - IPA

  Weigh PVP K-30 accurately and it is mixed with IPA to form a solution is used as binder solution and kept separately.
- Then the granulation, drying and sieving were followed by lubrication for final compression. Magnesium stearate and talc were weighed and they were passed through sieve#20.Then mixed with dried granules of Cimetidine in a polybag for 5minutes to get a uniform blend. Then the lubricated granules of Cimetidine were weighed accurately and fed into the die of single punch machinery and compressed. For this 9mm round punch was used for compression.

Formulation of effervescent floating tablets:

Development of effervescent floating sustained release tablets of Cimetidine was carried out. Sustained release tablets were prepared using formulae given below. Sustained release tablets were prepared on 16 station tablet compression machine by wet granulation. The tablets of different formulations were punched with 9mm round punch on compression machine. [10]

COMPOSITION OF EFFERVESCENT FLOATING TABLETS

Table no; 1 formulation table for effervescent floating sustained release tablets

Formulation	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8
Cimetidine	100	100	100	100	100	100	100	100
Xanthum gum	40	60	80	100	-	-	-	-
Guar gum	-	-	-	-	40	60	80	100
PVP K-30	22.5	22.5	22.5	22.5	22.5	22.5	22.5	22.5
NaHCO3	40	40	40	40	40	40	40	40
MCC	87.5	67.5	47.5	27.5	87.5	67.5	47.5	27.5
IPA	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Magnesium stearate	4	4	4	4	4	4	4	4
Talc	6	6	6	6	6	6	6	6
Total weight	300	300	300	300	300	300	300	300

Note: PVP- Polyvinyl pyrrolidone, IPA- Isopropyl alcohol. All the ingredients are in 'mg'.

EVALUATION OF GRANULES:

Angle of Repose:

The flow property was determined by measuring the Angle of Repose. In order to determine the flow property, the Angle of Repose was determined. It is the maximum angle that can be obtained between the free standing surface of a powder heap and the horizontal.

Angle of repose= $\tan^{-1}$ (h/r)

Where,

H = height of a pile (2 cm)

R = radius of pile base.

Procedure:

20gms of the sample was taken the sample was passed through the funnel slowly to form a heap. The height of the powder heap formed was measured. The circumference formed was drawn with a pencil on the graph paper. The radius was measured and the angle of repose was determined. This was repeated three times for a sample.[11]

Bulk density

Bulk density. Measuring the volume of known mass of powder sample and it is passed into the graduated cylinder and the ratio of given mass of powder and its bulk volume is known as bulk density.

Bulk density = M / V0

Where **M**= mass of the powder;

V0=bulk volume of the powder.

Limits:

It has been stated that the bulk density values having less than 1.2 g/cm3 indicates good packing and values greater than 1.5 g/cm3 indicates poor packing.

Tapped density

Weigh accurately a quantity of powder and transferred into a measuring cylinder and note down the volume as V0. Now the measuring cylinder is fixed to density determination apparatus, and tapped for 500 times until no further volume changes is observed then note down the volume Vr.

Tap density = M / Vr

Where M = mass of the powder,

Vr = final tapping volume of the powder.

Compressibility index and Hausner ratio

Bulk density and tapped density values were used to calculate the compressibility index and hausner ratio following is the equation:

Compressibility index = 100 × tapped density / bulk density

Hausner ratio = tapped density / bulk density

Flow properties and corresponding Angle of repose, Compressibility index and Hausner ratio[12]

TABLE NO 2: ACCEPTANCE CRITERIA OF FLOW PROPERTIES

Flow properties	Angle of repose(θ)	Compressibility Index (%)	Hausner ratio
Excellent	20-30	<10	1.00-1.11
Good	31-35	11-15	1.12-1.18
Fair	36-40	16-20	1.19-1.20
Passable	41-45	21-20	1.26-1.34
Poor	46-55	26-31	1.35-1.45
Very poor	56-65	32-37	1.46-1.59
Very very poor	> 66	>38	>1.6

POST COMPRESSION PARAMETERS

1. **Physical Appearance:**
   To be accepted by the consumer a tablet should be elegant in appearance it is necessary to determine the lot-to- lot uniformity and tablet-to- tablet uniformity.[13] It involves the measurement of size, shape, colour, presence or absence of odour, taste etc.
2. **Size & Shape:**
   Thickness is the only variable to calculate the size and shape of a tablet. Micro-meter is the device which is used to determine the thickness of the tablet. Controlled variation for tablet
   Thickness lies within a ± 5% standard value.
3. **Weight variation test:**
   This is an important in-process quality control test to be checked frequently (every half an hour). Corrections were made during the compression of tablets. Any variation in the weight of tablet (for any reason) leads to either under medication or overdose. So, every tablet in each batch should have a uniform weight. 20 tablets were weighed individually. Average weight was calculated from the total weight of all tablets. The individual weights were compared with the average weight. The percentage difference in the weight variation should be within the permissible limits (+5%). The percent deviation was calculated using the following formula.[14]

$$\% \text{ Deviation} = \frac{\text{Individual weight} - \text{Average weight}}{\text{Average weight}} \times 100$$

