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FORMULATION AND EVALUATION OF CLARITHROMYCIN EXTENDED RELEASE TABLET

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ABSTRACT

The design of extended release tablet by using natural polymers are becoming very popular in formulating oral controlled release tablet as they are biocompatible, biodegradable, non-toxic, cheap and easily available compared to synthetic polymers. The present investigation was planned to formulate and evaluate the clarithromycin once daily extended release tablets with natural polymers like guar gum and xanthan gum and in combination with HPMC K15M. Drug- excipient compatibility study was conducted using FTIR spectroscopy. A total of seven formulations were prepared with different combinations of polymers using wet granulation and compression method. Pre compression and post compression parameters were tested and *in vitro* drug release study was performed and the data were fitted into kinetic models. The selected best formulation (F_7) was kept for short-term accelerated stability studies (1 month at $40^oC \pm 2^oC$ / 75%±5% RH). FTIR analysis of spectra showed that there are no drug-excipients interactions and all the formulated tablets had acceptable physical properties. Drug content uniformity, hardness and thickness of best formulation (F_7) were found to be 99.7±0.004%, 4.8±0.21 Kg/cm^2 and 4.9±0.002mm. Formulation (F_7) showed release up to 94.81% in 0.1 N HCl and 88.4% in potassium phosphate buffer pH 6 in 24 hrs. The release mechanism of the best formulation (F_7) was found to be non fickian and Fick's law respectively, i.e., by both diffusion and erosion. It can be concluded that a successful once daily extended release tablets of Clarithromycin have been prepared by using the natural polymer such as guar gum.

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INTRODUCTION

The design of extended release tablet should be primarily aimed to achieve better predictability, reproducibility and increased bioavailability. The ideal drug delivery system should have the advantage of single dose for whole duration of treatment and it should deliver the active drug directly at specific site.[1] To maintain antimicrobial activity, frequent administration of conventional formulations of many antibiotics with short half-life is necessary. Otherwise, concentration under MIC occurs frequently in the course of anti-infective treatment, which induces antibiotic resistance.[2] Hydrophilic matrices containing swellable polymers are referred to as swellable Controlled-release systems or hydrophilic matrix tablets [3]. A number of polymers have been investigated to develop in situ gel-forming systems, due to the ability of these matrices to release an entrapped drug in aqueous medium and to regulate release of such drug by control of swelling and cross-linking.[3] Hydroxypropyl methylcellulose (HPMC), xanthan gum and guar gum are the polymers most widely used as gel-forming agents in the formulation of solid, liquid, semisolid and even controlled-release dosage forms.[3] Extended release dosage forms that allow at least a twofold reduction in dosage frequency as compared to that drug presented as an immediate release form. Ex: Controlled release, Sustained release.[4] Clarithromycin is a macrolide antibiotic, It prevents bacteria from growing by interfering with their protein synthesis. Clarithromycin binds to the subunit 50S of the bacterial ribosome and thus inhibits the translation of peptides.[5] Clarithromycin has similar antimicrobial spectrum as erythromycin but is more effective against certain gram-negative bacteria. Clarithromycin (CLAR) has a short half-life 2.5-3 hours. The usual oral dosage regimen is 250-500 mg every 4-6 hours and Gastric residence time of the conventional Clarithromycin dosage form is 0.5-2 hours. CLAR is having suitable properties stability in stomach pH and soluble in acidic pH.[6] The present study was undertaken to design the controlled release oral tablet to extended release of drug in order to; Increase bioavailability of the drug, Reduce the dosing frequency, Improve patient compliance. Thus, from the aforementioned facts, it becomes clear why the extended release drug delivery system for clarithromycin is better compared to conventional dosage forms. It is expected that controlled release of the drug would reduce plasma fluctuations and bring about optimized therapy of bacterial infection.

In the present investigation an attempt has been made to formulate and evaluate sustained release tablet of clarithromycin for better management of chronic disease. Our attempt has been to achieve a sufficiently prolonged release with the existing clinically used single unit extended release tablets providing a prolonged release for 24hrs. This would provide ample opportunity for the drug to get absorbed completely at a predictable rate.

MATERIALS & METHODS

Clarithromycin was provided as a gift sample from Zhejiang Better Pharmaceutical Co. Ltd. and HPMC K15M, xanthan gum, guar gum were purchased from Rolex Chemical Ltd. All other reagents and solvents used were of analytical grade.

Drug- Excipients Compatibility Studies [7]

Fourier transform infrared (FTIR) (Shimadzu 8300) spectroscopy was performed on each of the samples to determine the structure of the organic compounds and to identify the presence of specific functional groups within a sample. Spectra are obtained by passing infrared radiation through a sample and determining what fraction of incident radiation is absorbed at a particular energy. The energy of a peak in the spectrum corresponds to the frequency of vibration of part of the sample compound; 3-5 mg of composite sample was added to approximately 100 mg of KBr. The mixture was then ground to a fine powder using a mortar and pestle, and transparent discs were formed using a pellet press. The discs were then placed in the FTIR spectroscopy apparatus, and spectra were collected. The range of the collected spectra was 4000-400 cm^{-1}.

