Research Paper www.ijcps.com

International Journal of Chemical and Pharmaceutical Sciences
2013, Mar., Vol. 4 (1)

ISSN: 0976-9390
IJCPS

Formulation and evaluation of clarithromycin floating tablet

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ABSTRACT

The purpose of this investigation was to prepare a gastroretentive drug delivery system of clarithromycin. The present study outlines a systematic approach for design and development of hydrodynamically balanced tablets of clarithromycin to enhance the bioavailability and therapeutic efficacy of the drug.. Floating tablets of clarithromycin were prepared employing two different grades of, HPMC K4M, HPMC K10M, HPMC K15M, Chitoson by effervescent technique. Sodium bicarbonate was incorporated as a gas-generating agent. Drug-excipients compatibility studies were conducted using FTIR spectra. The floating tablets were evaluated for physical characteristics viz. uniformity of weight, hardness, friability, drug content, swelling index, in vitro buoyancy. Further, tablets were evaluated for in vitro release characteristics. The prepared tablets exhibited satisfactory physico-chemical characteristics. All the prepared batches showed good in vitro buoyancy. The tablet swelled radially and axially during in vitro buoyancy studies. HPMC K15M based matrix tablets showed significantly greater swelling indices compared with other batches. The tablets exhibited prolonged drug release profiles while floating over the dissolution medium. In vitro release mechanism was evaluated by subjecting the dissolution data to various kinetic models and the drug release was found to best fit to Korsemeyer – Peppas equation and followed by Higuchi model and Zero order rate kinetics. Comparison study with marketed product Clarithro ER showed that the optimized formulation F3 has better control over release rate in comparison with the marketed product.

Keywords: Floating tablets, clarithromycin, HPMC K15M, Zero order kinetics.

1. INTRODUCTION

Oral controlled drug delivery system should be primarily aimed at achieving more predictable and increased bioavailability of drugs. However, the development process is precluded by several physiological difficulties, such as an inability to restrain and localized the drug delivery system with in desired regions of GI tract and highly variable natures of gastric emptying process. It can be anticipated that, depending upon the physiological state of subject and design of pharmaceutical formulation, the emptying process can last from a few minutes to 12 hr. The relatively brief gastric emptying time in humans, which normally averages 2-3 hr. through the major absorption zone (stomach or upper part of intestine), can result in incomplete drug release from the drug delivery system leading to diminish efficiency of the administered dose. Thus control of placement of a drug delivery system in a specific region of GI tract offer numerous advantages, especially for drug with stability problem. Overall, the intimate contact of the drug delivery system with the absorbing membrane has the potential to maximize drug absorption and may also influence the rate of drug absorption. These considerations have lead to development of oral controlled release dosage forms possessing gastric retention capabilities.

The real issue in the development of oral controlled release dosage form is not just prolonging the delivery of drugs for more than 12 hrs but also to prolong the presence of dosage forms in the stomach or somewhere in small intestine. For instance, these will significantly extend the period of time over which drug may be released, and thus prolonged dosing intervals and increase patient compliance beyond the compliance level of existing controlled release dosage form.

GRDF will also greatly improve the pharmacotherapy of stomach itself through local drug release leading to high drug concentration at the gastric mucosa, which is sustained over long period of time. For example, eradication of *Helicobacter Pylori*, which requires the

administration of various medications several times a day according to complicated regimen and which frequently fails as a result of insufficient patient compliance, could perhaps be achieved more reliably using GRDF to administered smaller drug doses for fewer times.

The main objective of developing these systems is to increase the safety of product to extend its duration of action. Floating tablet of quinolone antibacterial agent like Ciprofloxacin was prepared with the aim to reduce bacterial colony by delivery of the drug in the upper gastrointestinal tract. Current therapy involves administration of proton pump inhibitor or surgery, in either case any bacterial colony might not reduce therefore there is strong need to deliver broad spectrum antibiotics like Ciprofloxacin, which can deliver the drug to the stomach and has long resident time in the gastric pouch. Buoyant tablet are one such a dosage form, which floats in gastric fluid for a longer time and delivery the drug in to the upper Gastrointestinal Tract (GIT), hence this work, is planned to deliver antibiotics like Ciprofloxacin as a floatable tablet. Selection of the best formulation based on using evaluation parameters like floating lag time, total floating time and release profile [1,2].