TABLE 3: LIMITS FOR TABLET WEIGHT VARIATION TEST

Average weight of tablet (mg)	% Difference allowed
130 or less	10%
From 130 to 324	7.5%
> 324	5%

Friability:

Friability test is one of the in process quality control test to determine whether the product will withstand the shocks during processing, handling, transportation, and shipment. Friability is defined as the loss in the weight of the tablet due removal of its fine particles from its surface. Friability of a tablet is measured with Roche friabilator.

Weigh about 10 collectively tablets from each batch and place them in the friabilator chamber. Now they were subjected to rolling, a free falls in the chamber from a height of 6cm which is rotated at a rate of 25 rpm. Repeat the procedure till the completion of 100 rotations (4 minutes), and now the tablets were taken out from the friabilator and note their weights.

The percentage friability was determined by the formula:

$$\% \text{ Friability} = (W_1 - W_2) / W_1 \times 100$$

W_1 = Weight of tablets before test

W_2 = Weight of tablets after test

Swelling Index Studies:

The swelling behavior of a dosage unit was measured by studying its weight gain. The swelling index of tablets was determined by placing the tablets in the basket of dissolution apparatus using dissolution medium as 0.1N HCl at 37±0.5°C. After 1, 4 and 6h each dissolution basket containing tablet was withdrawn, blotted with tissue paper to remove the excess water and weighed on the analytical balance (Schimdzu, AX 120). The experiment was performed in triplicate for each time point. Swelling index was calculated by using the following formula[15]

$$\text{Swelling index} = \frac{\text{(Wet weight of tablet – Dry weight of tablet)}}{\text{Dry weight of tablet.}}$$

In vitro Buoyancy studies:

The in vitro buoyancy was determined by floating lag time, and total floating time. (As per the method described by Rosa et al[39]) The tablets were placed in a 100ml beaker containing 0.1N HCl. The time required for the tablet to rise to the surface and float was determined as floating lag time (FLT) and the duration of the time the tablet constantly floats on the dissolution medium was noted as the Total Floating Time respectively (TFT).

In vitro Dissolution Studies

In vitro drug release studies were carried out using USP XXIV dissolution apparatus type II, with 900ml of dissolution medium maintained at 37±1°C for 12 hr, at 50 rpm, 0.1N HCl pH 1.2 for 8hrs for sustained release tablets. 5ml of sample was withdrawn at predetermined time intervals replacing with an equal quantity of drug free dissolution fluid. The samples withdrawn were filtered through 0.45µ membrane filter, and drug content in each sample was analyzed after suitable dilution by UV/Vis Spectrophotometer at 224nm and cumulative percent drug release was calculated.[16]

Release Kinetics

The analysis of drug release mechanism from a pharmaceutical dosage form is an important but complicated process and is practically evident in the case of matrix systems. As a model-dependent approach, the dissolution data was fitted to four popular release models such as zero-order, first-order, diffusion and Peppa's- Korsemeyer equations, which have been described in the literature. The order of drug

release from matrix systems was described by using zero order kinetics or first orders kinetics. The mechanism of drug release from the matrix systems was studied by using Higuchi equation and Peppa's-Korsemeyer equation.

Zero Order Release Kinetics

It defines a linear relationship between the fractions of drug released versus time.

$$Q = kot$$

Where, Q is the fraction of drug released at time t and ko is the zero order release rate constant.

A plot of the fraction of drug released against time will be linear if the release obeys zero order release kinetics.

First Order Release Kinetics:

Wagner assuming that the exposed surface area of a tablet decreased exponentially with time during dissolution process suggested that drug release from most of the slow release tablets could be described adequately by apparent first-order kinetics. The equation that describes first order kinetics is

$$In (1-Q) = - K1t$$

Where, Q is the fraction of drug released at time t and k1 is the first order release rate constant.

Thus, a plot of the logarithm of the fraction of drug remained against time will be linear if the release obeys first order release kinetics.

Higuchi equation:

It defines a linear dependence of the active fraction released per unit of surface (Q) on the square root of time.

$$Q=K2t½$$

Where, K2 is the release rate constant.

A plot of the fraction of drug released against square root of time will be linear if the release obeys Higuchi equation. This equation describes drug release as a diffusion process based on the Fick's law, square root time dependant.