Preparation of Matrix Tablets: [8, 9]

All the ingredients were weighed accurately. Clarithromycin, Xanthan Gum, Guar Gum, Microcrystalline Cellulose, Lactose Monohydrate, and H.P.M.C was passed through #40 mesh sieves & collected in a polybag. Above sifted materials was Loaded in a planetary mixer and mixed for 15min at slow speed. Accurately weighed PVP was mixed with required amount of IPA to prepare the binder solution. The above prepared binder solution was added to the contents of planetary mixer and obtained the wet dough mass. Wet mass was dried at 40°C-45°C by using digital hot air oven, till desired LOD is achieved. Dried granules was passed through # 22 mesh sieve and oversized granules passed through 2.0 mm multimill at medium speed in forward direction. Finally milled granules were passed through #22 mesh sieves.

Table 1: Ingredients used in the formulation.

Sl.no.	Excipients	F_1 mg/tab	F_2 mg/tab	F_3 mg/tab	F_4 mg/tab	F_5 mg/tab	F_6 mg/tab	F_7 mg/tab
1	Clarithromycin	500	500	500	500	500	500	500
2	Xanthan Gum	50	100	50	-	-	25	-
3	Guar Gum	-	-	50	100	50	25	75
4	HPMC K15M	50	-	-	-	50	50	-
5	Lactose Monohydrate	50	50	50	50	50	50	75
6	Microcrystalline Cellulose	25	25	25	25	25	25	25
7	PVP 5% solution	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
8	Magnesium stearate	2.5	2.5	2.5	2.5	2.5	2.5	2.5
9	Talc	2.5	2.5	2.5	2.5	2.5	2.5	2.5
10	Total weight	680	680	680	680	680	680	680

Evaluation of Powder Blend:

Pre-compression Parameters: [10, 11, 12]

Theoretical yield:

Theoretical yield was calculated based on the amount of solid added to solvent to prepare a solution.

Practical yield:

The dried product from the hot air oven was weighed.

Percentage yield:

It can be calculated by using the formula:

$$\%\text{Yeild} = \frac{\text{Practical yeild (microspheres)}}{\text{Theroretical yeild (drug + polymer)}} * 100$$

Flow Properties:

Bulk density (D_b):

It was measured by pouring the weighed powder into a measuring cylinder and the volume is noted. It is expressed in g/ml and expressed as:

$$D_b = M/V_b$$

Where, M = Mass of the powder and V_b = Bulk volume of the powder.

Tapped density (D_t):

It is the ratio of total mass of powder to the tapped volume of powder. The tapped volume was measured by tapping the powder to constant volume. It is expressed in g/ml and is given by:

$$D_t = M/V_t$$

Where, M = Mass of the powder and V_t = Tapped volume of the powder.

Carr's compressibility index (CI):

It indicates the ease with which a material can flow. It is expressed in percentage and is given by:

$$\text{Carr's Index (\%)} = \text{TBD} - \text{LBD} / \text{TBD} \times 100$$

Hausner ratio:

The Carr's index and Hausner ratio are measures of the propensity of a powder to be compressed.

$$\text{Hausner ratio} = \text{Tapped density} / \text{Bulk density}$$

Angle of repose:
The maximum angle which is formed between the surface of a pile of powder and horizontal surface is called the angle of repose.

$$\theta = \tan^{-1}\frac{h}{r}$$

Where θ =angle of repose, h is the height and r is the radius of pile. The powder mixture was allowed to flow through the funnel fixed to a stand at a definite height. Height and radius of the heap of powder formed was noted and angle of repose reported.

Post Compression Parameters:
Dimensions:
Thickness and diameter of the tablet was measured using Mitutoyo Digital Vernier caliper. Ten tablets of the formulation were picked randomly and measured individually.

Hardness:
Hardness was measured using Monsanto & Pfizer Hardness Tester. For each batch five tablets were used.

Friability:
Twenty tablets were weighed and placed in the Electrolab EF2 friabilator USP and apparatus was rotated at 25 rpm for 4 minutes. The tablets were dedusted and weighed again. The percentage friability is measured using the formula:

$$\textbf{Friability} = \{1-(W_t/W)\} \times 100$$

Where, F = Friability in percentage, W = Initial weight of tablets, W_t = Weight of tablets after friabiation

Drug content uniformity:
Ten tablets with pre-determined weight from each batch were taken and crushed in a mortar and weight and weight equivalent to one average tablet was taken, transferred to a 100 ml volumetric flask and 5 ml of acetone and 0.01 N HCl was added and volume was made up to 100 ml with 0.01 N HCl. The solution was filtered through a filter paper and the first few ml were discarded. The filtrate was sufficiently diluted and the absorbance was recorded against the blank at 264 nm. The drug content was calculated.