2. MATERIALS

Ciprofloxacin received as a gift sample from micro labs Ltd., Bangalore. The polymers Methocel K4M, Methocel K15M, were received as a gift sample from micro labs Ltd., Bangalore. Magnesium stearate, Sodium bicarbonate were purchased from S.D. fine chemicals Ltd. Ahmedabad, India, Lactose and purified talc were purchased from E. Merk (India) Ltd. Mumbai.

2.1. Formulation of hydrodyamically balanced tablets

Floating matrix tablets containing Clarithromycin were prepared by direct compression technique using varying concentrations of different grades of polymers with sodium bicarbonate.All the ingredients except magnesium stearate were blended in glass mortar uniformly. After sufficient mixing of drug as well as other components, magnesium stearate was added and further mixed for additional 2-3 minutes. The tablets were compressed with 13mm punch using hydraulic press. The weight of the tablets was kept constant for formulations F1 to F10. The composition of all formulations was given in Table 1.

2.2. Evaluation of hydrodynamically balanced tablets [3]

Evaluation was performed to assess the physicochemical properties and release characteristics of the developed formulations.

2.2.1. Evaluation of granules

2.2.1.2. Angle of Repose (θ)

The frictional forces in a loose powder or granules can be measured by angle of repose. This is the maximum angle possible between the surface of a pile of powder or granules and the horizontal plane. The granules were allowed to flow through the funnel fixed to a stand at definite height (H). The angle of repose was then calculated by measuring the height and radius of the heap of granules formed.

$\tan \theta = h/r$

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

2.2.1.3. Compressibility Index

The flowability of powder can be evaluated by comparing the bulk density (Do) and taped density (Df) of powder and the rate at which it packed down.

$$\text{Compressibility index (\%)} = \frac{Df - Do}{Df} \times 100$$

Do = Bulk density

Df = Tapped density

2.2.2. Evaluation of tablet[3]

2.2.2.1. Shape of tablets

Directly compressed tablets were examined under the magnifying lens for the shape of the tablet.

2.2.2.2. Tablet dimensions

Thickness and diameter were measured using a calibrated dial caliper. Three tablets of each formulations were picked randomly and thickness was measured individually [4] .

2.2.2.3. Thickness

The dimensions of the tablet like thickness, length were measured using vernier-calipers. Ten tablets were selected randomly for this test and the average value was reported.

2.2.2.4. Hardness

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets were determined using Monsanto hardness tester. It is expressed in kg/cm2. Three tablets were randomly picked and hardness of the same tablets from each tablets was determined [4].

2.2.2.5. Friability test

The friability of tablets were determined using Roche Friabilator. It is expressed in percentage (%). Ten tablets were initially weighed (Winitial) and transferred into friabilator. The friabilator was operated at 25rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed again (Wfinal). The % friability was then calculated by –

$$F = \frac{W\ initial - W\ final}{W\ initial} \times 100$$

% Friability of tablets less than 1% are considered acceptable.

2.2.2.6. Weight variation test

Ten tablets were selected randomly from each batch and weighed individually to check for weight variation. A little variation is allowed in the weight of a tablet by U.S. Pharmacopoeia. The following percentage deviation in weight variation is allowed [4].

2.2.2.7. Test for content uniformity

Tablet containing 500mg of drug is dissolved in 100ml of 0.1N HCl taken in volumetric flask. The drug is allowed to dissolve in the solvent. The solution was filtered, 1ml of filtrate was taken in 50ml of volumetric flask and diluted up to mark with 0.1N HCl and analysed spectrophotometrically at 203nm. The concentration of Clarithromycin in mg/ml was obtained by using standard calibration curve of the drug. Claimed drug content was 500mg per tablet. Drug content studies were carried out in triplicate for each formulation batch [3].

2.2.2.8. Tablet Density

Tablet density is an important parameter for floating tablets. The tablet will only float when its density is less than that of gastric fluid (1.004). The density was determined using following relationship.

$V = \pi r^2 h$

$d = m/v$

v = volume of tablet (cc)

r = radius of tablet (cm)

h = crown thickness of tablet (g/cc)

m = mass of tablet

2.2.2.9. Buoyancy / Floating Test

The time between introduction of dosage form and its buoyancy on the simulated gastric fluid and the time during which the dosage form remain buoyant were measured. The time taken for dosage form to emerge on surface of medium called Floating Lag Time (FLT) or Buoyancy Lag Time (BLT) and total duration of time by which dosage form remain buoyant is called Total Floating Time (TFT) [7].