Power Law:

In order to define a model, which would represent a better fit for the formulation, dissolution data was further analyzed by Peppa's and Korsemeyer equation (Power Law).

$$Mt/M(= K.tn$$

Where, Mt is the amount of drug released at time t and M(is the amount released at time (, thus the Mt/M(is the fraction of drug released at time t, k is the kinetic constant and n is the diffusion exponent. To characterize the mechanism for both solvent penetration and drug release n can be used as abstracted in Table. A plot between log of Mt/M(against log of time will be linear if the release obeys Peppa's and Korsemeyer equation and the slope of this plot represents "n" value.[17]

Table 4: Diffusion exponent and solute release mechanism for cylindrical shape

Diffusion Exponent	Overall solute diffusion mechanism
0.45	Fickian diffusion
0.45<n<0.89	Anomalous (non-fickian) diffusion
0.89	Case II transport
n>0.89	Super Case II transport

RESULTS AND DISCUSSION:

Preformulation Study:

A. Organoleptic Properties (Color, odor, taste and appearance)

Table 5 Results of identification tests of drug

S.NO	Parameter	Drug
1	Color	Fine White powder
2	Odor	Unpleasant odor
3	Taste	BitterTaste
4	Appearance	Crystalline powder.

B. Melting point determination: Drug: Cimetidine

Table 6: Results of Melting point determination test of drug

DRUG NAME	Observed Melting Point
Cimetidine	**141-143^{0}c**

C. Solubility

These tests were performed and the results are illustrated in the table

Table 7: showing the Solubility of Cimetidine (API) in various solvents.

Solvents	Solubility
Water	Freely soluble
Methanol	Freely Soluble
Ethanol	Freely soluble
Chloroform	Slightly soluble
Diethyl ether	Insoluble

DETERMINATION OF ABSORPTION MAXIMA OF CIMETIDINE:

10 mg pure drug was dissolved in methanol and was diluted to give concentration of 100 µg/ml and was scanned between 200 nm and 400 nm for the determination of λ_{max}. The wavelength of 224 nm was selected as for λ_{max}. The same was used for further analysis of drug solution and absorbance of final standard solution was measured at 224 nm.

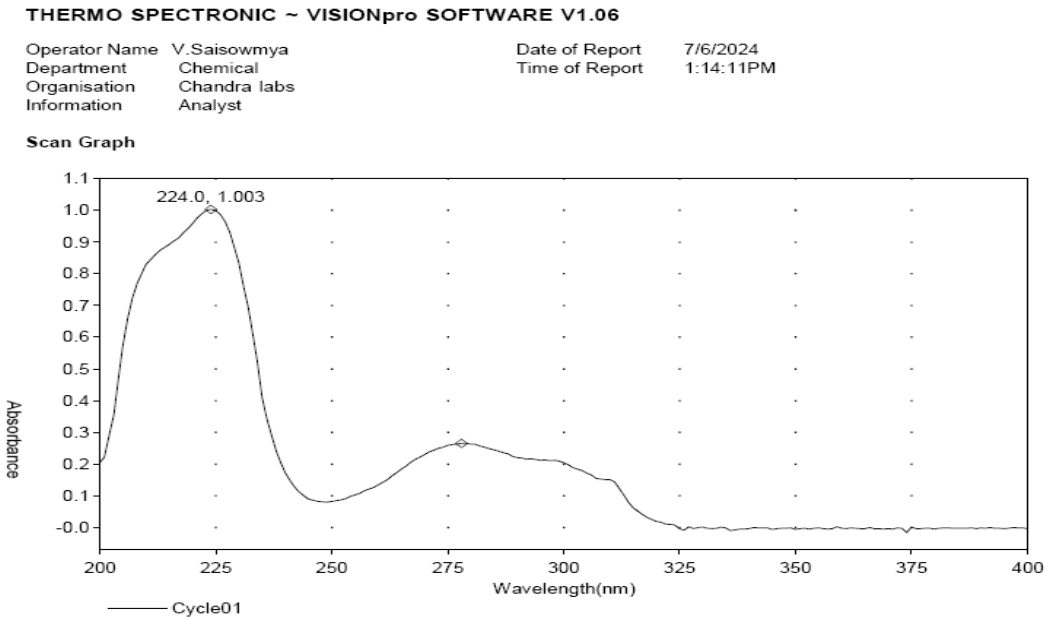

Fig : 1 Cimetidine UV spectrum at 226nm in 0.1N HCl

Standard Graph of Cimetidine:

The standard graph of Cimetidine has shown good linearity with R^2 values 0.998 in 0.1N HCl, which suggests that it obeys the "Beer-Lambert's law".

