



## FORMULATION AND EVALUATION OF CLARITHROMYCIN GASTRORETENTIVE DOSAGE FORM

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### ABSTRACT

The present study investigates the formulation of floating sustained release tablets of Clarithromycin, by using a combination of hydrophilic polymers (different grades of hydroxypropyl methylcellulose), Kollidon SR and an effervescent substance (sodium bicarbonate). The formulations were evaluated to study the effect of sodium bicarbonate concentration on the floating lag time, total duration of floating, in vitro dissolution release profile and the effect of different fillers and ethyl cellulose concentration on the release profile of drug. It was found that among all the formulations, formulation F4 (HPMC K15M, Avicel 102 pH and sodium bicarbonate) was found to be the optimum formulation as it had good swelling property, floating time and drug release. The drug release of optimized formulation was found to follow Zero order, Higuchi and Korsmeyer-Peppas kinetic models.

**Keywords:** Clarithromycin, Floating, Gastroretentive, Hydroxy propyl methyl cellulose.

### INTRODUCTION

Over the years there has been available a variety of drug modification and dosage forms, with which we have attempted to control the time course and specificity of drugs in the body. To maximize drug utilization, it is necessary to deliver the drug to its target tissue in the correct amount at the proper time to elicit the desired response. Moreover, drug delivery must be continued at a rate such that the condition in question is cured or controlled in a minimum time with the fewest side effects.<sup>1</sup>

Formulation of Gastroretentive Dosage Forms containing suitable drug candidates which would remain in the stomach and/or upper part of gastrointestinal tract for a prolonged period of time there by maximizing the drug release at desired site within the time before Gastroretentive Dosage Forms left the stomach and/or upper part of the gastrointestinal tract, has provoked a great deal of increased interest in the formulation of such drugs as floating drug delivery system. *H.pylori* which is believed to cause gastric or peptic ulcer can be eradicated by the use of antibiotics like Clarithromycin which has been selected to be formulated as floating drug delivery system.

Clarithromycin is stable in gastric acidic medium and has a narrow absorption window in gastrointestinal tract, rapid gastrointestinal absorption, highly soluble at acidic pH, no effect of food on absorption and it has higher eradication rate in vivo to *H. pylori*. Hence increasing the gastric retention time of the drug in the stomach may improve its bioavailability and therapeutic efficacy.

### MATERIALS AND METHODS

#### Materials

Clarithromycin (as a gift sample from Alembic limited, Baddi H.P), Hydroxy propyl methyl cellulose (as a gift sample from Colorcon Asia Pvt.Ltd., Goa), Kollidon SR (BASF India Ltd, Mumbai),

Microcrystalline cellulose (Avicel PH102 was obtained as a gift sample from Signet chemical company, Mumbai), Ethyl cellulose and Magnesium stearate (S D Fine Chemicals Ltd., Mumbai), Lactose DC and Talc (Loba Chemicals. Pvt. Ltd., Mumbai), Sodium bicarbonate (Ranbaxy Fine chemicals Ltd. New Delhi).

Tablet compression machine (16 Station) (Model No: CMD<sub>3</sub>-16/CMDB<sub>3</sub>-16), Cadmach Machinery Company Pvt. Ltd., Ahmedabad.

### METHODS

#### Pre formulation studies

Physical properties like Bulk density, Tapped density, Hausner's ratio<sup>2</sup> and Angle of repose<sup>3</sup> of the drug and excipients were determined and shown in table 1.

#### Formulation of Clarithromycin floating matrix tablets

Floating hydrophilic matrix tablets were prepared by direct compression technique<sup>4</sup> using different grades of polymer of varying concentrations as well as different concentrations of sodium bicarbonate and varying ratios of microcrystalline cellulose. (The compositions of all the formulations are shown in Table 2.)

All the ingredients except magnesium stearate and talc were blended in glass mortar and pestle uniformly. After sufficient mixing of the drug as well as other components, magnesium stearate and talc were added and further mixed for additional 2-3 min. The physical properties of the mixtures were evaluated and shown in Table 3. The tablets were compressed using 19.9×9 punch on a 16 station rotary tablet punching machine. The weights of the tablets were kept constant for all formulations, which were 804 mg for formulation F1 to formulation F9 and 840 mg for F10 to F12.

Drug-polymer interactions were determined by IR spectra and shown in figures 1and 2.