2.2.2.10. Swelling study

The swelling behaviour of a dosage form is measured by studying its weight gain or water uptake. The dimensional changes can be measured in terms of the increase in tablet diameter and/or thickness over time. Water uptake is measured in terms of percent weight gain, as given by the equation [7].

$$WU = \frac{W1 - W0}{W0} \times 100$$

Wt = Weight of dosage form at time t.

W0 = Initial weight of dosage form

2.2.2.11. Effect of hardness on Buoyancy Lag Time (BLT) or Floating Lag Time (FLT)

Formulation F2 was selected to study the effect of hardness on buoyancy lag time. The tablets of batch F2 were compressed at three different compression pressures to get the hardness of 5kg/cm2, 7kg/cm2 and 9kg/cm2. The tablets were evaluated for Buoyancy Lag Time. The method followed is same as that of Buoyancy test [7].

2.2.2.12. In-vitro Dissolution Study

In-vitro release studies were carried out using USP XXIII dissolution test apparatus. 900ml of 0.1N HCl (pH 1.2) was filled in dissolution vessel and the temperature of the medium was set at $37^0C \pm 0.10^0C$. For the study ring/mesh assembly was used. The tablet was put inside the ring assembly and placed inside the dissolution vessel. The speed was set at 50 rpm. 1ml of sample was withdrawn at predetermined time intervals for 8 hours and same volume of fresh medium was replaced. The samples were analyzed for drug content against 0.1N HCl as a blank at λmax 203nm using U.V. spectrophotometer [6].

2.2.2.13. Curve fitting analysis

The mechanism of Clarithromycin released from the matrix system was studied by fitting the dissolution data obtained to following equation.

1. Korsmeyer – Peppas equation
2. Zero order equation
3. Higuchi square root equation

2.2.2.14. Comparison with commercial marketed product

The promising formulation was compared with marketed productformulation by checking various physicochemical parameters.

2.2.2.15. Stability study

The optimum formulation was tested for a period of 12 weeks at 40c with 75% rh for drug content and other parameters.

3. RESULTS AND DISCUSSION

3.1. Compatibility study

Compatibility studies were performed using IR spectrophotometer. The IR spectrum of pure drug and physical mixture of drug and polymer were studied.

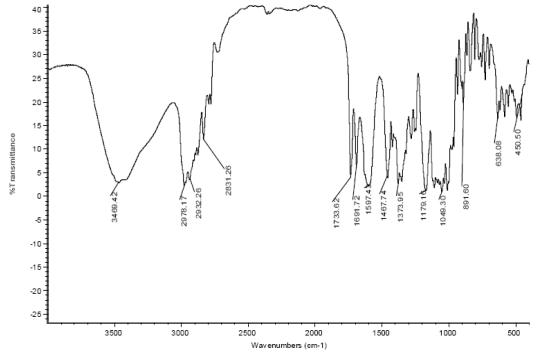

Figure - 1: IR spectra for clarithromycin

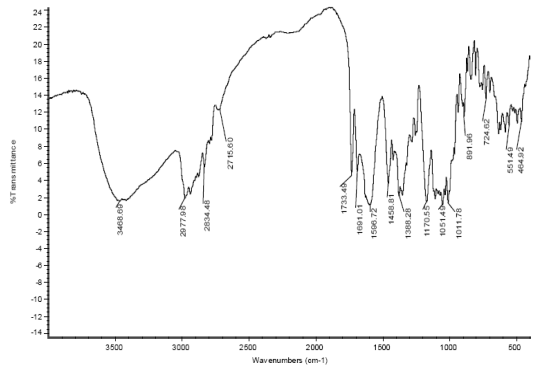

Figure – 2: IR Spectra of HPMC K15M

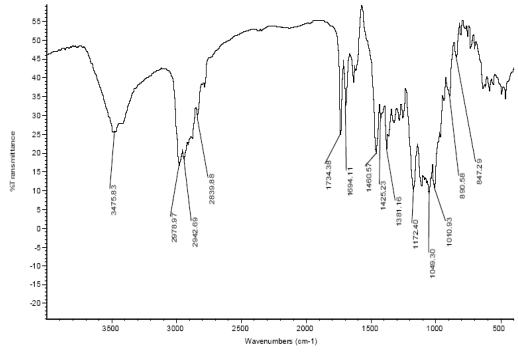

Figure - 3: IR Interpretation of physical mixture

The characteristic absorption peaks of Clarithromycin were obtained at 891.60cm-1, 1049.30cm-1, 1373.95cm-1, 1691.72cm-1.

The peaks obtained in the spectras of each formulation correlates with the peaks of drug spectrum. This indicates that the drug is compatible with the formulation components. The spectras for all formulations are shown in Fig. 1 - 3.