Table No:8 Concentration and absorbance's of Cimetidine in 1.2pH 0.1N HCl

Concentration	Absorbance
0	0
10	0.145
20	0.324
30	0.515
40	0.695
50	0.889
60	0.994

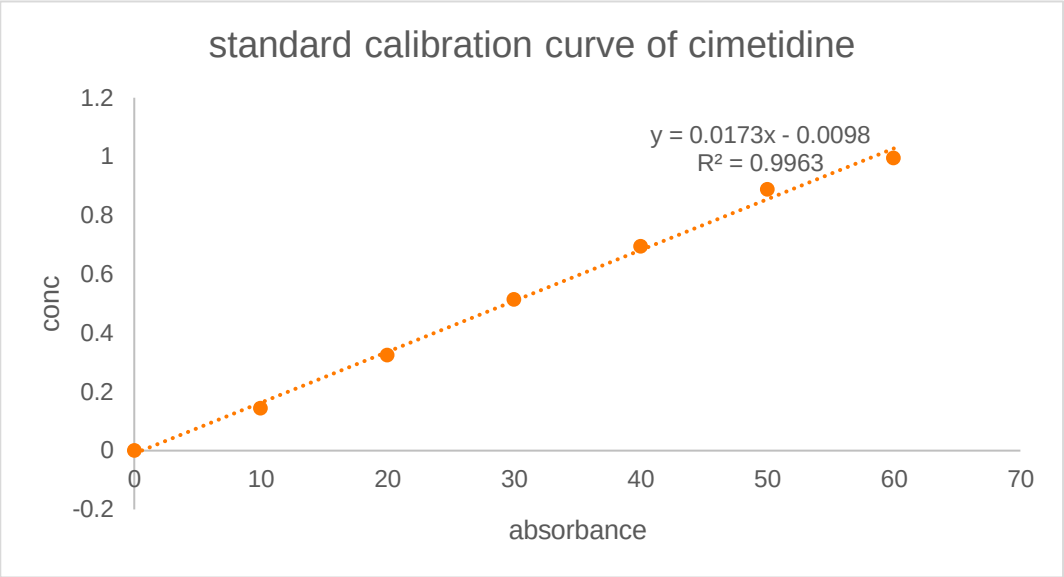

Fig: 2 Calibration curve of Cimetidine in 1.2pH 0.1N HCl

FTIR COMPATABILITY STUDIES

The spectrum obtained after the analysis is shown in Figure No: The spectrum of the standard and the samples were then superimposed to find out any possible interactions between the drug and the polymers. All the characteristic peaks of Cimetidine mentioned in fig .3 were also found in the spectrum formulations. The results suggest that the drug is intact in the formulations and there is no interaction found between the drug and the excipients.