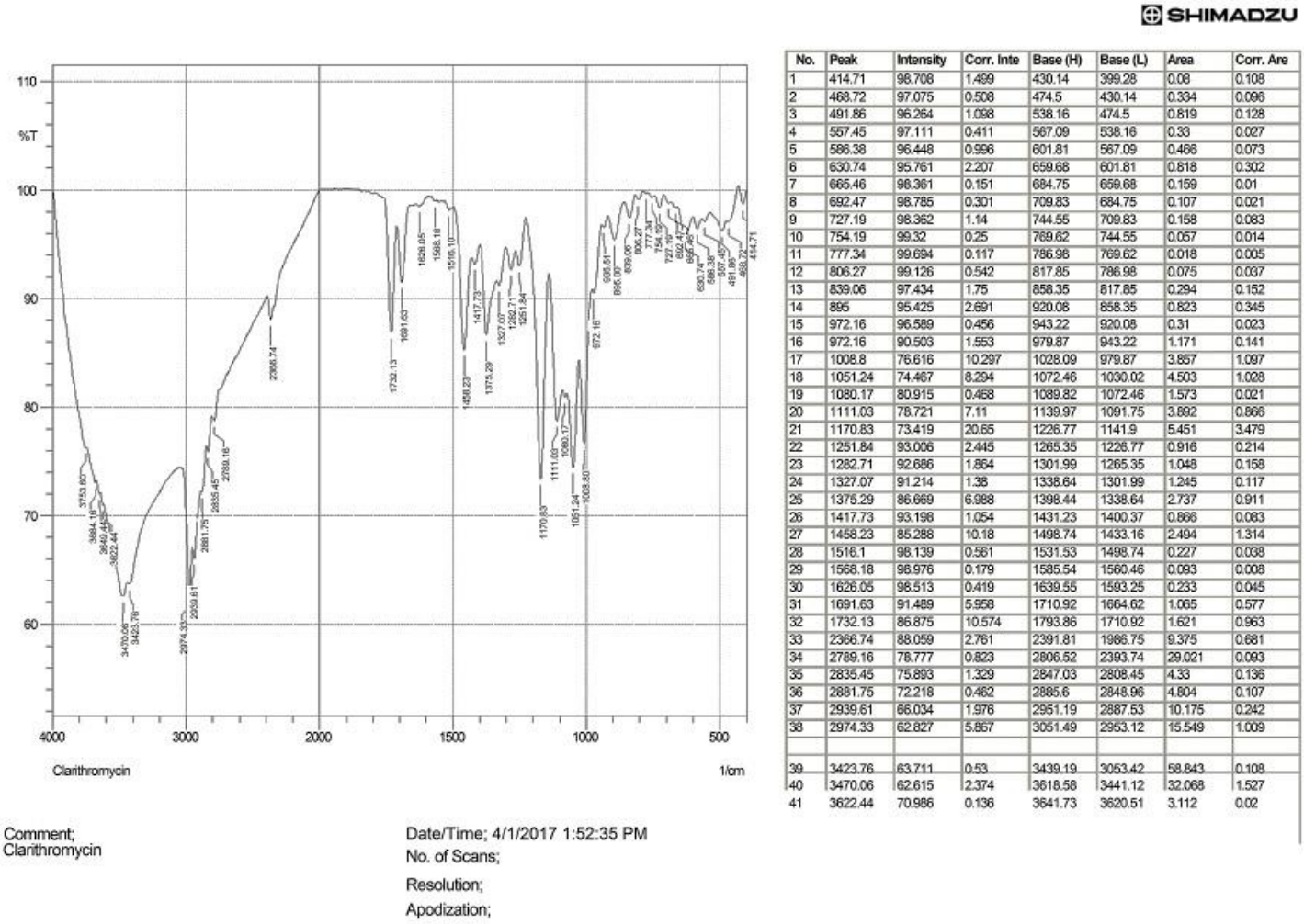
***In vitro* dissolution studies:** [13,14]
Dissolution test was performed using a USP type-2 paddle apparatus at 37 ± 0.5°C in 900 ml of 0.1 N HCl and Potassium phosphate buffer pH 6 with a speed of 50 rpm. Samples (2ml) were withdrawn at 15, 30 min, and 1, 2, 3, 4, 5, 6, 8, 24 hours as per regulations of USFDA and medium was replenished with fresh dissolution fluid and samples were measured using a UV spectrophotometer at a 264 nm wavelength.

***In-Vitro* drug release kinetics** [15]
The release data of selected formulation (F_7) obtained was fitted into various mathematical models using PCP Disso – V2.08 software. The parameters 'n' and time component 'k', the release rate constant and 'R', the regression co-efficient were determined by Krosmeyer – Peppas equation to understand the release mechanism. To examine the release mechanism of Losartan potassium from the microsphere formulations, the release data was fitted into Krosmeyer – Peppas equation:

$$\mathbf{M_t / M_\infty = K\, t^n}$$

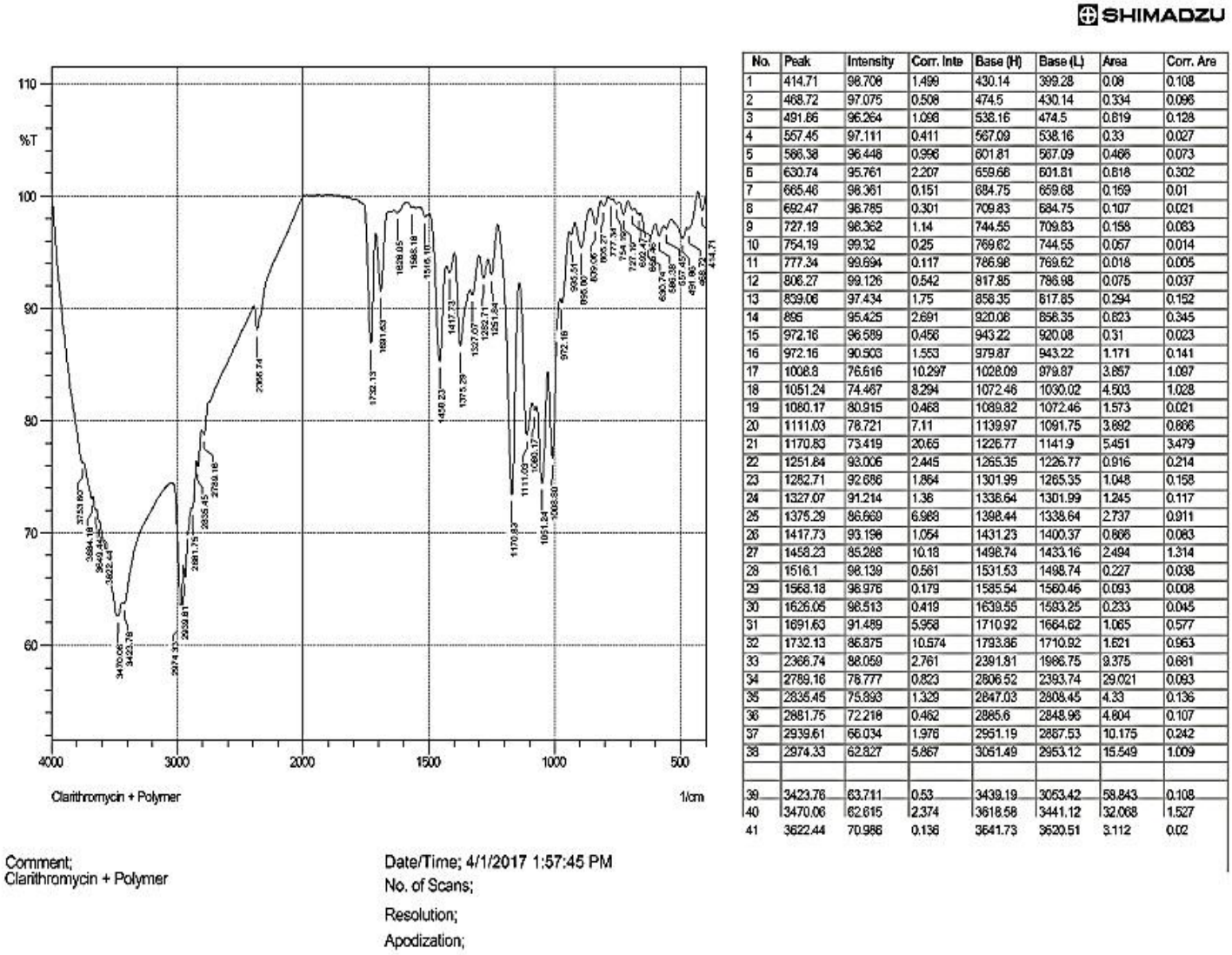
Where, Mt / **M**∞ = the fractional release of drug, t = release time, K = A constant incorporating structural and geometrical Characteristics of the device, n = the diffusional exponent and characterize the type of release mechanism during the release process.

RESULTS & DISCUSSION
Preformulation Studies:
FTIR Compatibility Study
FTIR spectra of the drug and physical mixture of drug and polymers were recorded in the range of 500-4000 cm^{-1}. Clarithromycin showed some prominent and characteristic peaks at 1691 cm^{-1} refers to -C=O stretching vibration from ketone group, 1732 cm^{-1} refers to -O-C=O stretching vibration in the lactone ring, 1051 cm^{-1} and 1107 cm^{-1}, refers to the -O-ether functional bands. In IR spectra of drugs with polymers all characteristic peaks were undisturbed which indicated no strong interaction between the drug and excipients. FTIR spectra of the drug and physical mixture of drug and polymers are shown in Fig. 1&2.