3.2. Evaluation of granules

3.2.1 Angle of repose

The values obtained for angle of repose for all formulations are tabulated in Table5. The values were found to be in the range from 240.88' to 29.30'. This indicates good flow property of the powder blend (Table 2).

3.2.2. Compressibility Index

Compressibility index value ranges between 12.30% to 16.34% indicating that the powder blend have the required flow property for direct compression (Table 2).

3.2.3. Swelling Study

Swelling ratio describes the amount of water that is contained within the hydrogel at an equilibrium and is a function of the network structure, hydrophilicity and ionization of the functional groups. Swelling study was performed on all the batches for 5 hr. The results of swelling index is given in Table 3. While the plot of swelling index against time (hr) is depicted in figure 4.From the results it was concluded that swelling increases as the time passes because the polymer gradually absorb water due to hydrophilicity of polymer. The outermost hydrophilic polymer hydrates and swells and a gel barrier is formed at the outer surface.

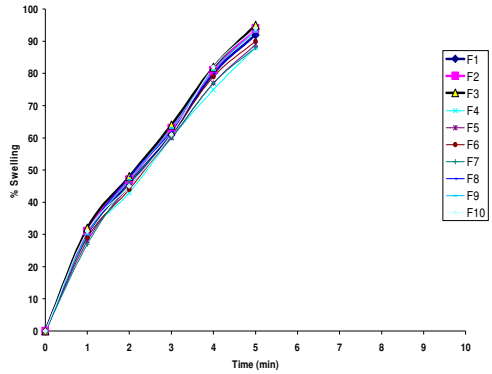

Figure - 4: Swelling Index

As the gelatinous layer progressively dissolves and/or is dispersed, the hydration swelling release process is repeated towards new exposed surfaces, thus maintaining the integrity of the dosage form. In the present study, the higher

swelling index was found for tablets of batch F3 containing HPMC K15M having nominal viscosity of 15,000 cps. Thus, the viscosity of the polymer had major influence on swelling process, matrix integrity, as well as floating capability, hence from the above results it can be concluded that linear relationship exists between swelling process and viscosity of polymer.

3.2.4. Effect of hardness on buoyancy lag time

The effect of hardness on buoyancy lag time for batch F3was studied. The results of floating lag time of tablet having hardness of 5kg/cm2, 7kg/cm2 and 9kg/cm2 were 102, 480 and 650 sec respectively as tabulated in Table 9. The plot of floating lag time (sec) V/s hardness (kg/cm2). Batch F3 was selected for the study because it showed buoyancy lag time of 49 sec at hardness of 4kg/cm2.Buoyancy of the tablet was governed by both the swelling of the hydrocolloid particle on surface when it contacts the gastric fluid which in turn results in an increase in the bulk volume and the presence of internal void space in the dry center of the tablet (porosity). On increasing the hardness of the tablets results in increased buoyancy lag time which might be due to high compression resulting in reduction of porosity of the tablet and moreover, the compacted hydrocolloid particles on the surface of the tablet cannot hydrate rapidly when the tablet reaches the gastric fluid and as a result of this, the capability of the tablet to float is significantly reduced.

3.2.5. *In-vitro* dissolution study

The in-vitro drug release profile of tablet from each batch (F1 to F10) were shown in Table10. The plot of % cumulative drug release V/s time (hr) was plotted and depicted as shown in figure 5. For in-vitro dissolution study ring mesh device was used. The reason is that when paddle apparatus is used, the tablets would rise and eventually stick to the flange of the rotating shaft resulting in partial surface occlusion. In case of basket apparatus, it ensures full exposure of all surfaces of hydrophilic swelling tablets that may stick to bottom of dissolution vessel if paddle apparatus was used. However, it was observed that after 5-7 hr the tablets had swollen to such an extent that they were completely constricted by the radius of the basket and completely filled the bottom of the basket. Once the dosage forms completely fills the basket, tablet is unable to swell further and move in unimpeded fashion leading to limited drug release. In order to overcome these drawbacks ring mesh device is employed in the study.

From the in-vitro dissolution data it was found that formulation F4 containing chitosan alone released 97.2% of drug within 6 hr of the study indicating that the polymer amount is not sufficient to control the drug release.Formulation F3 containing HPMC K15M showed better control of drug release than chitosan alone, and released 96.3% drug at the end of 10 hr. Tablet of batch F1, F2 and F3 contained same amount of polymer of different grades viz. HPMC K4M, HPMC K15M and combination of HPMC K4M and K15M which showed drug release rate of 93.6%, 92.1% and 89.3% respectively. Out of all the ten formulations batch F3 showed better control over drug release indicating that the release was decreased when the viscosity of the polymer was increased.

