



PREPARATION AND EVALUATION OF GASTRORETENTIVE FLOATING MATRIX TABLETS OF CLARITHROMYCIN

Zeenaath Unnisa¹ and Pamu Sandhya^{*2}

^{1,*2} Department of Pharmaceutics, Shadan Women's College of Pharmacy, Khairatabad, Hyderabad, 500004

*Corresponding Author Email: sandhyapasikanti@gmail.com

ABSTRACT

In the present research work gastro retentive floating matrix formulation of Clarithromycin by using various hydrophilic polymers were developed. Initially analytical method development was done for the drug molecule. Absorption maxima was determined based on that calibration curve was developed by using different concentrations. Gas generating agent sodium bicarbonate concentration was optimized. Then the formulation was developed by using different concentrations of polymers of various grades of HPMC as polymeric substances. The formulation blend was subjected to various pre-formulation studies, flow properties and all the formulations were found to be good indicating that the powder blend has good flow properties. Among all the formulations the formulations HPMC K15M as polymer were retarded the drug release up to desired time period i.e., 12 hours in the concentration of 180 mg. whereas in low concentrations the polymer was unable to produce the desired action. (F3 Formulation, 98.56% Drug release). The formulations prepared with HPMC K100M were also retarded the drug release for more than 12 hours. Hence, they were not considered. The optimized formulation dissolution data was subjected to release kinetics, from the release kinetics data it was evident that the formulation followed zero order mechanism of drug release.

Key words:

Clarithromycin, HPMC polymers, Floating tablets.

INTRODUCTION

Oral controlled release drug delivery has recently been of increasing interest in pharmaceutical field to achieve improved therapeutic advantages, such as ease of dosing administration, patient compliance and flexibility in formulation. Drugs that are easily absorbed from gastrointestinal tract (GIT) and have short half-lives are eliminated quickly from the systemic circulation. Frequent dosing of these drugs is required to achieve suitable therapeutic activity. To avoid this limitation, the development of oral sustained-controlled release formulations is an attempt to release the drug slowly into the gastrointestinal tract (GIT) and maintain an effective drug concentration in the systemic circulation for a long time. After oral administration, such a drug delivery would be retained in the stomach and release the drug in a controlled manner, so that the drug could be supplied continuously to its absorption sites in the gastrointestinal tract (GIT).

Basic Gastrointestinal Tract Physiology Stomach

The stomach is J-shaped organ located in the upper left-hand portion of the abdomen, just below the diaphragm. Due to its small surface area very, little absorption takes place from the stomach. It provides barrier to the delivery of drugs to small intestine.

Stomach is divided into 3 regions: fundus, body, and antrum (or pylorus). The proximal part made of fundus and body acts as a reservoir for undigested material, whereas the distal region (pylorus) is the main site for mixing motions and act as a pump for gastric emptying by propelling actions.^{3,4}

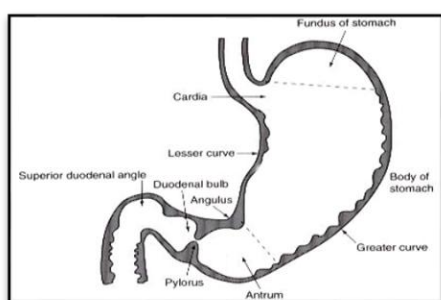


Figure 1: Anatomy of Stomach

Gastric emptying

The total transit time of foods and dosage forms in human from stomach to ileocecal junction is approximately 3 to 6 hours and 6 to 10 hours in fasted and fed states respectively. Process of gastric emptying occurs during fasting as well as fed states. The pattern of motility is however distinct in the 2 states.

During the fasting state an interdigestive series of electrical events take place, which cycle both through stomach and intestine every 2 to 3 hours. This is called the interdigestive myoelectric cycle or migrating myoelectric cycle (MMC), which is further divided into following 4 phases as described by Wilson and Washington.⁶ which is shown in the figure 1.

- Phase I (basal phase) lasts from 40 to 60 minutes with rare contractions.
- Phase II (pre burst phase) lasts for 40 to 60 minutes with intermittent action potential and contractions. As the phase progresses the intensity and frequency also increase gradually.
- Phase III (burst phase) lasts for 4 to 6 minutes. It includes intense and regular contractions for short period. It is due to this wave that all the undigested material is swept out of the stomach down to the small intestine. It is also known as the housekeeper wave. As phase III of one cycle reaches the end of the small intestine, phase III of the next cycle starts in the duodenum.
- Phase IV lasts for 0 to 5 minutes and occurs between phases III and I of two consecutive cycles.⁷

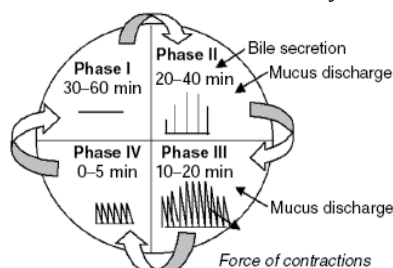


Figure 2: Illustration of four phases in Migrating Myoelectric Cycle (MMC)