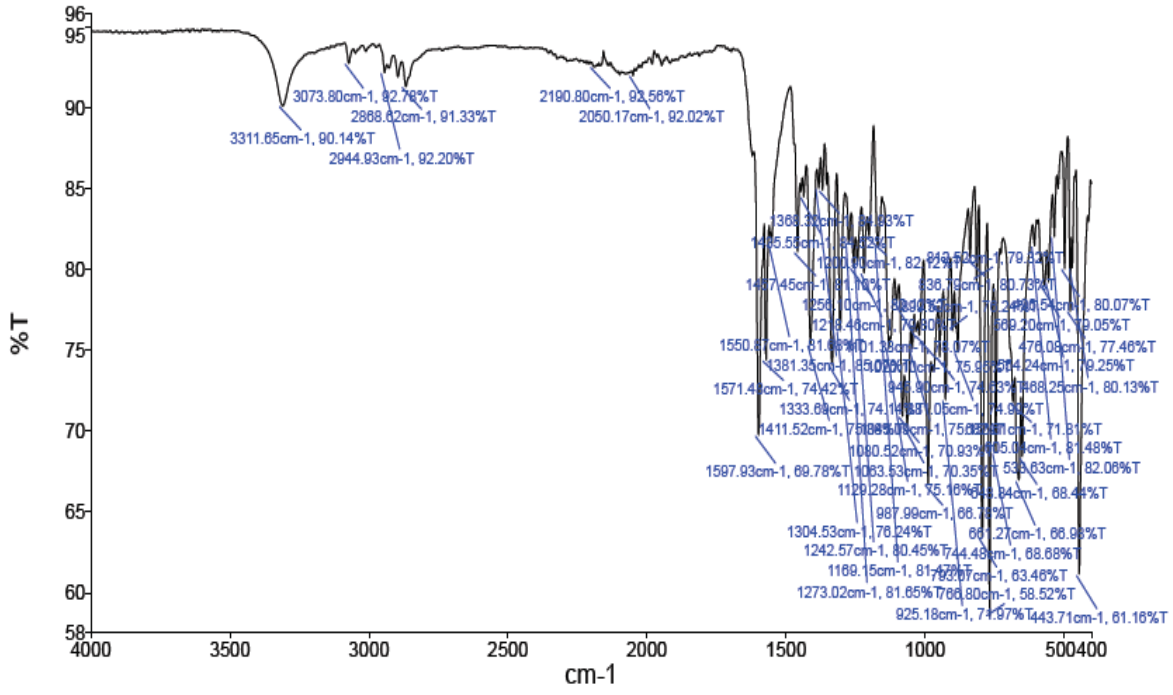

Fig:3 FTIR graph of Pure Cimetidine drug

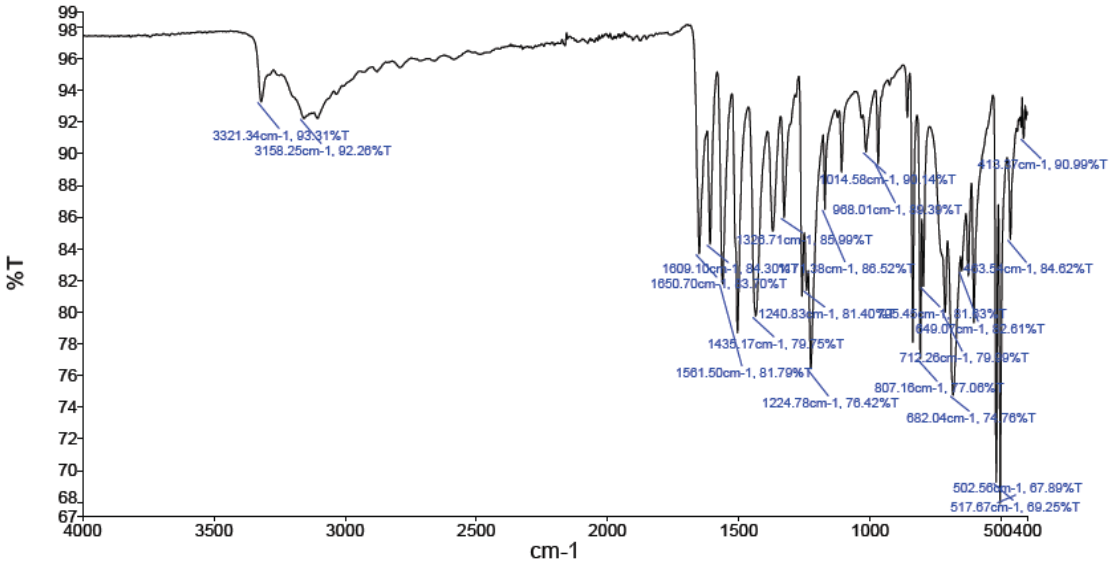

Fig:4 FTIR graph of Cimetidine optimized formulation with Excipients

Table 9: FTIR Spectra of Cimetidine Final formulation

Characteristic peak	Observed range	Pure drug	Optimised formulation
N-H	3400-3200	3311.65	3321.34
C═N	1690-1540	1597.93	1561.50

FTIR studies were performed to understand the compatibilities between the drug with different excipients. The figures above illustrate that the functional groups like N-H Stretching with the observation range of 3400-3200 has peaks at 3311.65 in pure drug, 3321.34 drug and excipient. Similarly the functional group C═N Stretching has a peak range of 1690-1540 has peaks at 1597.93 in pure drug, 1561.50 drug and excipient.

PRE COMPRESSION PARAMETERS

Characterization of Blends

The blends for Bucoadhesive tablets were characterized with respect to angle of repose, bulk density, tapped density, Carr's index, and Hausners ratio. Angle of repose was less than 30° and Carr's index values were less than 20 for the blend of all the batches indicating excellent to good flowability and compressibility. Hausner's ratio was less than 1.11 for all the batches indicating excellent flow properties.

Table No 10: pre compression parameters for cimetidine effervescent floating Tablet

Formulations	Angle of Repose (θ)	Loose Bulk Density (g/ml)	Tapped Bulk Density (g/ml)	Carr's index	Hausner's ratio	RESULT
F1	28.38±0.06	0.614±0.01	0.754±0.04	18.56±0.05	1.22±0.03	Excellent
F2	27.36±0.04	0.661±0.01	0.812±0.03	18.59±0.06	1.22±0.02	Excellent
F3	25.55±0.03	0.648±0.02	0.793±0.02	18.28±0.03	1.22±0.03	Excellent
F4	29.11±0.06	0.612±0.01	0.761±0.03	19.57±0.03	1.24±0.02	Excellent
F5	27.72±0.07	0.665±0.01	0.826±0.02	19.49±0.03	1.23±0.02	Excellent
F6	28.14±0.07	0.661±0.03	0.820±0.03	19.39±0.05	1.24±0.02	Excellent
F7	28.39±0.06	0.674±0.02	0.842±0.03	19.95±0.02	1.27±0.04	Excellent
F8	26.31±0.02	0.659±0.02	0.830±0.02	20.60±0.01	1.25±0.04	Excellent

From the above pre-compression parameters it was clear evidence that granules has excellent flow properties.