3.2.6. Curve Fitting Analysis

The results of dissolution data fitted to various drug release kinetic equations. Peppas model was found to be best fitted in all dissolution profile having higher correlation coefficient (r value) followed by Higuchi model and Zero Order

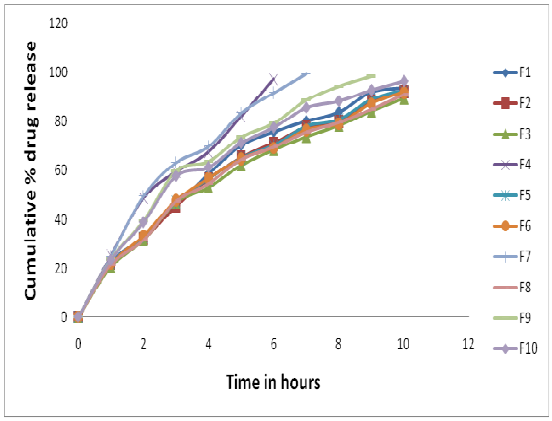

Figure - 5: In Vitro drug release plot for Formulation F1-F10

Release equation. The kinetic values obtained for different formulations are tabulated in Table11. Korsemeyer-Peppas model indicates that release mechanism is not well known or more than one type of release phenomena could be involved. The 'n' value could be used to characterize different release mechanisms as:

The results are reported in Table 9 and in the present study 'n' value ranges between 0.64 to 0.76 for all ten batches. It ranges between 0.5 to 1, so it was concluded that the drug release occurred via non-Fickian diffusion, which shows that the release from initially dry, hydrophilic glassy polymers that swell when added to water and become rubbery show anomalous diffusion as a result of the rearrangement of macromolecular chains.

Table - 1: Formulation of hydrodynamically balanced tablets of clarithromycin (in mgs)

Ingredients(in mgs)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Clrithromycin	500	500	500	500	500	500	500	500	500	500
HPMC K 4 M	200	-	-	-	100	100	100	-	-	-
HPMC K 10M	-	200	-	-	100	-	-	100	100	
HPMC K 15M	-	-	200	-	-	100	-	100		100
Chitosan	-	-	-	200	-	-	100		100	100
Sodium bicarbonate	80	80	80	80	80	80	80	80	80	80
Lactose	10	10	10	10	10	10	10	10	10	10
Mag.stearate	10	10	10	10	10	10	10	10	10	10

Table - 2: Angle of Repose, Compressibility Index

Batch	Angle of repose	Compressibility index
F1	24.30 ^{o}	12.30
F2	25.41 ^{o}	14.58
F3	26.77 ^{o}	15.67
F4	28.56 ^{o}	16.34
F5	24.72 ^{o}	14.12
F6	25.28 ^{o}	14.48
F7	27.08 ^{o}	14.59
F8	25.63 ^{o}	14.74
F9	28.45 ^{o}	15.34
F10	29.88 ^{o}	15.41

Table - 3: Swelling Index of Tablets of Batch F1 to F10

Time in Hrs	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
1	30	31	32	29	28	29	27	30	30	31
2	46	47	48	43	45	44	46	48	47	45
3	61	63	64	60	60	61	60	62	63	61
4	80	81	82	75	77	79	77	80	81	82
5	92	94	95	88	89	90	88	92	93	94

Table - 4: Physical Properties of Tablets of Batch F1 to F10

Batch	Diameter	thickness	hardness	friability	Weight variation	Drug content
F1	12.99 ±0.04	5.16 ±0.01	4.5 ±0.47	0.41	800.65 ±1.29	97.01
F2	12.98 ±0.01	5.15 ±0.02	4.4 ±0.1	0.40	800.41 ±1.12	98.35
F3	12.98 ±0.006	5.14 ±0.01	4.4 ±0.32	0.36	800.50 ±1.74	99.50
F4	12.98 ±0.07	5.16 ±0.01	4.3±0.42	0.38	800.05 ±1.37	97.40
F5	12.98 ±0.04	5.15 ±0.03	4.2±0.41	0.37	801.10 ±1.13	99.40
F6	12.99 ±0.067	5.12 ±0.06	4.1±0.54	0.38	799.55 ±1.18	98.01
F7	12.98 ±0.05	5.16 ±5.15	4.2±0.32	0.42	799.85 ±1.65	99.21
F8	12.99 ±0.06	5.15 ±0.02	4.3±0.65	0.38	800.03 ±1.11	98.69
F9	12.98 ±0.02	5.16 ±0.03	4.4±0.41	0.39	800.68 ±1.35	98.98
F10	12.98 ±0.056	5.18 ±0.01	4.5±0.35	0.37	801.65 ±1.49	98.40