Types of Floating Drug Delivery Systems (FDDS)

Based on the mechanism of buoyancy, two distinctly different technologies have been utilized in development of FDDS, which are

- I. Effervescent System, and
- II. Non-Effervescent System

Advantages Of FDDS

- Floating dosage forms such as tablets or capsules will remain in the solution for prolonged time even at the alkaline pH of the intestine.
- FDDS are advantageous for drugs meant for local action in the stomach e.g.: Antacids
- FDDS dosage forms are advantageous in case of vigorous intestinal movement and in diarrhoea to keep the drug in floating condition in stomach to get a relatively better response.

Disadvantages OF FDDS

- Floating systems are not feasible for those drugs that have solubility or stability problems in gastric fluids.
- Drugs such as Nifedipine, which is well absorbed along the entire GI tract and which undergo significant first-pass metabolism, may not be suitable candidates for FDDS since the slow gastric emptying may lead to reduced systemic bioavailability. Also there are limitations to the applicability of FDDS for drugs that are irritant to gastric mucosa.

Suitable Drug Candidates for Gastroretention

- In general, appropriate candidates for GRDF are molecules that have poor colonic absorption but are characterized by better absorption properties at the upper parts of the GIT:
- Narrow absorption window in Gastro Intestinal tract, e.g., Riboflavin and Levodopa.
- Primarily absorbed from stomach and upper part of GI tract, e.g., calcium supplements, Chlordiazepoxide and cinnarizine.
- Drugs that act locally in the stomach, e.g., antacids and misoprostol.
- Drugs that degrade in the colon, e.g., ranitidine HCl and metronidazole.
- Drugs that disturb normal colonic bacteria, e.g., amoxicillin trihydrate.

LITERATURE REVIEW

Patel *et al.*, (2012) formulated and evaluated bi-layer tablet containing Metoprolol succinate as extended-release form and Ramipril as immediate release form. Acting by different mechanisms, Metoprolol succinate and Ramipril in combination would produce an additive

antihypertensive effect. Although an enhanced antihypertensive effect can be obtained by using a larger dose of a single drug, this may increase the incidence of side effects.

Prashanth et al., (2012) developed a novel oral pulsatile drug delivery system based on enteric coated time release press coated (ETP) tablet. Tablet containing mainly three layers; a theophylline core tablet by direct compression, outer shell by different weight ratio of hydrophobic polymer of ethyl cellulose (EC) and hydrophilic excipients such as low-substituted hydroxy propyl cellulose (L-HPC) or hydroxypropyl methylcellulose (HPMC) and top layer of enteric coated polymer like Eudragit L-100.

Jain Sheetal et al (2012) developed and evaluated floating pulsatile tablets of Lornoxicam which releases no drug during floating in stomach followed by rapid and burst release in distal small intestine to achieve a chronotherapeutic release of Lornoxicam for relieve the complications associated with rheumatoid arthritis. The system developed consists of drug containing core tablets, which were coated with pH- dependent polymer Eudragit S100 and outer effervescent layer of polymers and sodium bicarbonate showed floating in acidic medium with no drug release followed by rapid release of drug in basic medium.

Sameer Singh et al (2011) developed the floating tablets of captopril by using different grade of HPMC. Lactose and citric acid were used in different concentration as a channeling and chelating agent to obtain best optimized formulation and designed to prolong the gastric residence time (GRT). Results revealed that the effect of channeling and chelating agent at different concentration had significant effect on the release of the drug from hydrophilic matrix tablet.

Gottimukkala Jayapal Reddy et al (2011) developed and optimized a controlled- release floating tablet of highly water-soluble drug Nizatidine in an effort to increase its gastric retention time in the stomach. The tablets were prepared by direct compression method and Hydroxy propyl methyl cellulose (HPMC) of different viscosity grades, Carboxymethyl cellulose Sodium (NaCMC) were incorporated as retarding polymers. Sodium bicarbonate was incorporated as effervescent agent. The formulation F6 with HPMC K 4M exhibited floating lag time of less than 1min and floating time of more than 12 hrs.

Jadhavmayur.N et al (2010) investigated gastro retentive drug delivery system of Famotidine. Floating tablets of Famotidine were prepared by employing polymers like Guar gum and Xanthan gum by effervescent technique. The tablets were prepared by direct compression method.

The polymers were used individually as well as in combination to formulate floating tablets.

D. M. Sakarkar et al (2009) formulated gastro retentive floating tablets of carbamazepine and to optimize drug release profile. Hydroxy propyl methyl cellulose (HPMC) of different viscosity grades and ethyl cellulose were used in formulating the gastric floating drug delivery system (GFDDS). Main effect and interaction terms of the formulation variables could be evaluated in terms of drug release. It was found that both HPMC viscosity, the presence of ethyl cellulose and their interaction had significant impact on the release and floating properties of the delivery system.