No.	Peak	Intensity	Corr. Inte	Base (H)	Base (L)	Area	Corr. Are
1	414.71	98.708	1.499	430.14	399.28	0.08	0.108
2	468.72	97.075	0.508	474.5	430.14	0.334	0.096
3	491.86	96.264	1.098	538.16	474.5	0.819	0.128
4	557.45	97.111	0.411	567.09	538.16	0.33	0.027
5	586.38	96.448	0.996	601.81	567.09	0.466	0.073
6	630.74	95.761	2.207	659.68	601.81	0.818	0.302
7	665.46	98.361	0.151	684.75	659.68	0.159	0.01
8	692.47	98.785	0.301	709.83	684.75	0.107	0.021
9	727.19	98.362	1.14	744.55	709.83	0.158	0.083
10	754.19	99.32	0.25	769.62	744.55	0.057	0.014
11	777.34	99.694	0.117	786.98	769.62	0.018	0.005
12	806.27	99.126	0.542	817.85	786.98	0.075	0.037
13	839.06	97.434	1.75	858.35	817.85	0.294	0.152
14	895	95.425	2.691	920.08	858.35	0.823	0.345
15	972.16	96.589	0.456	943.22	920.08	0.31	0.023
16	972.16	90.503	1.553	979.87	943.22	1.171	0.141
17	1008.8	76.616	10.297	1028.09	979.87	3.857	1.097
18	1051.24	74.467	8.294	1072.46	1030.02	4.503	1.028
19	1080.17	80.915	0.468	1089.82	1072.46	1.573	0.021
20	1111.03	78.721	7.11	1139.97	1091.75	3.892	0.866
21	1170.83	73.419	20.65	1226.77	1141.9	5.451	3.479
22	1251.84	93.006	2.445	1265.35	1226.77	0.916	0.214
23	1282.71	92.686	1.864	1301.99	1265.35	1.048	0.158
24	1327.07	91.214	1.38	1338.64	1301.99	1.245	0.117
25	1375.29	86.669	6.988	1398.44	1338.64	2.737	0.911
26	1417.73	93.198	1.054	1431.23	1400.37	0.866	0.083
27	1458.23	85.288	10.18	1498.74	1433.16	2.494	1.314
28	1516.1	98.139	0.561	1531.53	1498.74	0.227	0.038
29	1568.18	98.976	0.179	1585.54	1560.46	0.093	0.008
30	1626.05	98.513	0.419	1639.55	1593.25	0.233	0.045
31	1691.63	91.489	5.958	1710.92	1664.62	1.065	0.577
32	1732.13	86.875	10.574	1793.86	1710.92	1.621	0.963
33	2366.74	88.059	2.761	2391.81	1986.75	9.375	0.681
34	2789.16	78.777	0.823	2806.52	2393.74	29.021	0.093
35	2835.45	75.893	1.329	2847.03	2808.45	4.33	0.136
36	2881.75	72.218	0.462	2885.6	2848.96	4.804	0.107
37	2939.61	66.034	1.976	2951.19	2887.53	10.175	0.242
38	2974.33	62.827	5.867	3051.49	2953.12	15.549	1.009
39	3423.76	63.711	0.53	3439.19	3053.42	58.843	0.108
40	3470.06	62.615	2.374	3618.58	3441.12	32.068	1.527
41	3622.44	70.986	0.136	3641.73	3620.51	3.112	0.02

Fig. 1: IR spectra of Clarithromycin.



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41	3622.44	70.986	0.136	3641.73	3620.51	3.112	0.02

Fig. 2: IR spectra of physical mixture of Clarithromycin and polymers.

Formulation & Design:

Seven formulations of extended release tablets were prepared (F_1 to F_7) using various polymers such as HPMC K15M, guar gum and xanthan gum in different ratios. The tablets were prepared by wet granulation method using PVP 5% solution as binding agent. The concentration of binding agent was decreased for better control of drug release. Microcrystalline cellulose and lactose monohydrate were used as diluents and magnesium stearate and talc were used as a lubricant in appropriate concentration. All the formulations were prepared by keeping constant tablet weight of 680 mg with an average hardness 4.5 kg/cm^2.

Evaluation of Powder blends:

Pre Compression Evaluation

The pure drug has Carr's Index about 31.03 and Hausner Ratio 1.45, indicating that it is a poor candidate for direct compression technique. The drug blend which was prepared by wet granulation technique was found to have Carr's compressibility index less than 25% and Hausner ratio less than 1.30 for all the formulation blends indicating that the blend has passable flow property. (Table 2)

Post Compression Evaluation:

Physicochemical Properties

The prepared tablets were subjected to preliminary characterization such as hardness, thickness, % weight variation, friability and drug content. Evaluation studies indicated that, the values of various parameters were within the permissible limits of pharmacopoeia for all the formulations. (Table 3)

***In-vitro* Drug Release Profile**

Formulation F_1 and F_2 showed drug release less than ideal release in 0.1N HCl and potassium phosphate buffer pH 6 in 24 hours. This may be due to the high viscosity of HPMC K15M and stability of Xanthan gum in pH range of 2-10 which blocks the release of drug completely. But by using guar gum in the formulation F_4, F_3, F_5 and F_6 showed the drug release was increased in 0.1N HCl and potassium phosphate buffer pH 6 in 24 hours. This may be due to the viscosity of guar gum which remains stable in solution over pH range 5-7. But strong acids cause hydrolysis and loss of viscosity, and alkalies in strong concentration also tend to reduce viscosity. Another trial (F_7) was formulated by further decreasing the guar gum concentration. F_7 was able to sustained the drug release up to 24th hr. i.e., 94 % and 88 % of drug was released up to 24th hour in 0.1 N HCl and potassium phosphate buffer pH 6 respectively. The dissolution profile of F_1 to F_7 are shown in Fig. 3 & 4.

Table 2: Characterization of granules of F_1 - F_7.

F.No.	Angle of repose θ^0 ±S.D (n=3)	Loose bulk density (g/ml) ±S.D (n=3)	Tapped bulk density (g/ml) ±S.D (n=3)	% Compressibility ±S.D (n=3)	Hausner ratio ±S.D (n=3)
Pure drug	27.13±0.990	0.400±0.002	0.580±0.009	31.03±0.07	1.45±0.028
F_1	29.84±0.787	0.371±0.002	0.447±0.009	18.30±1.70	1.22±0.018
F_2	27.18±1.250	0.374±0.006	0.492±0.011	23.90±1.67	1.31±0.027
F_3	29.75±2.180	0.379±0.006	0.461±0.010	17.84±0.98	1.21±0.024
F_4	29.68±0.900	0.357±0.000	0.447±0.009	18.12±1.73	1.22±0.019
F_5	27.51±0.500	0.406±0.004	0.461±0.010	12.17±1.12	1.13±0.012
F_6	26.48±0.110	0.430±0.000	0.508±0.010	14.42±0.99	1.16±0.023
F_7	28.74±0.110	0.361±0.000	0.440±0.008	18.18±0.98	1.22±0.028

Table 3: Post compression evaluation of F_1 - F_7.