Table 1: Physical properties of drug and excipients

Parameter	Bulk density (g/cm <sup>3</sup> )	Tapped density (g/cm <sup>3</sup> )	Compressibility index	Hausner's ratio	Angle of repose $\theta$
Drug (Clarithromycin)	0.532	0.641	17.00	1.20	29°40'
HPMC K 15M	0.338	0.500	32.40	1.48	31°06'
HPMC K100M	0.342	0.510	32.94	1.49	30°52'
HPMC K100LV	0.333	0.489	31.90	1.47	32°72'
Kollidon SR	0.439	0.510	13.92	1.16	25°53'
Ethyl cellulose	0.294	0.373	21.18	1.27	23°47'
Avicel PH 102	0.352	0.439	19.82	1.25	29°03'
Lactose DC	0.555	0.684	18.86	1.23	27°11'
Sodium bicarbonate	0.833	1.316	36.70	1.58	29°83'

Table 2: Composition of Floating tablets of Clarithromycin

Ingredients (mg)	Formulation code											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Clarithromycin	402	402	402	402	402	402	402	402	402	402	402	402
HPMC K 15M	134	-	134	134	134	-	134	90	-	-	-	-
HPMC K100M	-	134	-	-	-	134	-	-	-	-	-	-
HPMC K100LV	-	-	-	-	-	-	-	44	134	-	-	-
Kollidon SR	-	-	-	-	-	-	-	-	-	268	268	268
Sodium bicarbonate	-	-	50	100	200	100	100	100	100	50	50	50
Avicel 102 pH	250	250	200	150	50	150	-	150	150	107	53.4	-
Ethyl cellulose	-	-	-	-	-	-	-	-	-	-	53.6	107
Lactose DC	-	-	-	-	-	-	150	-	-	-	-	-
Magnesium Stearate	10	10	10	10	10	10	10	10	10	10	10	10
Talc	5	5	5	5	5	5	5	5	5	-	-	-
Silicon dioxide	3	3	3	3	3	3	3	3	3	3	3	3
Total (mg)	804	804	804	804	804	804	804	804	804	804	804	804

Table 3: Physical properties of Formulation F1 to Formulation F12

Formulation code	Bulk density (g/cm <sup>3</sup> )	Tapped density (g/cm <sup>3</sup> )	Compressibility Index	Hausner ratio	Angle of repose $\theta$
F1	0.446	0.526	20.64	1.26	24° 56'
F2	0.450	0.568	20.64	1.26	24° 19'
F3	0.463	0.595	22.18	1.29	25° 08'
F4	0.510	0.625	18.40	1.23	26° 05'
F5	0.543	0.735	26.12	1.35	22° 73'
F6	0.515	0.632	18.52	1.23	25° 94'
F7	0.538	0.694	22.48	1.29	26° 68'
F8	0.490	0.610	19.67	1.24	25° 44'
F9	0.485	0.617	21.39	1.27	27° 18'
F10	0.485	0.575	15.65	1.19	30° 42'
F11	0.481	0.568	15.32	1.18	30° 77'
F12	0.476	0.568	16.20	1.19	30° 75'

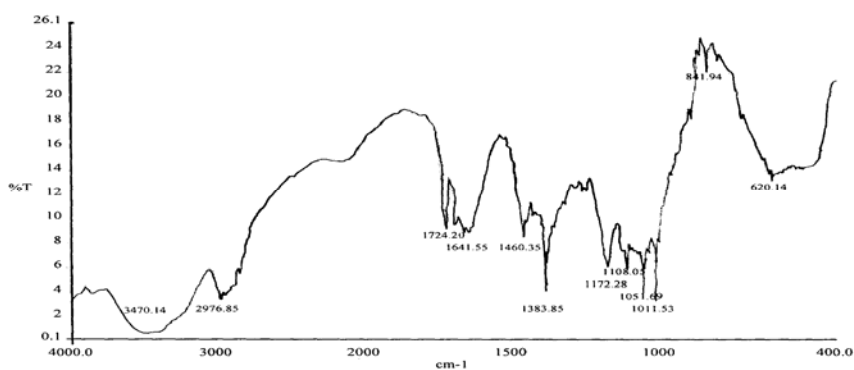


Fig. 1: IR spectrum of tablet powder of formulation F3



Fig. 2: IR spectrum of tablet powder of formulation F11

### Evaluation of clarithromycin floating tablets

#### Physical evaluation of Clarithromycin floating matrix tablets

All the prepared floating hydrophilic tablets were evaluated for the physical properties like Hardness<sup>5</sup>, Friability<sup>5</sup> and Weight variation<sup>6</sup> and the results are shown in Table 4.

#### Evaluation of floating properties

##### Determination of floating lag time and total floating time<sup>7</sup>

The time taken for dosage form to emerge on to the surface of medium is called floating lag time (FLT) and duration of time by which the dosage form constantly emerges on surface of medium is called Total Floating Time (TFT).

One tablet from each formulation was placed in USP type II dissolution apparatus containing 900 ml of 0.1 N HCl (pH 1.2) using paddle at a rotational speed of 100 rpm. The temperature of medium and the duration of time by which the tablet constantly remains on the surface of the medium were noted. The floating lag time and total floating time of tablet of each formulation is shown in Table 4.