METHODOLOGY

Analytical method development:

Determination of absorption maxima:

A solution containing the concentration 10 µg/ ml drug was prepared in 0.1N HCl UV spectrums was taken using Double beam UV/VIS spectrophotometer. The solution was scanned in the range of 200-400.

Preparation calibration curve:

100mg of clarithromycin pure drug was dissolved in 100ml of 0.1NHCl (stock solution) 10ml of solution was taken and make up with 100ml of 0.1N HCl (100µg/ml). From this 10ml was taken and make up with 100 ml of 0.1N HCl (10µg/ml). The above solution was subsequently diluted with 0.1N HCl to obtain series of dilutions Containing 2,4,6,8 and 10 µg/ml of clarithromycin per ml of solution. The absorbance of the above dilutions was measured at 274 nm by using UV-Spectrophotometer taking 0.1N HCl as blank.

Drug – Excipient compatibility studies

Fourier Transform Infrared (FTIR) spectroscopy

The physical properties of the physical mixture were compared with those of plain drug. Samples was mixed thoroughly with 100mg potassium bromide IR powder and compacted under vacuum at a pressure of about 12 psi for 3 minutes. The resultant disc was mounted in a suitable holder in Perkin Elmer IR spectrophotometer and the IR spectrum was recorded from 3500 cm to 500 cm. The resultant spectrum was compared for any spectrum changes.

Preformulation parameters

The quality of tablet, once formulated by rule, is generally dictated by the quality of physicochemical properties of blends. There are many formulations and process variables involved in mixing and all these can affect the characteristics of blends produced.

Angle of repose

The frictional force in a loose powder can be measured by the angle of repose. It is defined as, the maximum angle possible between the surface of the pile of the powder and

the horizontal plane. The angle of repose was calculated using the following formula:

$$\tan \theta = h / r$$

Tan θ = Angle of repose

h = Height of the cone; r = Radius of the cone base

Table 1: Angle of Repose values

Angle Of Repose	Nature of Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Bulk density

Density is defined as weight per unit volume. Bulk density, is defined as the mass of the powder divided by the bulk volume and is expressed as gm/cm³. The bulk density of a powder primarily depends on particle size distribution, particle shape and the tendency of particles to adhere together.

Tapped density

After carrying out the procedure as given in the measurement of bulk density the cylinder containing the

sample was tapped using a suitable mechanical tapped density tester that provides 100 drops per minute and this was repeated until difference between succeeding measurement is less than 2 % and then tapped volume, V measured, to the nearest graduated unit.

Measures of powder compressibility:

The Compressibility Index (Carr's Index) is a measure of the propensity of a powder to be compressed. It is determined from the bulk and tapped densities. In theory, the less compressible a material the more flowable it is.

Table 2: Carr's index values

Carr's index	Properties
5 – 15	Excellent
12 – 16	Good
18 – 21	Fair to Passable
2 – 35	Poor
33 – 38	Very Poor
>40	Very Very Poor

Hausner ratio is an indirect index of ease of powder flow. It is calculated by the following formula.

Hausner's Ratio = Tapped density / Bulk density

Table 3: Hausner ratio values

Hausner ratio range	Flow characteristic
< 1.25	Good flow
1.25- 1.5	Moderate flow
> 1.5	Poor flow

Formulation development of Tablets

All the formulations were prepared by direct compression. The compressions of different formulations are given in Table 3. The tablets were prepared as per the procedure given below and aim is to prolong the release of Clarithromycin. Total weight of the tablet was considered as 650mg.

Procedure:

- 1) Clarithromycin and all other ingredients were passed through sieve no $\neq$ 60.

- 2) All the ingredients were mixed thoroughly by triturating up to 15 min.
- 3) The powder mixture was lubricated with talc.
- 4) The tablets were prepared by using direct compression method.

Optimization of Sodium bicarbonate concentration

Sodium bicarbonate was employed as effervescent gas generating agent. It helps the formulation to float. Various concentrations of sodium bicarbonate were employed; floating lag time and floating duration were observed.

Based on the concentration of sodium bicarbonate was finalized and preceded for further formulations.

Table 4: Optimization sodium bicarbonate concentration

S. No	Excipient Name	EF1	EF2	EF3
1	Clarithromycin	250	250	250
2	HPMC K 100M	100	100	100
4	NaHCO ₃	75	100	125
5	Mg. Stearate	6.5	6.5	6.5
6	Talc	6.5	6.5	6.5
7	MCC pH 102	212	187	162

All the quantities were in mg.

Based on the floating lag time and floating duration the concentration of sodium bicarbonate was optimised.