Formulation	Hardness (Kg/cm^2) ±S.D(n=6)	Thickness (mm) ±S.D (n=6)	Weight variation (mg) ±S.D(n=20)	Friability (%)	Drug content (%) ±S.D (n=3)
F_1	4.8±0.56	5.12±0.001	677±4.32	0.06	100±1.100
F_2	4.5±0.45	5.21±0.003	679±2.58	0.05	98.6±0.001
F_3	4.1±0.76	5.10±0.004	682±2.43	0.09	99.4±0.003
F_4	4.6±0.43	5.09±0.002	679±2.65	0.04	101.3±1.31
F_5	4.5±0.12	5.10±0.006	681±1.40	0.07	98.8±0.002
F_6	4.7±0.32	5.11±0.001	680±1.20	0.10	99.2±0.004
F_7	4.8±0.21	4.90±0.002	680±1.10	0.08	99.7±0.04

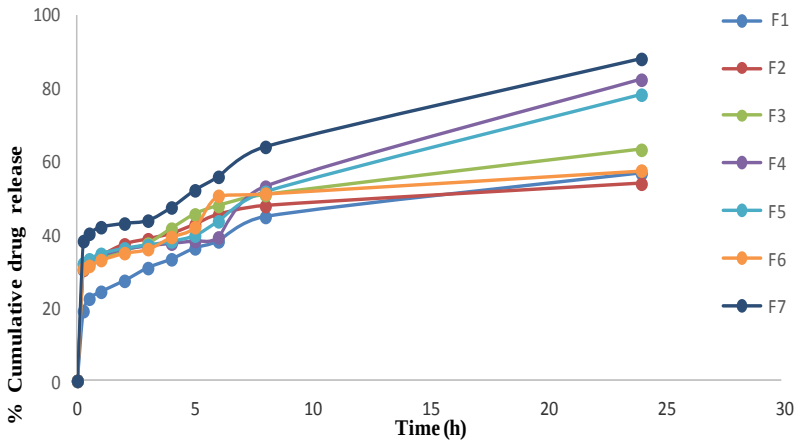


Fig. 3: *In vitro* release profile F_1 - F_7 in 0.1N HCl.

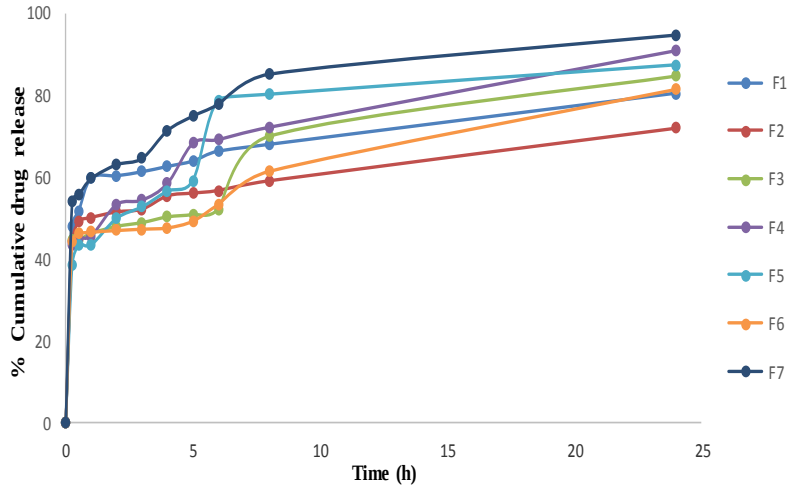


Fig. 4: *In vitro* release profile F_1-F_7 in Potassium phosphate Buffer pH 6.

***In-Vitro* Drug Release Kinetics:**

The curve fitting results of the release rate profile for the selected formulation was subjected to data analysis. It was found that the selected formulations were fitted into Korsmeyer-Peppas model, which is the best fitted model as per cumulative drug releasing data in 0.1 N HCl after 24 hours and also it fitted into First order model as per cumulative drug releasing data in potassium phosphate buffer pH 6 after 24 hours. From the Korsmeyer-Peppas equation and first order equation k and R values were calculated. The values are shown in Table 4 and Table 5 respectively. From Korsmeyer-Peppas equation model the 'n' value was found to be between 0.13 and 0.27, indicating that the mechanism of release in 0.1 N HCl is Quasi-fickian diffusion mechanism as the *n* values for these formulations were less than 0.5. From first order kinetic model the R value was found to be 0.93, indicating that the mechanism of releasing in potassium phosphate buffer pH 6 is Fick's first law diffusion mechanism. (Table 4&5) & (Fig. 5&6)

Table 4: Release kinetics data for F7 in 0.1 N HCl.

	Zero order	Korsmeyer-Peppas	Higuchi	First Order
$K_{0(Slope)}$	2.299376	0.1305		-0.044
R^2	0.4099	0.9327	0.6774	0.8601
	2.2994		K_1	0.102

Table 5: Release kinetics data for F_7 in potassium phosphate buffer pH 6.