##### Effect of buoyancy on floating<sup>8</sup>

The result of the in vitro buoyancy study of formulation F4 is shown in Figure 3. The figure clearly indicates the floating lag time of the Clarithromycin tablets and the floating and swelling tendency of the formulation.

#### Effect of hardness on floating

The tablets of formulation F4 were compressed by using three different compression pressures to get hardness of 5 kg/cm<sup>2</sup>, 7 kg/cm<sup>2</sup>, 10 kg/cm<sup>2</sup> and 15 kg/cm<sup>2</sup>. The tablets were evaluated for determination of floating lag time.

The plot of floating lag time (sec) vs hardness (Kg) depicted as Figure 4.

#### Swelling study of Clarithromycin floating tablets<sup>9,10</sup>

For each formulation, one tablet was weighed and placed in a beaker containing 200 ml of distilled water. After each hour the tablet was removed from beaker and weighed again upto 8 h. The swelling study was not performed for formulations F1 and F2 as the tablets of these formulations did not float in floating property studies. The percentage weight gain by the tablet was calculated by the formula.

$$\text{Swelling index (S.I)} = \{(W_t - W_0) / W_0\} \times 100$$

Where, S.I. = Swelling index

$W_t$  = Weight of tablet at time  $t$

$W_0$  = Weight of tablet before immersion.

The swelling index of tablets was given in Table 4 and the plot of Swelling index Vs Time (h) depicted as Figures 5 and 6.