Table 5: Formulation of floating tablets

Formulation No.	Clarithromycin	HPMC K15M	HPMC K100M	HPMC K4 M	Carbopol 934 p	NaHCO ₃	Mag. Stearate	Talc	MCC pH 102
F1	250	60	--	--	50	100	6.5	6.5	177
F2	250	120	--	--	50	100	6.5	6.5	117
F3	250	180	--	--	50	100	6.5	6.5	57
F4	250	--	60	--	50	100	6.5	6.5	177
F5	250	--	120	--	50	100	6.5	6.5	117
F6	250	--	180	--	50	100	6.5	6.5	57
F7	250	--	--	60	50	100	6.5	6.5	177
F8	250	--	--	120	50	100	6.5	6.5	117
F9	250	--	--	180	50	100	6.5	6.5	57

All the quantities were in mg

Evaluation of post compression parameters for prepared Tablets

The designed formulation compression coated tablets were studied for their physicochemical properties like weight variation, hardness, thickness, friability and drug content.

Weight variation test

To study the weight variation, twenty tablets were taken and their weight was determined individually and

collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of determining the drug content uniformity.

$$\% \text{ Deviation} = (\text{Individual weight} - \text{Average weight} / \text{Average weight}) \times 100$$

Table 6: Pharmacopoeial specifications for tablet weight variation

Average weight of tablet (mg) (I.P)	Average weight of tablet (mg) (U.S.P)	Maximum percentage difference allowed
Less than 80	Less than 130	10
80-250	130-324	7.5
More than	More than 324	5

Hardness: Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. For each formulation, the hardness of three tablets was determined using Monsanto hardness tester and the average is calculated and presented with deviation.

Thickness: Tablet thickness is an important characteristic in reproducing appearance. Tablet thickness is an important characteristic in reproducing appearance. Average thickness for core and coated tablets is calculated and presented with deviation.

Friability: It is measured of mechanical strength of tablets. Roche friabilator was used to determine the friability by following procedure. Prewedged tablets were placed in the friabilator. The tablets were rotated at 25 rpm

for 4 minutes (100 rotations). At the end of test, the tablets were re weighed, loss in the weight of tablet is the measure of friability and is expressed in percentage as:

$$\% \text{ Friability} = [(W1-W2) / W] \times 100$$

Where, W1 = Initial weight of three tablets

W2 = Weight of the three tablets after testing

Determination of drug content:

Ten tablets were finely powdered quantities of the powder equivalent to one tablet weight of Clarithromycin were accurately weighed, transferred to a 100 ml volumetric flask containing 50 ml water and were allowed to stand to ensure complete solubility of the drug. The solution was suitably diluted and the absorption was determined by UV-Visible spectrophotometer. The drug concentration was calculated from the calibration curve.

In vitro Buoyancy studies:

The in vitro buoyancy was determined by floating lag time, and total floating time. 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 duration of time the tablet constantly floats on the dissolution medium was noted as Total Floating Time respectively (TFT).

In vitro drug release studies

Dissolution parameters:

Apparatus	--	USP-II,
Paddle Method		
Dissolution Medium	--	0.1 N HCl
RPM	--	50
Sampling intervals (hours)	--	0.5,1,2,3,4,5,6,7,8,10,11,12.
Temperature	--	37°C ± 0.5°C

As the preparation was for floating drug release given through oral route of administration, different receptors fluids are used for evaluation the dissolution profile.

Procedure:

900ml of 0.1 HCl was placed in vessel and the USP apparatus-II (Paddle Method) was assembled. The medium was allowed to equilibrate to temp of 37° ± 0.5°C. Tablet was placed in the vessel and the vessel was covered the apparatus was operated for 12 hours and then the medium 0.1 N HCl was taken and process was continued from 0 to 12 hrs at 50 rpm.

Application of Release Rate Kinetics to Dissolution Data:

Various models were tested for explaining the kinetics of drug release. To analyse the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

Zero order release rate kinetics:

To study the zero-order release kinetics the release rate data are fitted to the following equation.

$$F = K_0 t$$

Where, 'F' is the drug release at time 't', and 'K₀' is the zero order release rate constant. The plot of % drug release versus time is linear.

First order release rate kinetics: The release rate data are fitted to the following equation

$$\text{Log}(100-F) = kt$$

A plot of log cumulative percent of drug remaining to be released vs. time is plotted then it gives first order release.

Higuchi release model: To study the Higuchi release kinetics, the release rate data were fitted to the following equation.

$$F = k t^{1/2}$$

Where, 'k' is the Higuchi constant.

In Higuchi model, a plot of % drug release versus square root of time is linear.

Korsmeyer and Peppas release model:

The mechanism of drug release was evaluated by plotting the log percentage of drug released versus log time according to Korsmeyer-Peppas equation. The exponent 'n' indicates the mechanism of drug release calculated through the slope of the straight line.

$$M_t / M_\infty = K t^n$$

Where, M_t / M_∞ is fraction of drug released at time 't', k represents a constant, and 'n' is the diffusional exponent, which characterizes the type of release mechanism during the dissolution process. For non-Fickian release, the value of n falls between 0.5 and 1.0; while in case of Fickian diffusion, n = 0.5; for zero-order release (case I transport), n=1; and for supercase II transport, n > 1. In this model, a plot of log (M_t / M_∞) versus log (time) is linear.