POST

COMPRESSION PARAMETERS

Table No: 11 Post Compression Parameters for Cimetidine effervescent floating Tablet

F.Code	Hardness (kg/cm^2) †	Thickness (mm) ‡	Weight (mg) ‡	Friability (%)
F1	4.25±0.02	3.40±0.03	300±0.01	0.58±0.05
F2	4.53±0.02	3.32±0.03	301±0.03	0.50±0.05
F3	4.46±0.01	3.40±002	300±0.03	0.52±0.05
F4	4.31±0.03	3.40±0.01	299±0.02	0.33±0.05
F5	4.59±0.03	3.41±0.01	301±0.03	0.31±0.03
F6	4.87±0.02	3.21±0.01	300±0.03	0.32±0.05
F7	4.94±0.05	3.11±0.02	300±0.05	0.45±0.04
F8	4.81±0.06	3.11±0.03	300±0.04	0.49±0.01

The results of the uniformity of weight, hardness, thickness, friability, and drug content of the tablets are given in Table. All the tablets of different batches complied with the official requirements of uniformity of weight as their weights varied between 299.2±0.02 and 301±0.03mg. The hardness of the tablets ranged from 4.25±0.02 to 4.94±0.05 kg/cm2 and the friability values were less than 0.5% indicating that the Effervescent floating tablets were compact and hard. The thickness of the tablets ranged from 3.11±0.02 to 3.41±0.01 mm. Thus all the physical attributes of the prepared tablets were found be practically within control.

Table no 12: Post compression parameters of % drug content, floating lag time, swelling index, floating duration

Formulation Code	Drug content (%)	Floating lag time(sec)	Swelling index (%)	Floating duration(hrs)
F1	98.42±0.01	25	121.12	>12
F2	99.40±0.05	24	139.45	>12
F3	98.34±0.02	15	142.05	>12
F4	98.45±0.04	45	144.85	>12
F5	99.34±0.05	54	129.18	>12
F6	99.29±0.01	2min	142.61	>12
F7	97.38±0.02	1min 24sec	145.24	>12
F8	99.43±0.01	3mins	156.18	>12

The results of the Floating lag time (sec), Swelling index (%), Floating duration (hrs), and drug content of the tablets are given in Table. All the tablets of different batches complied with the official requirements of Floating lag time (sec) varied between 1min 24sec and 3mins. The Swelling index **(%)** of the tablets ranged from 121.2 to 156 and Floating duration (hrs) values were less than >12. All the formulations satisfied the content of the drug as they contained 98 to 101 % of Cimetidine and good uniformity in drug content was observed. Thus all the physical attributes of the prepared tablets were found be practically within control.

INVITRO DISSOLUTION STUDIES FOR FLOATING SR TABLETS -DISSOLUTION STUDY:

Buffer Stage:

Medium : 0.1N HCl adjusted to 1.2pH
Type of apparatus : USP - II (paddle type)
RPM : 50
Volume : 900ml
Time : 8hrs

In-Vitro Drug Release Studies for SR tablets

Table 12: cumulative percentage drug release from sustained release tablets

Time	F1	F2	F3	F4	F5	F6	F7	F8
0	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
1	12.04	11.5	10.21	16.51	11.23	12.5	11.3	16.15
2	28.5	36.14	35.24	31.24	28.42	26.14	30.14	26.16
3	59.26	64.21	57.17	50.27	45.16	42.18	48.22	45.28
4	94.15	92.5	72.28	67.19	65.33	68.27	64.56	60.61
6	--	--	94.17	80.45	90.12	92.18	80.24	78.18
8	--	--	--	92.17	--	--	98.17	94.27