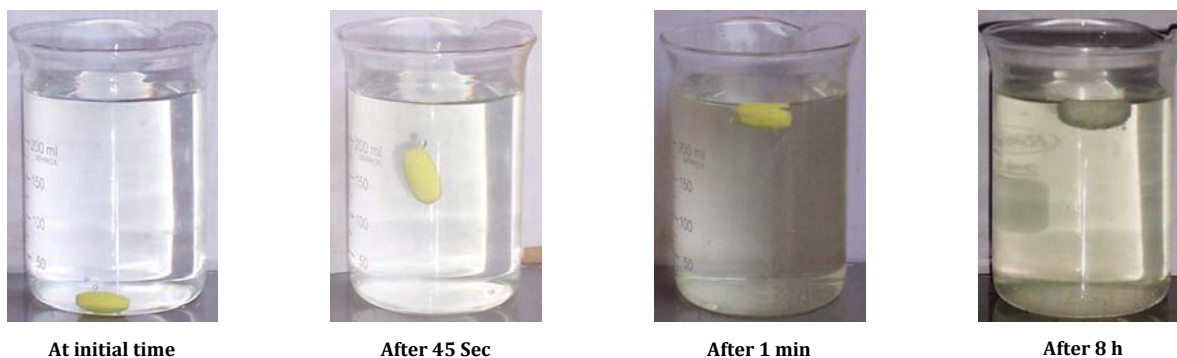


Fig. 3: in Vitro buoyancy study of formulation F4

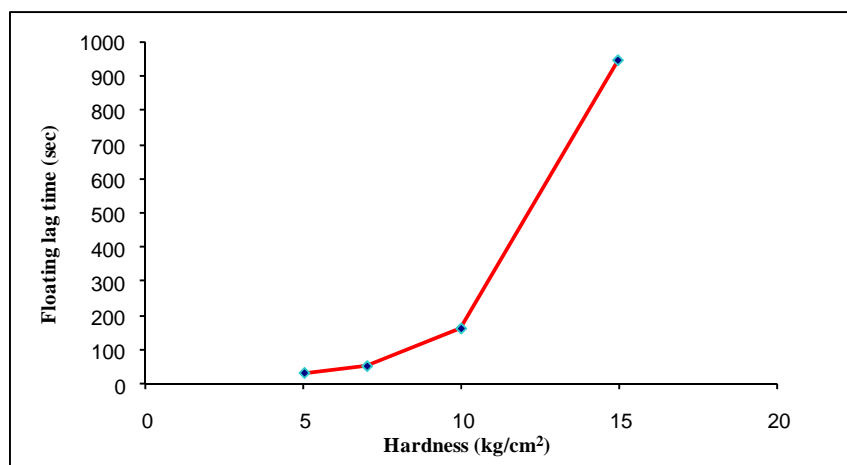


Fig. 4: Effect of hardness on floating lag time of tablet of formulation F4

Table 4: Physical properties of tablets of each formulation

Formulation code	Average weight of tablets (mg) $\pm$ S.D n=20	Hardness kg/cm <sup>2</sup> $\pm$ S.D (n=5)	Percentage friability	Floating lag time (sec)	Total floating time (h)	Swelling index at the end of 8 <sup>th</sup> h
F1	804 $\pm$ 1.86	6.0 $\pm$ 0.61	0.53	--	--	--
F2	805 $\pm$ 1.50	6.2 $\pm$ 0.27	0.59	--	--	--
F3	805 $\pm$ 1.07	6.6 $\pm$ 0.42	0.59	240	>12	240
F4	803 $\pm$ 1.37	6.4 $\pm$ 0.42	0.56	50	>12	238
F5	806 $\pm$ 1.12	6.3 $\pm$ 0.27	0.53	30	>12	231
F6	808 $\pm$ 1.23	6.5 $\pm$ 0.35	0.53	65	>12	267
F7	803 $\pm$ 1.74	6.6 $\pm$ 0.22	0.57	45	>12	226
F8	808 $\pm$ 1.23	6.3 $\pm$ 0.27	0.55	60	>12	202
F9	804 $\pm$ 1.49	6.6 $\pm$ 0.42	0.57	50	6.5	16
F10	840 $\pm$ 1.30	5.2 $\pm$ 0.27	0.21	70	>12	89
F11	841 $\pm$ 1.19	5.1 $\pm$ 0.22	0.25	105	>12	85
F12	840 $\pm$ 1.30	5.2 $\pm$ 0.27	0.27	125	>12	69

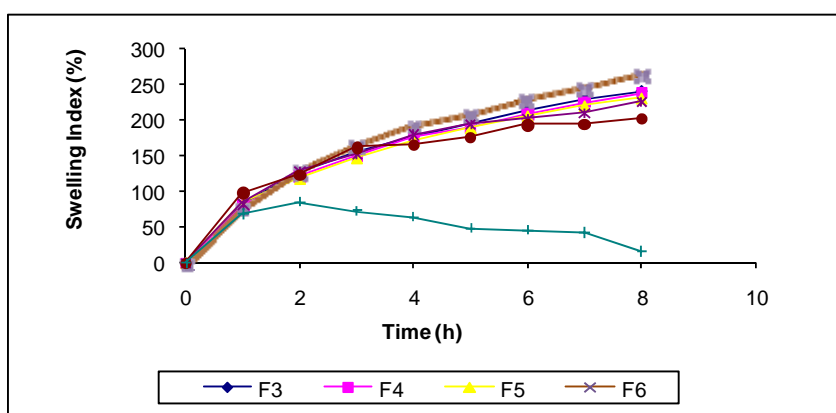


Fig. 5: Swelling studies of Clarithromycin floating tablets of formulation F3 to F9

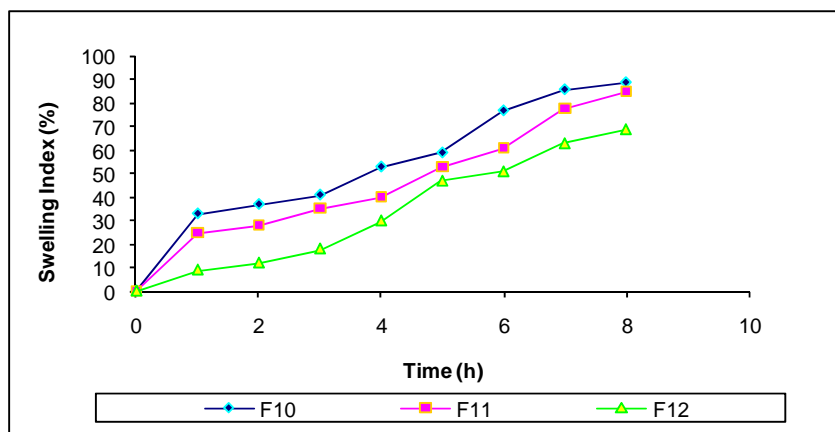


Fig. 6: Swelling studies of Clarithromycin floating tablets of formulation F10 to F12

#### Assay of clarithromycin floating matrix tablets

##### Mobile Phase

A mixture of 0.067M Potassium di-hydrogen phosphate solution containing acetonitrile and methanol in a ratio of 40:30:30 was prepared.

1 mg per ml of n-hexane sulphonic acid sodium salt was added, filtered and degassed.

#### Standard preparation

100 mg Clarithromycin RS was weighed accurately and transferred into a dry 100 ml volumetric flask, 50 ml of methanol was added and sonicated to dissolve. The resulting solution was diluted upto 100 ml with methanol.

#### Assay preparation

Accurately counted number of tablets were finely powdered and the powder equivalent to 2 g of Clarithromycin was accurately weighed

and transferred to a 500 ml standard volumetric flask. To this 250 ml of methanol was added and sonicated for 30 min. The resulting solution was diluted with methanol to 500 ml and the insoluble matter was allowed to settle. The resulting solution was diluted to get a concentration of about 1 mg/ml. A portion of this solution was passed through a filter having a porosity of 0.5  $\mu$ m.

#### Chromatographic system

The tablets were analyzed by HPLC with UV100 detector (210nm), isocratic pump, column L1 (Hypersil, 250 mm  $\times$  4.6 mm, 5  $\mu$ m) at a flow rate of 2 ml/min and the retention time of sample as 4-5 min.