Hixson-Crowell release model:

$$(100-Q_t)^{1/3} = 100^{1/3} - K_{HC}.t$$

Where, k is the Hixson-Crowell rate constant.

Hixson-Crowell model describes the release of drugs from an insoluble matrix through mainly erosion. (Where there is a change in surface area and diameter of particles or tablets).

RESULTS AND DISCUSSION

The present study was aimed to developing gastro retentive floating tablets of Clarithromycin using various HPMC polymers. All the formulations were evaluated for physicochemical properties and invitro drug release studies.

Analytical Method

Graphs of Clarithromycin was taken in Simulated Gastric fluid (pH 1.2) at 274nm

Table 7: Observations for graph of Clarithromycin in 0.1N HCl (274 nm)

Conc.[µg/l]	Abs
2	0.235
4	0.356
6	0.468
8	0.565
10	0.685

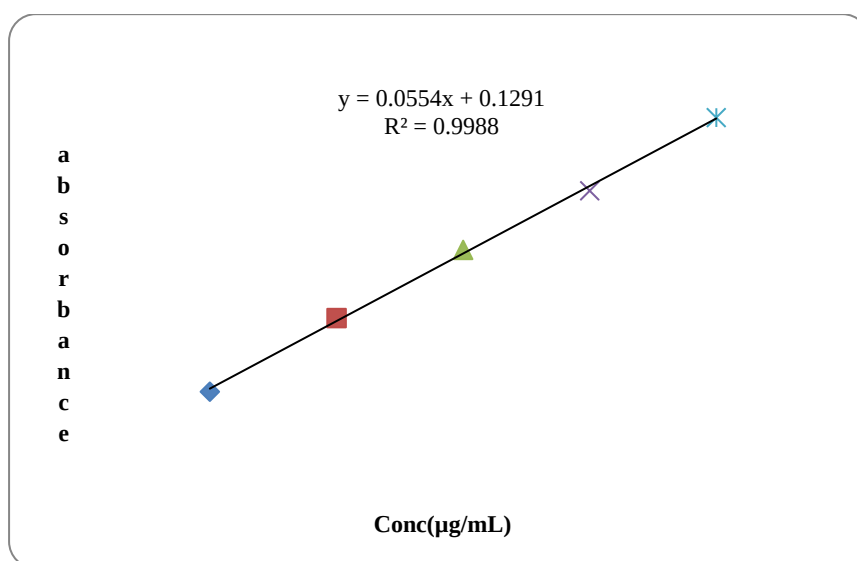


Figure 3: Standard graph of Clarithromycin in 0.1N HCl

Drug – Excipient compatibility studies

Fourier Transform-Infrared Spectroscopy:

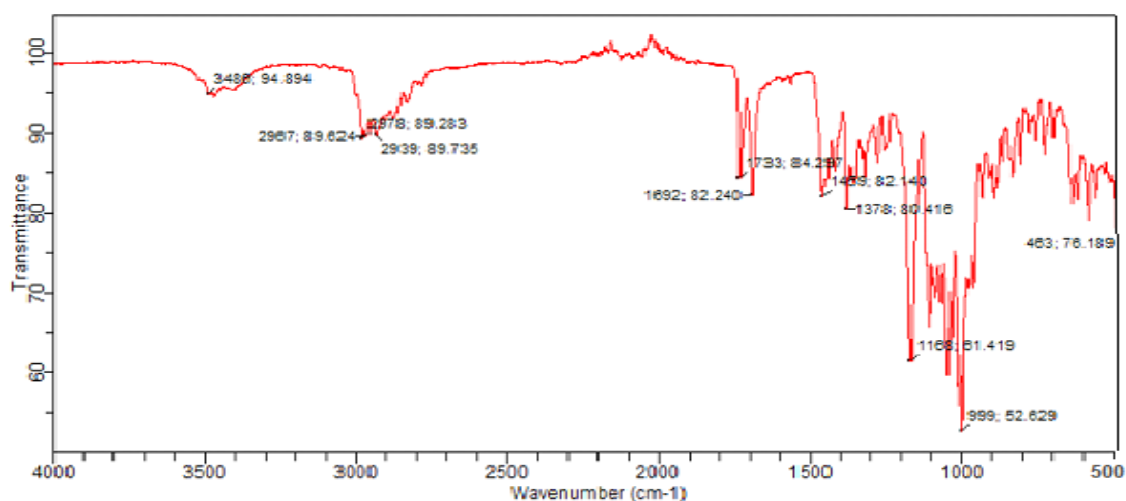


Figure 4: FT-IR Spectrum of Clarithromycin pure drug

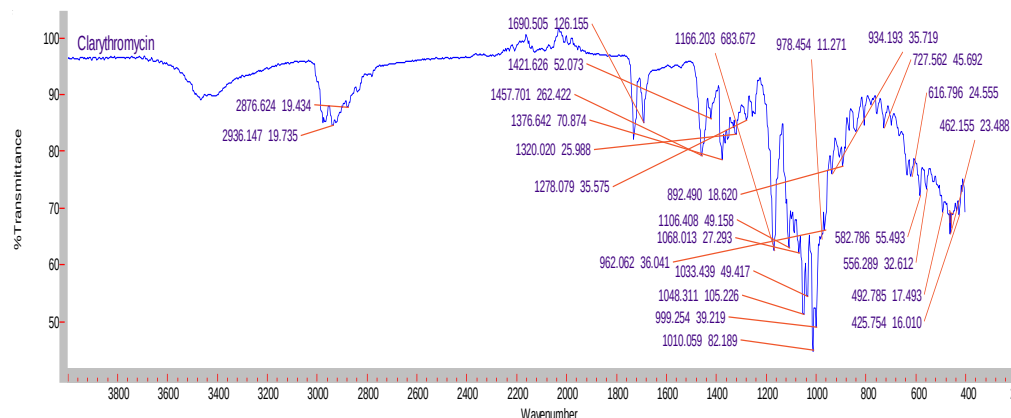


Figure 5: FT-IR Spectrum of Optimized Formulation

Pre-formulation parameters of blend

Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.41 to 0.50(gm/cm³) showing that the powder has good flow properties. The tapped density of all

the formulations was found to be in the range of 0.50 to 0.58 showing the powder has good flow properties. The compressibility index of all the formulations was found to be ranging from 14 to 18 which show that the powder has good flow properties. All the formulations have shown the Hausner ratio ranging between 0 to 1.21 indicating the powder has good flow properties.

Table 8: Pre-formulation parameters of blend

Formulation Code	Angle of Repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
F1	27.91	0.45	0.55	18.18	1.22
F2	28.23	0.47	0.55	14.54	1.17
F3	29.34	0.50	0.58	13.79	1.16
F4	26.71	0.46	0.55	16.36	1.19
F5	29.34	0.50	0.58	13.79	1.16
F6	28.23	0.47	0.55	14.54	1.17
F7	29.34	0.50	0.58	13.79	1.16
F8	26.78	0.41	0.50	18	1.21
F9	26.78	0.44	0.53	16.98	1.20

Optimization of sodium bicarbonate concentration

The formulation containing sodium bicarbonate in 100 mg concentration showed less floating lag time of 5 min and the tablet was in floating condition for more than 12 hours.

Quality Control Parameters For tablets

Tablet quality control tests such as weight variation, hardness, and friability, thickness, and drug release studies in different media were performed on the tablets.

Table 9: *Invitro* quality control parameters for tablets

Formulation codes	Weight variation(mg)	Hardness (kg/cm ²)	Friability (%loss)	Thickness (mm)	Drug content (%)	Floating lag time (min)
F1	655.5	4.5	0.51	4.8	98.76	5.0
F2	654.4	4.5	0.51	4.9	97.45	5.2
F3	650..6	4.4	0.52	4.9	99.34	5.5
F4	651.6	4.5	0.53	4.9	101.87	5.1
F5	650.4	4.4	0.54	4.7	100.14	5.0
F6	649.7	4.5	0.50	4.5	98.56	5.4
F7	651.3	4.5	0.53	4.4	98.42	5.5
F8	650.2	4.4	0.50	4.7	99.65	5.6
F9	654.3	4.4	0.51	4.6	100.12	5.7

All the parameters such as weight variation, friability, hardness, thickness and drug content were found to be within limits.

In-Vitro Drug Release Studies

Table 10: Dissolution Data of Clarithromycin Tablets Prepared with HPMC K15M

Time (h)	Cumulative Percent Drug Dissolved		
	F1	F2	F3
0.5	35.56	24.67	10.45
1	57.45	38.98	16.54
2	75.23	43.44	19.89
3	86.48	51.23	27.99
4	99.43	64.25	34.19
5		78.90	39.66
6		89.56	41.77
7		97.66	55.23
8			64.89
9			72.22
10			80.90
11			88.66
12			98.56