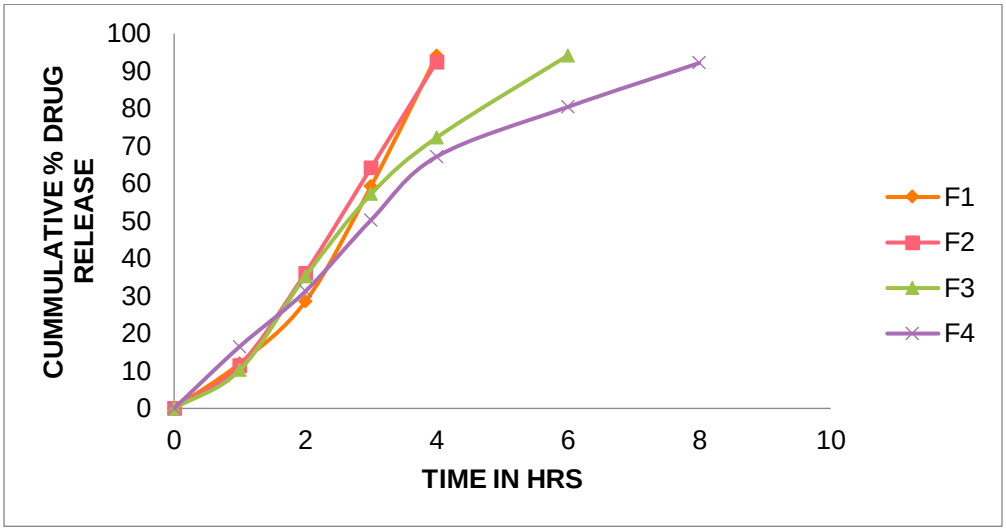

Fig: 5 dissolution graph for Cimetidine floating tablets formulations F1-F4

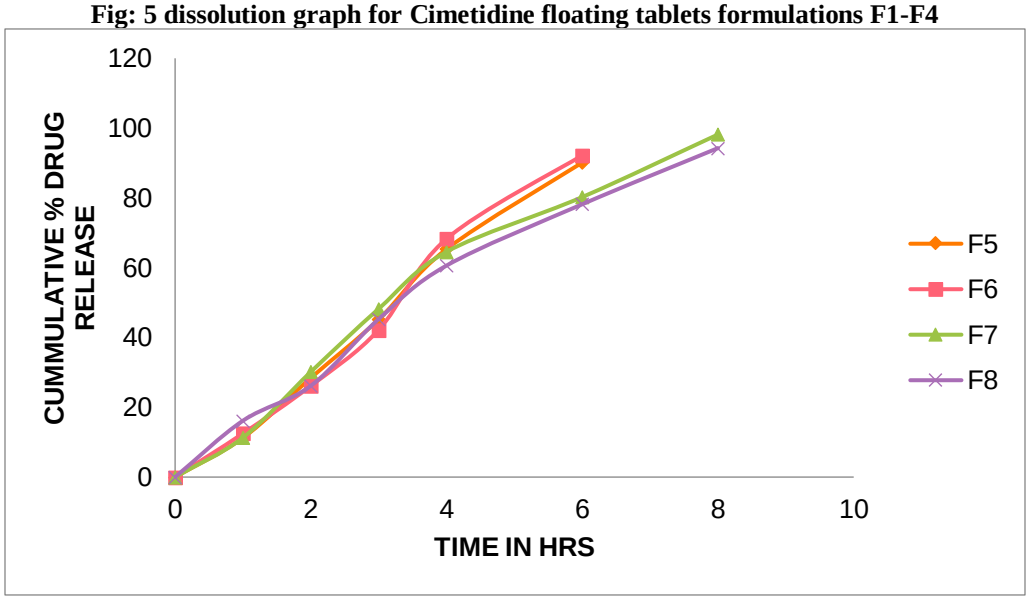

Fig: 6 dissolution graph for Cimetidine floating tablets formulations F5-F8

In-vitro drug release study

The In-vitro drug release study has been done for various formulations (F1-F8). The different ratios of polymers were used. The results shown that as the proportion of polymers in the formulation increases, cumulative percent drug released was found to be reduced. Among the 8 batches, formulation F1 and F2 have released 94.15% and 92.5% drug release in 4th hr respectively, F3, F5& F6 formulations shows 94.17%, 90.12% and 92.18% drug release in 6th hr respectively, Whereas F4, F7& F8 formulations shows 92.17%, 98.17% and 94.27% drug release in 8th hr respectively. Among all formulations F7 formulations was optimized based on sustained drug release and

highest drug release at 98.17% at 8th hr.

Discussion of dissolution

The results of *in-vitro* drug release studies in 0.1N HCl (from 1 to 12 hours), initially the aim was to select optimum concentration of individual polymers of different concentration for SR tablets. Hence the tablets containing, floating tablets of drug (Cimetidine) were prepared by altering the concentration of different natural polymers.

Discussion for *in-vitro* release of Cimetidine Sustained release tablet

From the table, it was confirmed that the F7 formulation floating tablets fulfill the sustained release theory, In that the Guar gum was used separately in the formulations, but increasing the polymer concentration, it was clearly identified that the drug release was retarded.

KINETIC RELEASE MODELS:

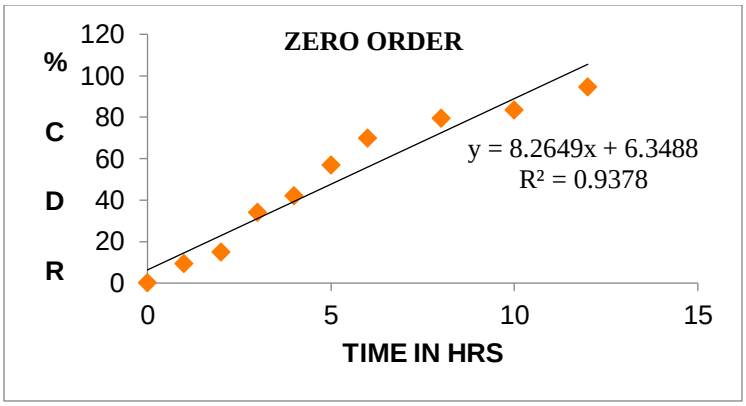

Fig: 7 Zero order release graph for F7 sustained release formulation

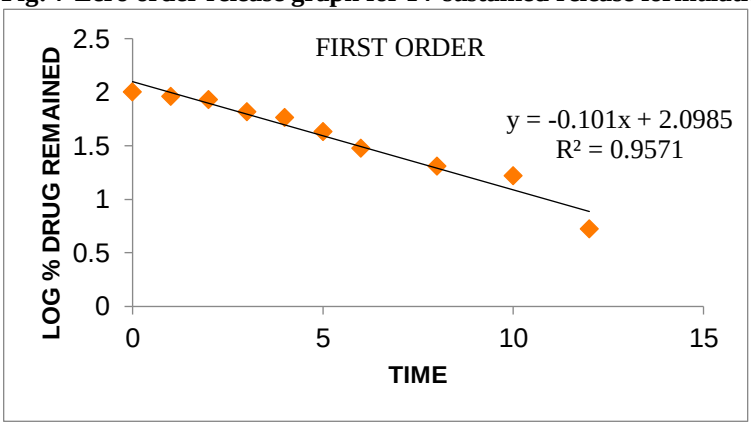

Fig: 8 First order release graph for F7 sustained release formulation

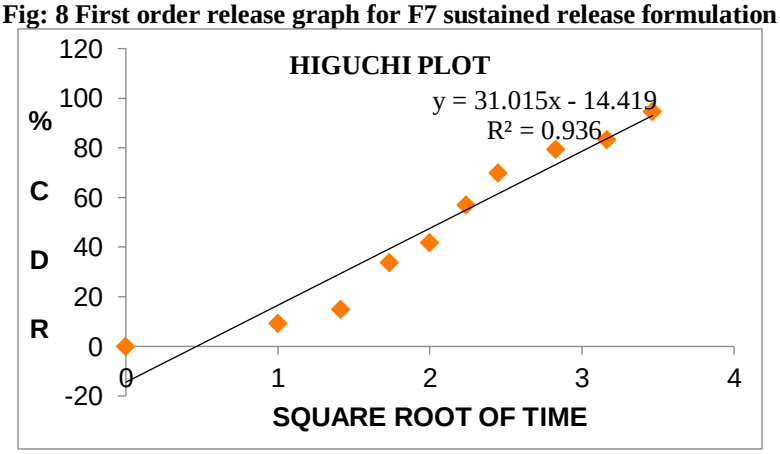

Fig: 9 Higuchi model graph for F7 sustained release formulation

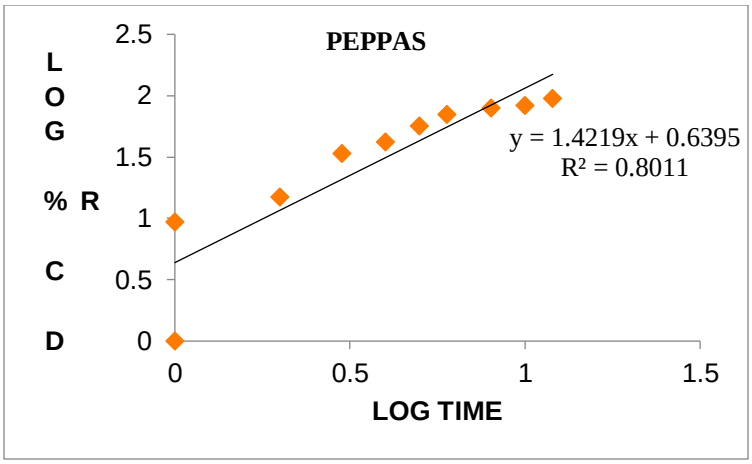

Fig: 10 Peppas model for F7 sustained release formulation

Table no 13: release kinetics for F7 formulation for sustained release tablets

PARAMETERS	ZERO	FIRST	HIGUCHI	Korsmeyer-PEPPAS
	% CDR Vs T	Log % Remain Vs T	%CDR Vs √T	Log C Vs Log T
Slope	12.59	-0.199	36.95	1.677
Intercept	4.344	2.201	-12.79	0.683
R 2	0.9378	0.9571	0.936	0.8011

Drug release kinetics

In-vitro drug release data of all the effervescent floating tablet formulations was subjected to goodness of fit test by linear regression analysis according to 0, 1st, Higuchi's and Korsmeyer-Peppas models to ascertain the mechanism of drug release. From the above data, it can be seen the formulation, F7 have displayed first order release kinetics. And follows higuchi mechanism of release.

CONCLUSION:

The Floating Sustained released tablets using effervescent agent containing Cimetidine SR tablets were successfully prepared and evaluated further the in-vivo studies and pharmacokinetic studies can b \e done and commercialized.

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