#### PROCEDURE

A solution of 20  $\mu$ l of the standard preparation and assay preparation were injected into the chromatogram, chromatograph was recorded and the response of the major peak was measured. The amount of Clarithromycin was calculated by the formula.

$$\text{Percentage purity} = (R_u/R_s) \times (W_s/W_u) \times (W_a/W_d) \times S_p$$

Where,  $R_u$  and  $R_s$  are the peak responses obtained from the assay preparation and standard preparation respectively,  $W_s$  and  $W_u$  are the weights of standard and assay sample respectively,  $W_a$  and  $W_d$  are the average weights of Clarithromycin floating tablets and labelled amount of Clarithromycin in mg in each tablet and  $S_p$  is the percentage purity of the standard drug.

#### In vitro dissolution study

Dissolution of the tablet of each formulation was carried out using USP type II apparatus using paddle.<sup>11,12</sup>

Dissolution of the tablets was performed by using 900 ml of 0.1N HCl (pH 1.2) as the dissolution medium at a temperature of  $37 \pm 0.5^\circ\text{C}$ .

One tablet was placed in each dissolution vessel and the rotational speed of paddle was set at 100 rpm. Samples of 5 ml were withdrawn and replaced with the same volume of fresh dissolution medium at times 0.5, 1, 2, 4, 6 and 10 h respectively. The collected samples were analyzed for drug content by HPLC-UV (210 nm), in which the sample solution was filtered and 20  $\mu$ l of the filtrate was injected into the chromatogram. The chromatograph was recorded and the areas for the respective peaks were measured. The percentage of cumulative drug released was calculated using the formula,

$$\text{Percentage drug release} = (R_d/R_s) \times (W_s/100) \times (D_v/W_d) \times S_p$$

Where,  $R_d$  and  $R_s$  are the peak responses obtained from the dissolution sample preparation and standard preparation respectively,  $W_s$  and  $W_d$  are the weights of standard and labelled amounts of Clarithromycin in mg present in each tablet respectively,  $D_v$  is the volume of the dissolution medium taken and  $S_p$  is the percentage purity of the standard drug, Clarithromycin.

The in vitro release profiles of Clarithromycin from each formulation are shown in Figures 9 and 10.

#### Drug release kinetics

For finding out mechanism of drug release from floating hydrophilic matrix tablet, the dissolution data obtained from the above experiments were treated with the different release kinetic equations<sup>13,10</sup>, and shown in table 5.