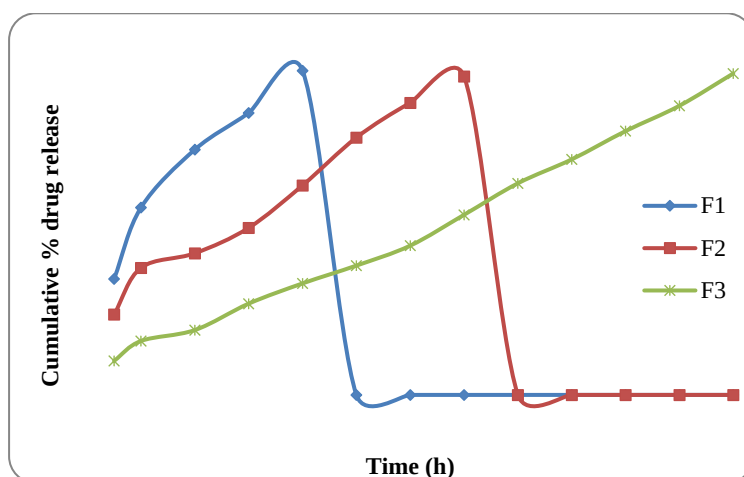


Figure 6: Dissolution profile of F1, F2, F3

Table 11: Dissolution Data of Clarithromycin Tablets Prepared with HPMC K 100M

Time (h)	Cumulative Percent Drug Dissolved		
	F4	F5	F6
0.5	22.77	16.90	9.89
1	30.21	27.55	16.76
2	39.54	39.20	22.53
3	51.20	48.13	27.43
4	69.66	54.76	33.66
5	77.33	69.87	37.11
6	90.10	78.23	44.67
7	95.77	85.40	53.87
8		92.33	61.30

9	97.66	69.10
10		78.20
11		84.22
12		90.33

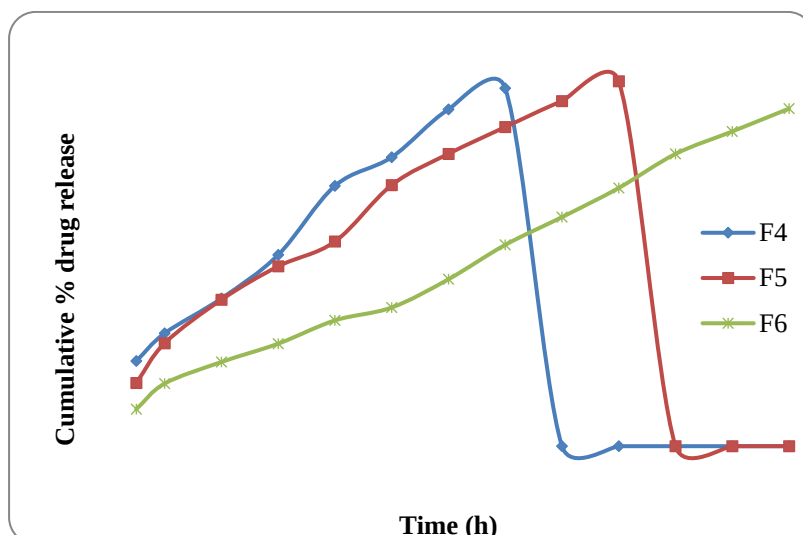


Figure 7: Dissolution profile of F4, F5, F6

Table 12: Dissolution Data of Clarithromycin Tablets Prepared with HPMC K 4 M

Time (H)	Cumulative Percent Drug Dissolved		
	F7	F8	F9
0.5	43.32	28.04	18.87
1	77.22	53.81	27.19
2	96.90	69.43	43.32
3		83.52	57.13
4		97.33	69.71
5			85.97
6			95.77
7			
8			
9			
10			
11			
12			

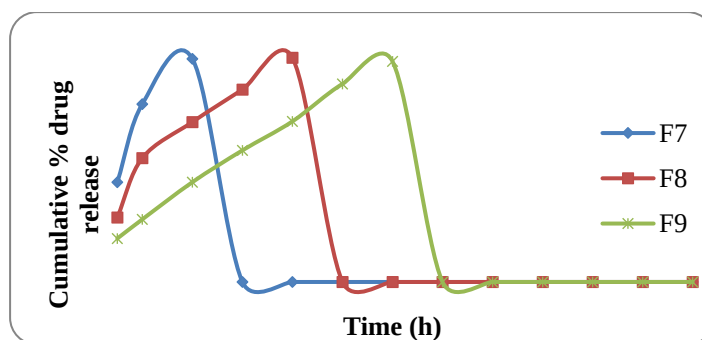


Figure 8: Dissolution profile of F7, F8, F9

From the dissolution data it was evident that the formulations prepared with HPMC K15M as polymer were retarded the drug release up to desired time period i.e., 12 hours in the concentration of 180 mg. whereas in low concentrations the polymer was unable to produce the desired action. (F3 Formulation 98.56% Drug release)

Whereas the formulations prepared with HPMC K100M were retarded the drug release in more than 12 hours in higher concentration. In lower concentrations the polymer was unable to retard the drug release.

The formulations prepared with HPMC K4M showed very less retardation capacity hence they were not considered.