Table - 5: Tablet Density, Buoyancy Lag Time, TotalFloatingTime

Batch	Tablet density	Buoyancy lag time (sec)	Total floating time(Hrs)
F1	0.93	62	>12
F2	0.88	54	>12
F3	0.82	49	>12
F4	0.99	134	>6
F5	0.85	58	>12
F6	0.89	55	>12
F7	0.95	125	>7
F8	0.86	118	>12
F9	0.93	107	>9
F10	0.90	102	>10

Table – 6: n value of different kinetic machanism

n	Mechanism
0.5	Fickian diffusion (Higuchi Matrix)
0.5 < n < 1	Non-Fickian diffusion
1	Case II transport

Table - 7: Effect of Hardness on Buoyancy Lag Time of Batch F3

Hardness in kg/cm²	Buoyancy Lag Time (sec)
4kg/cm²	49
5kg/cm²	102
7kg/cm²	480
9kg/cm²	650

Table - 8: Cumulative % Drug Released from Tablet Formulations F1 to F10.

Time in Hrs	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
1	22.51	21.64	20.70	25.24	21.96	21.64	24.94	21.45	23.73	23.41
2	32.43	31.97	31.54	48.67	32.65	33.34	49.57	31.52	39.47	38.72
3	45.56	45.35	46.87	59.43	47.24	47.72	63.27	47.28	59.84	57.62
4	58.53	56.59	53.12	67.56	56.57	56.78	69.81	54.58	63.71	61.28
5	70.20	65.41	62.14	81.98	65.12	64.84	83.53	64.39	73.59	71.17
6	75.67	71.28	68.45	97.24	70.24	69.38	91.75	69.47	79.28	77.47
7	80.12	77.67	73.85		77.98	76.51	99.42	75.52	88.69	85.53
8	83.76	80.12	78.34		80.79	79.20		79.47	94.35	88.26
9	91.89	88.43	84.35		88.97	87.36		84.91	98.43	92.74
10	93.65	92.11	89.43		92.64	91.95		90.93		96.31

Table - 9: Kinetic Values Obtained From F3 plot Formulation.

Formulation	Zero order R^2	First order R^2	Higuchi R^2	Korsmeyer -Peppas R^2	n	Best fit model
F3	0.944	0.985	0.955	0.996	0.647	Peppas

Table – 10: Comparison of Optimization formulation F3 with marketed product.

Time in Hrs	F3	Marketed product
1	20.70	24.31
2	31.54	34.25
3	46.87	48.63
4	53.12	59.47
5	62.14	66.65
6	68.45	74.74
7	73.85	78.96
8	78.34	81.94
9	84.35	90.70
10	89.43	92.31

Table – 11: Kinetic studies of optimum formulation F3

Time in hours	√ T	Log T	Cumulative % drug release	Cumulative % drug remain	Log cumulative % drug release	Log cumulative % drug remain
0	0	0	0	100	0	2
1	1.0	0	20.70	79.3	1.315	1.899
2	1.414	0.301	31.54	68.46	1.498	1.835
3	1.732	0.477	46.87	53.13	1.670	1.725
4	2.0	0.602	53.12	46.88	1.725	1.670
5	2.236	0.698	62.14	37.86	1.793	1.578
6	2.449	0.778	68.45	31.55	1.835	1.498
7	2.645	0.845	73.85	26.15	1.868	1.417
8	2.828	0.903	78.34	21.66	1.893	1.335
9	3.0	0.954	84.35	15.65	1.926	1.194
10	3.162	1.0	89.43	10.57	1.951	1.024

Table – 12: Characteristics of optimized tablet.