	Zero order	Korsmeyer-Peppas	Higuchi	First Order
K0(Slope)	2.531237	0.1678	-	-0.033
R2	0.6711	0.8019	0.8432	0.9378
	2.5312		K_1	0.075

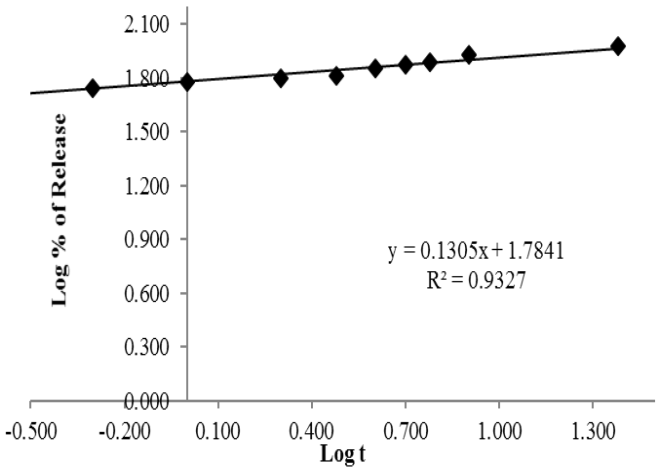


Fig. 5: Korsmeyer-Peppas Model for F_7 in 0.1 N HCl.

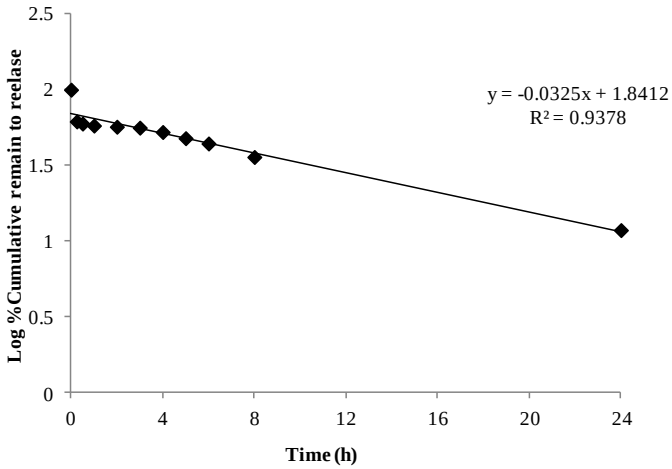


Fig. 6: First Order Release for F_7 in Potassium phosphate Buffer pH 6.

Accelerated Stability Studies:

Accelerated stability studies were carried out for the selected formulation (F_7) as per ICH guidelines for 1 months. The formulation showed good stability and values are under permissible limits. No considerable changes in drug release profiles were observed. Thus it can be concluded that the F_7 were found to be stable over a period of time and release the drug in controlled manner without dose dumping. (Table 6 &7) and (Fig. 7).

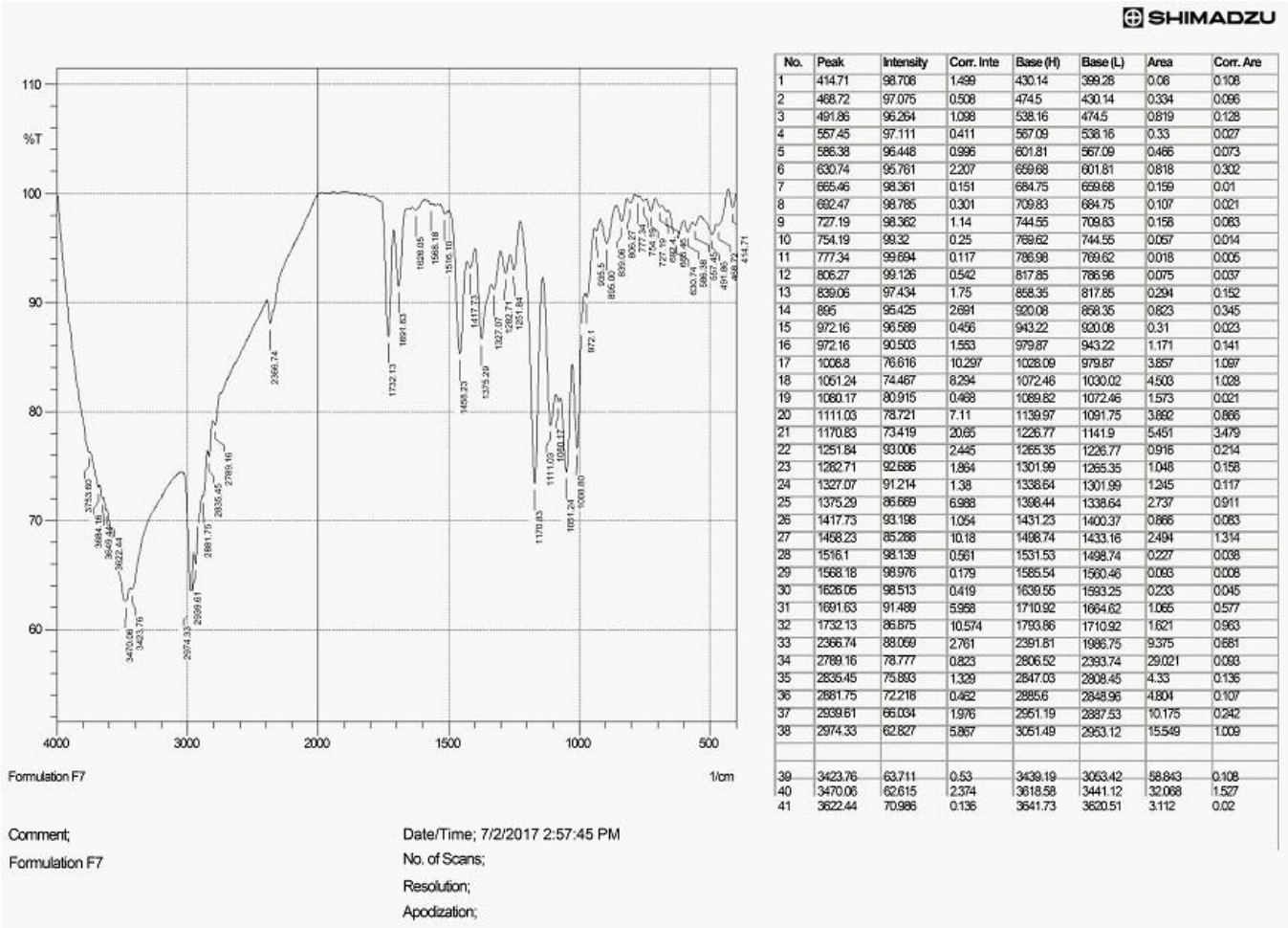
Table 6: Post compression parameters for F_7 tablet (Pre and Post accelerated stability study).