Application of Release Rate Kinetics to Dissolution Data:

Various models were tested for explaining the kinetics of drug release. To analyse the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

Table 13: Release kinetics data for optimised formulation

Cumulative (%) Release Q	Time (T)	Root (T)	Log (%) Release	Log (T)	Log (%) Remain	Cumulative % Release / T	1/Cum % Release	Peppas Log Q/100	% Drug Remaining
0	0	0			2.000				100
10.45	0.5	0.707	1.019	0.301	1.952	20.900	0.0957	-0.981	89.55
16.54	1	1.000	1.219	0.000	1.921	16.540	0.0605	-0.781	83.46
19.89	2	1.414	1.299	0.301	1.904	9.945	0.0503	-0.701	80.11
27.99	3	1.732	1.447	0.477	1.857	9.330	0.0357	-0.553	72.01
34.19	4	2.000	1.534	0.602	1.818	8.548	0.0292	-0.466	65.81
39.66	5	2.236	1.598	0.699	1.781	7.932	0.0252	-0.402	60.34
41.77	6	2.449	1.621	0.778	1.765	6.962	0.0239	-0.379	58.23
55.23	7	2.646	1.742	0.845	1.651	7.890	0.0181	-0.258	44.77
64.89	8	2.828	1.812	0.903	1.545	8.111	0.0154	-0.188	35.11
72.22	9	3.000	1.859	0.954	1.444	8.024	0.0138	-0.141	27.78
80.9	10	3.162	1.908	1.000	1.281	8.090	0.0124	-0.092	19.1
88.66	11	3.317	1.948	1.041	1.055	8.060	0.0113	-0.052	11.34
98.56	12	3.464	1.994	1.079	0.158	8.213	0.0101	-0.006	1.44

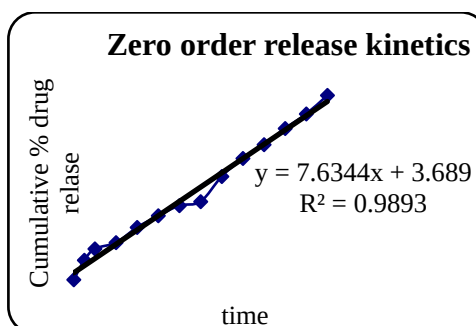


Figure 9: Zero order release kinetics graph

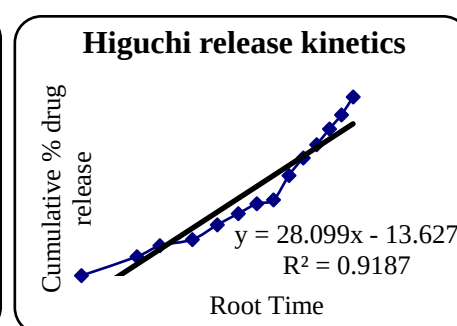


Figure 10: Higuchi release kinetics graph

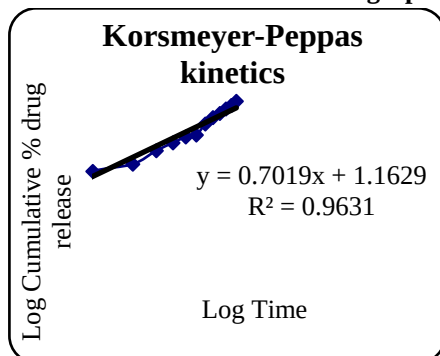


Figure 11: Korsmeyer-Peppas kinetics

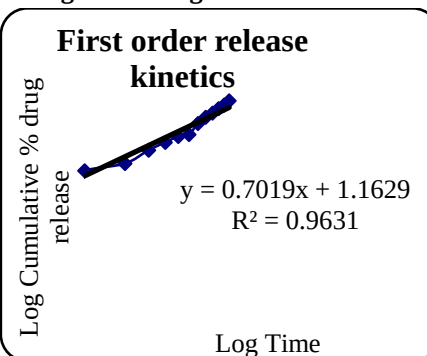


Figure 12: First order release kinetics

From the above graphs it was evident that the formulation F3 was followed Zero order release mechanism.

CONCLUSION

In the present research work gastro retentive floating matrix formulation of Clarithromycin by using various hydrophilic polymers were developed. Initially analytical method development was done for the drug molecule. Absorption maxima was determined based on that calibration curve was developed by using different concentrations. Gas generating agent sodium bicarbonate concentration was optimized. Then the formulation was developed by using different concentrations of polymers of various grades of HPMC as polymeric substances. The formulation blend was subjected to various pre-formulation studies, flow properties and all the formulations were found to be good indicating that the powder blend has good flow properties. Among all the formulations the formulations HPMCI K15M as polymer were retarded the drug release up to desired time period i.e., 12 hours in the concentration of 180 mg. whereas in low concentrations the polymer was unable to produce the desired action. (F3 Formulation, 98.56% Drug release). The formulations prepared with HPMC K100M were also retarded the drug release for more than 12 hours. Hence, they were not considered. The optimized formulation dissolution data was subjected to release kinetics, from the release kinetics data it was evident that the formulation followed zero order mechanism of drug release.

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***Corresponding author Email address:**

sandhyapasikanti@gmail.com