	Drug Content (%) ± SD	Hardness (Kg/cm²) ±SD	Floating behaviour	
			Floating lag time (sec)	Floating duration (hrs)
After one month	89.24±0.029	4.4 ±0.32	49	13
After two months	89.04±0.024	4.5 ±0.43	52	13
After three months	88.87±0.025	4.56 ±0.36	58	12

Table – 13: *In-Vitro* drug release study

Time (in hours)	Cumulative drug release after one month	Cumulative drug release after two months	Cumulative drug release after three months
0	0.000	0.00	0.00
1	20.67	20.57	20.07
2	31.34	31.68	31.64
3	46.80	47.20	46.60
4	52.08	53.12	53.01
5	62.01	62.23	62.07
6	68.25	69.23	69.68
7	73.98	74.20	75.03
8	78.18	79.28	80.20
9	84.30	84.75	84.93
10	89.43	89.38	89.33

3.2.7. Pharmacokinetic studies

Kinetic plots of formulation F3

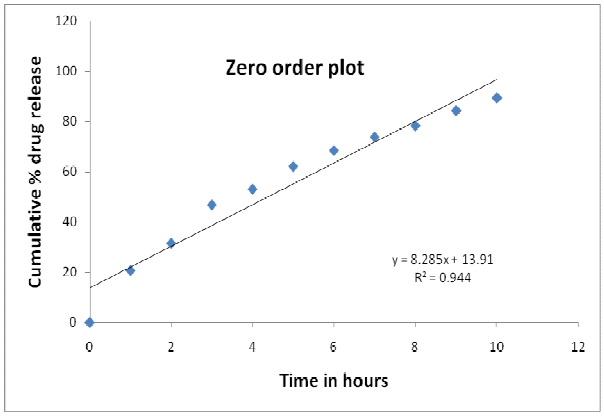

Figure - 6: Zero order plot

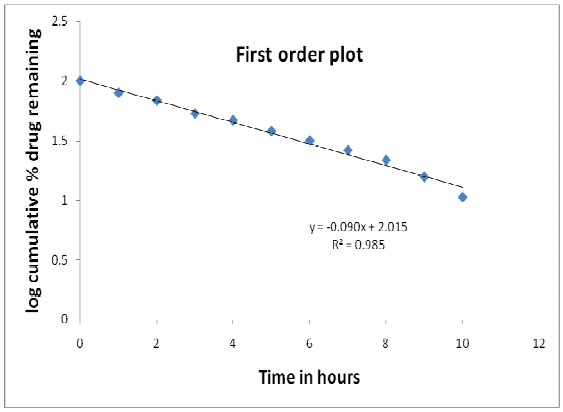

Figure -7: First order plot

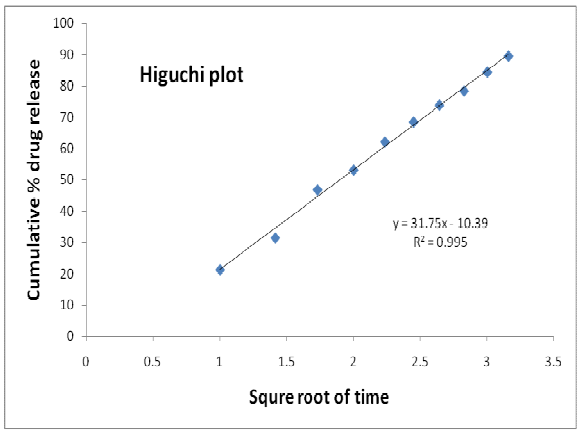

Figure - 8: Higuchi plot

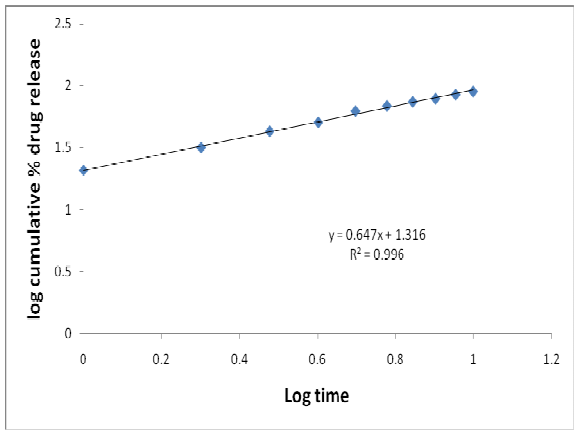

Figure - 9: Korsmeyer peppas plot

3.2.8.Comparison with Commercial Marketed Product

The promising formulation (F3) as found by evaluation studies was compared with marketed product Clarithro ER (500mg). The evaluation parameters tested and compared were drug content uniformity and in-vitro dissolution profile. The values obtained for in vitro dissolution study are recorded in Table 8.