Zero order release equation:  $Q = K_0 t$

Higuchi's square root of time equation:  $Q = K_H t^{1/2}$

Korsmeyer and Peppas equation:  $F = (M_t/M) = K_m t^n$

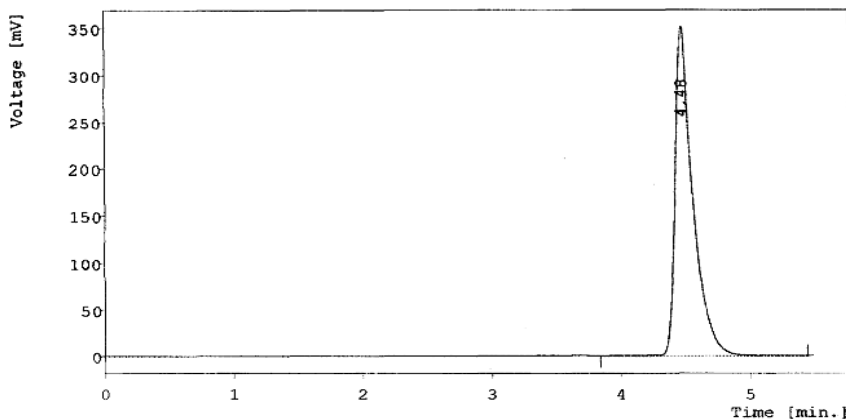


Fig. 7: Chromatogram of standard Clarithromycin

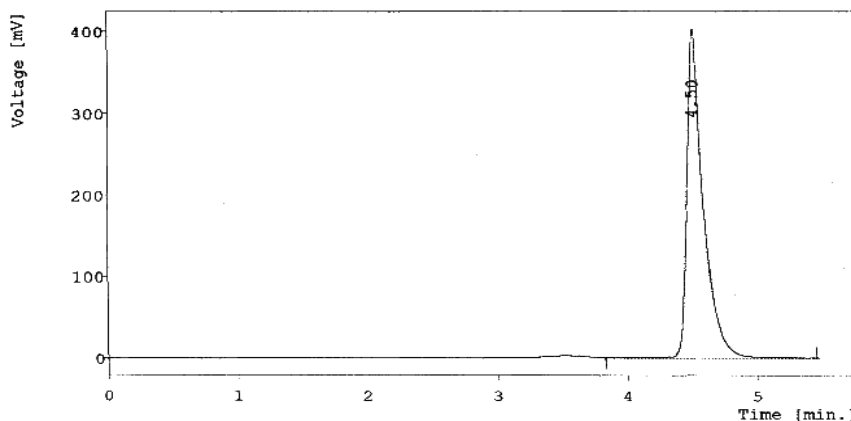


Fig. 8: Chromatogram of test Clarithromycin

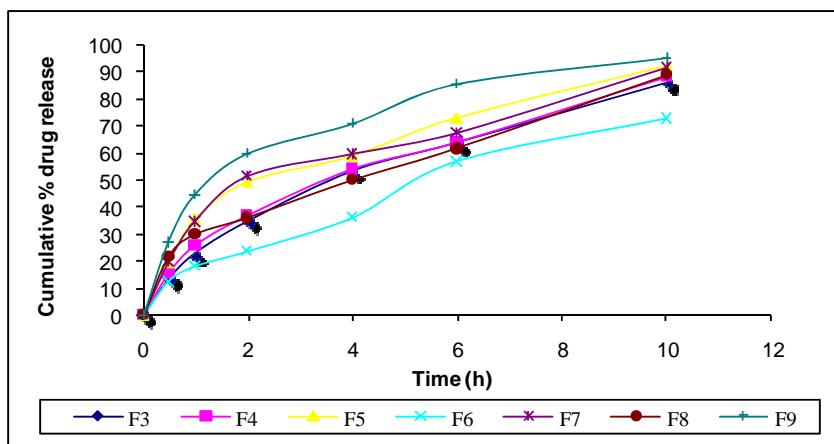


Fig. 9: Comparative dissolution profile of Clarithromycin floating tablets for formulation F3 to F9 in 0.1N HCL pH 1.2

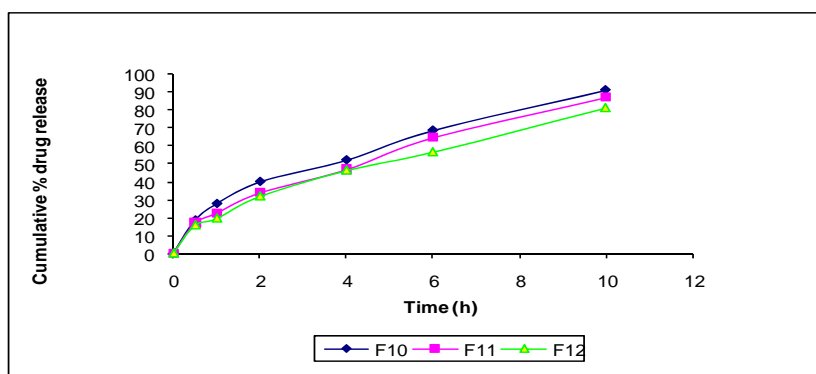


Fig. 10: Effect of Ethyl cellulose on drug release from Kollidon-SR matrix of formulation F10 to F12

Table 5: Kinetic treatment to dissolution data of tablets of formulation F3 to F12

Formulation	Zero order		Higuchi		Korsmeyer-Peppas		
	r <sup>2</sup>	K	r <sup>2</sup>	K	r <sup>2</sup>	K	n
F3	0.9817	7.5464	0.9994	29.947	0.9988	0.5753	0.619
F4	0.9846	7.4200	0.9986	29.374	0.9988	0.5330	0.5708
F5	0.9638	7.1018	0.9912	28.469	0.9928	0.4046	0.5096
F6	0.9889	6.4900	0.9880	25.275	0.9891	0.6252	0.6040
F7	0.9568	6.8338	0.9836	27.384	0.9842	0.3959	0.5078
F8	0.9973	6.9700	0.9894	26.955	0.9834	0.4710	0.4962
F9	0.9303	6.7537	0.9787	27.696	0.9943	0.3376	0.4165
F10	0.9886	7.5237	0.9973	29.588	0.9969	0.5126	0.5268
F11	0.9937	7.4753	0.9954	29.188	0.9978	0.5857	0.5567
F12	0.993	6.8974	0.9957	26.958	0.9979	0.6040	0.5595

**RESULTS AND DISCUSSION**

On the basis of preliminary identification test it was found that all three grades of HPMC complied the preliminary identification test as specified in USP XXIV. From the IR spectrum of tablet formulations F3 and F11 it was found that it had no significant difference of peak pattern in IR spectrum of pure drug, polymer and excipients as shown in Figures 1 and 2.

The physical parameters of drug as well as excipients showed that these were considerably good to be formulated as tablets using direct compression technique (Table 1).

From the physical parameters of tablets of each formulation it was found that the tablets of all batches had desirable physical characteristics (Table 3).