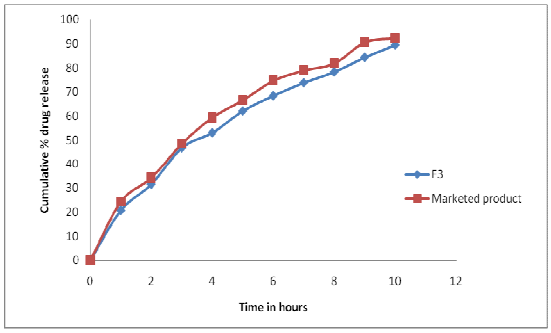

Figure - 10: A Plot for comparison between optimized formulation F3 with Marketed product

The mean value of drug content uniformity observed was 99.28%. The marketed product gave 92.31% of drug release in 10 hrs of dissolution study. In-vitro dissolution profile of marketed product in comparison to the formulated batches were shown graphically in Figure 10 and showed that the formulation F3 with 89.4% of drug release has better control over release of drug in comparison to marketed product.

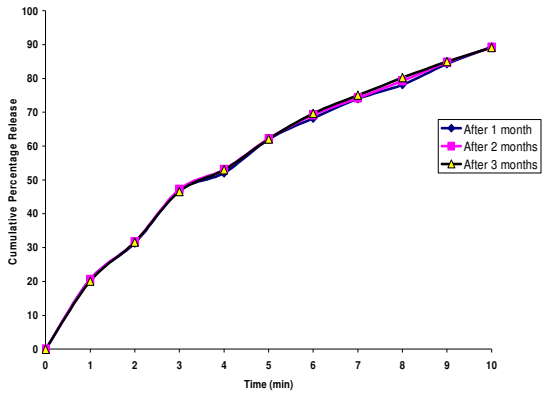

Figure - 11: In Vitro Drug Release Study

The tablets were investigated at 40°C/75%RH For 3 months. From the data, The Formulation is found to be stable under the conditions mentioned before since there was no significant change in the percentage amount of drug content and drug release. Thus, it was found that the Fioating tablets of clarithromycin (F3) were stable under these conditions at least for three months.

4. CONCLUSION

In the present study Gastroretentive delivery systems of Clarithromycin were successfully developed in the form of Hydrodynamically Balanced Tablets to improve the local action and ultimately its bioavailability.The tablets were formulated using different grades of polymers (HPMC K4M, HPMC K15M and Chitosan) and effervescing agent (NaHCO3).IR spectra studies revealed that the drug and the polymers used were compatible. The evaluation parameters like hardness, friability and content uniformity were within the limits for various batches formulated.Buoyancy lag time, Total floating time, tablet density, Swelling studies showed satisfactory results for batch F1, F2, F3, F5, F6 and F8. The formulation F3 was evaluated for effect of hardness on floating lag time, and the results showed that the floating lag time increased as hardness increased due to reduction in porosity.In-vitro dissolution of batch F3 containing HPMC K15M showed good drug release rate in comparison to remaining batches containing chitosan, HPMC K4M, HPMC K10M which were not able to sustain their release up to 10 hrs. Formulations subjected to curve fitting analysis showed to best fit Korsemeyer – Peppas equation and followed non-Fickinian diffusion mechanism.Comparison study with marketed product Clarithro ER showed that the optimized formulation F3 has better control over release rate in comparison with the marketed product.Hence it was concluded that formulation F3 containing HPMC K15M showed better controlled drug release rate in comparison to other polymers and showed that the release decreases as the viscosity of the polymer increases.From the findings obtained, it can be concluded that:-Hydrodynamically Balanced Tablets of an antibacterial drug Clarithromycin can be formulated as an approach to increase gastric residence time and thereby improve its bioavailability.Among the polymers used to improve the gastric residence, cellulose polymers HPMC K4M, HPMC K15M showed better control over drug release in comparison to polysaccharide polymer Chitosan.Formulated tablets gave satisfactory results for various physicochemical evaluation for tablets like Tablet dimensions, Hardness, Friability, Weight variation, Tablet density, Swelling index and Content uniformity.Overall, tablets of batch F3 possessed quick buoyancy lag time and good total floating time.Variation on hardness on tablet of batch F3 was found to effect the floating lag time of the tablet as hardness increased.In-vitro release rate showed that the drug release was better controlled in formulation F3 shows better control drug release in comparision to other

formulation.Formulated floating tablets best fitted to Peppas model followed by Higuchi model and Zero order rate kinetics.Formulation F3 has better Sustained drug release in comparison to marketed product Clarithro ER.The present work can be continued further to prove its stability during shelf life, in-vivo gastric residence time by using gamma scintigraphy and establishment of in vitro – in vivo correlation.

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