The results of studies on floating properties of tablets showed that all tablets except tablets of formulations F1 and F2 had good floating properties (Table 4), which might be due to absence of sodium

bicarbonate in the formulations. Incorporation of sodium bicarbonate helps to improve floating properties by reacting with gastric fluid when the dosage form comes in contact and produce carbon dioxide gas which when entrapped inside the hydrophilic matrices leads to increase in volume of dosage form resulting in lowering of density and that the dosage form starts to float.<sup>14</sup>

The effect of sodium bicarbonate concentration on floating lag time was studied from formulations F3, F4 and F5. The results showed that (Table 4) as the amount of sodium bicarbonate increases, the floating lag time decreases.<sup>8</sup>

From the results of dissolution profiles of F3, F4 and F5, an initial burst effect upto 1 h and higher drug release at the end of 10 h was found in F5 formulation than F3 and F4. It might be due to high amount of gas generating agent (sodium bicarbonate), which creates path for drug release by increasing pore size of matrix and increasing gas pressure inside the matrix. The rate of drug release

was found to increase with increasing weight ratio of sodium bicarbonate. This is the direct result of the porous nature of the sodium bicarbonate containing beads. The high amount of sodium bicarbonate may lead to matrix failure resulting into dose dumping.<sup>15</sup> Hence to avoid such complication, formulation F5 was discontinued from the study. Thus, it may be concluded that sodium bicarbonate (100 mg per tablet) was essential to achieve optimum in vitro buoyancy and in vitro drug release.

From the results of total floating time, it was found that higher viscosity grades of HPMC had good sustaining properties for tablets of all formulations except tablets of batch F9, which had good duration of floating as the tablets dissolved within 6.5 h which might be due to low viscosity of the polymer used in the formulation.<sup>16</sup>

From the results of swelling study it was found that swelling index increases as the time passes (Figure 6 and Table 4) because the polymer gradually absorbed water due to its hydrophilic nature and swelling capacity. The swelling index increases with time upto 2 h in case of tablets of formulation F9 that might be due to the low viscosity of polymer (100 cps) and after 2 h, the polymer chain relaxation was a dominating phenomenon as swelling reaches thresholds resulting in lowering of swelling index. Thus, the viscosity of polymer had major influence on swelling process, matrix integrity and floating capability. The higher swelling index was found for tablets of formulation F6, which contain HPMC K100 M having nominal viscosity of 1, 00,000 cps. Thus it was concluded that there might be a linear relationship between the swelling process and the viscosity of polymer and that the water absorption rate increases as the viscosity of the polymer increases and thus, at the end of the experiment, polymer of higher viscosity showed the maximum absorption.<sup>17</sup> The effect of filler was found to be of little effect on swelling behaviours, as the ratio of microcrystalline cellulose:lactose changed from 100:0 to 0:100. The swelling index after reaching certain threshold started to decline as the lactose content was increased. Lactose is water soluble filler and gets leached from the tablets when it comes in contact with water. From the study of swelling process, it was observed that the tablets of batch F3 to F7 had good swelling properties and ultimately matrix integrity.

The in vitro dissolution was carried out for all batches except formulation F1 and F2, as the tablets of these batches had no floating properties. From the dissolution data (Figure 9), it was shown that tablets of formulation F7 gave comparatively good dissolution profile as like formulation F4, despite the presence of same amount of high viscosity grade of HPMC (15,000 cps). The good dissolution profile might be due to high amount of water-soluble filler lactose, which creates the path for drug release, and weakens the matrixing ability of polymer. The high amount of lactose in matrix along with the drug, which is also highly soluble, may lead to matrix failure resulting in dose dumping (Figure 9). Also tablets of formulation F7 gave higher floating time as compared to F4 which might be due to the presence of higher amount of lactose than formulation F4, as it is well known to the ordinary art of excipients that the lactose has higher density than microcrystalline cellulose resulting in higher floating lag time.<sup>18</sup> Hence to avoid such complications formulation F7 was discontinued from the study.

To investigate the effect of small variation on viscosity in drug release formulation F8 was prepared by substituting 35% of the HPMC K15 M with HPMC K 100 LV. From the results, it was found that it had almost negligible effect on drug release. The higher release was found only for 1 h, which was the period of burst effect, after which no significant difference was observed. The finding was also supported by Li and co-workers who reported<sup>19</sup> that there was a significant difference in the burst effect from formulations fabricated with polymers of different viscosities but no significant difference was observed for second phase of drug release which might suggest that the initial burst effect was followed by the completion of a stable gel layer which, in turn, controls the drug release from the dosage forms.

The results of the swelling study indicated the importance of the use of higher viscosity polymer (formulation F4 Vs F8), as after 8 h

swelling layer remains intact as well as swelling index increases with time of formulation F4 than formulation F8. Hence tablets of formulation F4 was selected as the optimum formulation among all the formulation and was taken for further study.

It was also observed that the release rate was decreased when the viscosity and/or content of the polymer was increased. A linear relationship was found between the viscosity of the polymer and release rate of drug from the drug delivery system. As the viscosity and/or the content of HPMC increased, the release rate of drug decreased.<sup>18</sup>

From the overall dissolution profiles it was concluded that the drug release rate was decreased as the viscosity of HPMC increases (Figure 9). This can probably be attributed to the different diffusion and swelling behaviours of the polymer. With the increasing macromolecular weight, the degree of entanglement of the polymer chains increases. Thus the mobility of the macromolecule in a fully swollen system decreases. According to free volume of theory of diffusion, as the probability for a diffusing molecule to jump from one cavity into another, decreases. This leads to decreased drug diffusion co-efficient and decreases release rate with increase in molecular weight or viscosity of the polymer.

From the dissolution profiles of tablets of all formulations, the initial burst effect was observed to some extent which might be due to inherent characteristics of HPMC matrices which showed an initial burst of drug release, owing to the time required for the formation of an efficient gel layer which was particularly evident for highly soluble drugs<sup>10</sup> as Clarithromycin is highly soluble at low pH.

It was also concluded that the type of filler had significant influence on drug release from the drug delivery systems (Figure 9). It was concluded that a shift from water insoluble filler to water-soluble filler altered the dissolution profile of drug, which might probably due to reduction in tightness of the swollen hydrogel.<sup>20</sup>

Buoyancy of the tablet was governed by both the swelling of the hydrocolloid particle on surface when it contacts the gastric fluids, which in turn results in an increase in the bulk volume and the presence of internal void space in the dry centre of the tablet (porosity)<sup>7</sup>.

On increasing the hardness of tablets of formulation F4 from 5 Kg/cm<sup>2</sup> to 15 Kg/cm<sup>2</sup> resulted in drastically increased lag time (Figure 4) which might be due to high compression resulting in reduction of porosity of the tablets and moreover, the compacted surface of the hydrocolloid particles on the surface of the tablet cannot hydrate rapidly when the tablets contacts the gastric fluids and as a result of this, the capability of the tablet to float is significantly reduced.<sup>7, 18</sup>

Kollidon SR can be effectively used for formulating floating drug delivery system of Clarithromycin. Tablets can be prepared at low compression force, which can float for entire study period. This is because of the plastic behaviour of polyvinyl acetate and povidone combination leading to retention of high porosity. This results in the dosage form to float in the dissolution medium. Retention of high porosity is due to the unique ability of the plastic polymer (PVA) and binder (PVP) in the formulation to form good tablets at a very low compression force. At a low compression pressure tablets with conventional excipients may not eject out from the die in an intact form.<sup>21</sup>

Tablets containing Kollidon-SR and ethyl cellulose did not show any swelling, this might be because of non-swelling nature of PVA and PVP (Table 4 and Figure 5).

From the dissolution profiles of formulations F10, F11 and F12, it was concluded that the release rate decreases as the concentration of ethyl cellulose increases. This might be because of the hydrophobic nature and drug retarding property of ethyl cellulose. So it can be used successfully for retarding the release of the drug beyond 12 h from Kollidon-SR matrix tablets (Figure 9).

The floating lag time increases for formulations from F10 to F12. This might be due to decrease in concentration of Micro crystalline cellulose. Micro crystalline cellulose absorbs 0.1 N HCL from the

dissolution medium, which should be used for gas generation (act as wicking agent in floating formulation).

From the results of dissolution data fitted to various drug release kinetic equations (Table 6), the Higuchi model and Korsmeyer-Peppas ( $n > 0.45$ ) model were found to be the best fitted in all the dissolution profiles having higher correlation co-efficient followed by zero order drug release equation. It was concluded that the drug release occurred via anomalous diffusion mechanism coupled with erosion. Hence the drug release was controlled by more than one process from hydrophilic matrices of HPMC. In the present study it was also found that all formulations except formulations F3 and F5 containing 12 % w/w of sodium bicarbonate and drug release followed square root of time dissolution profile.<sup>22, 23</sup>

#### CONCLUSION

Floating matrix tablets of Clarithromycin were prepared using different grades of HPMC and varying concentrations of sodium bicarbonate, a gas-generating agent along with varying ratios of microcrystalline cellulose and lactose as filler.

Tablets were subject to various evaluation parameters such as hardness, weight variation, friability, floating property studies, swelling studies and in vitro drug release studies. It was revealed that tablets of all batches had acceptable physical parameters. Tablets of formulation F4 had good floating properties along with good swelling behaviours and in vitro drug release.

Tablets of formulation F4 was selected as an optimum formulation and was evaluated for further parameters like effect of hardness on floating lag time.

It was observed that tablets of all batches followed Higuchi's square root of time profile and Korsmeyer-Peppas equation followed by zero order drug release profiles. Thus it can be concluded that the drug release occurred via anomalous diffusion mechanism coupled with erosion and hence the drug release was controlled by more than one process.

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