Code	Colour	Weight variation (mg) ±S.D(n=20)	Thickness mm (±SD) (n=6)	Hardness kg/cm^2(±SD)	Friability%
F_7 (Pre-study)	white	680±1.1	4.8±0.21	4.9±0.002	0.08
F_7 (Post-study)	white	679±1.1	4.8±0.4	4.9±0.003	0.08

Table 7: Post compression parameters for F_7 tablet (Pre and Post accelerated stability study).

Code	Drug content% ±SD (F_7)*	%CDR ±SD (F_7)* in 0.1N HCl at 24 h.	%CDR ±SD (F_7)* in Potassium Phosphate Buffer pH 6 at 24 h.
F_7	99.7±0.004	94.81±1.2	88.2±1.2
F_7	99.0±0.002	93.91±1.1	87.1±1.1

*n=3 (in Triplicate).



No.	Peak	Intensity	Corr. Inte	Base (H)	Base (L)	Area	Corr. Are
1	414.71	98.708	1.499	430.14	399.28	0.08	0.108
2	468.72	97.075	0.508	474.5	430.14	0.334	0.096
3	491.86	96.264	1.098	538.16	474.5	0.819	0.128
4	557.45	97.111	0.411	567.09	538.16	0.33	0.027
5	586.38	96.448	0.996	601.81	567.09	0.466	0.073
6	630.74	95.761	2.207	659.68	601.81	0.818	0.302
7	665.46	98.361	0.151	684.75	659.68	0.159	0.01
8	692.47	98.785	0.301	709.83	684.75	0.107	0.021
9	727.19	98.362	1.14	744.55	709.83	0.158	0.083
10	754.19	99.32	0.25	769.62	744.55	0.057	0.014
11	777.34	99.694	0.117	786.98	769.62	0.018	0.005
12	806.27	99.126	0.542	817.85	786.98	0.075	0.037
13	839.06	97.434	1.75	858.35	817.85	0.294	0.152
14	895	95.425	2.691	920.08	858.35	0.823	0.345
15	972.16	96.589	0.456	943.22	920.08	0.31	0.023
16	972.16	90.503	1.553	979.87	943.22	1.171	0.141
17	1006.8	76.616	10.297	1028.09	979.87	3.857	1.097
18	1051.24	74.467	8.294	1072.46	1030.02	4.503	1.028
19	1080.17	80.915	0.468	1069.82	1072.46	1.573	0.021
20	1111.03	78.721	7.11	1139.97	1091.75	3.892	0.866
21	1170.83	73.419	20.65	1226.77	1141.9	5.451	3.479
22	1251.84	93.006	2.445	1265.35	1226.77	0.916	0.214
23	1282.71	92.686	1.864	1301.99	1265.35	1.048	0.158
24	1327.07	91.214	1.38	1338.64	1301.99	1.245	0.117
25	1375.29	86.669	6.988	1398.44	1338.64	2.737	0.911
26	1417.73	93.198	1.054	1431.23	1400.37	0.866	0.083
27	1458.23	85.288	10.18	1498.74	1433.16	2.494	1.314
28	1516.1	98.139	0.561	1531.53	1498.74	0.227	0.038
29	1568.18	98.976	0.179	1585.54	1560.46	0.093	0.008
30	1626.05	98.513	0.419	1639.55	1593.25	0.233	0.045
31	1691.63	91.489	5.958	1710.92	1664.62	1.065	0.577
32	1732.13	86.875	10.574	1793.86	1710.92	1.621	0.963
33	2366.74	88.069	2.761	2391.81	1986.75	9.375	0.881
34	2789.16	78.777	0.823	2806.52	2393.74	29.021	0.093
35	2835.45	75.893	1.329	2847.03	2808.45	4.33	0.136
36	2881.75	72.218	0.462	2885.6	2848.96	4.804	0.107
37	2939.61	66.034	1.976	2951.19	2887.53	10.175	0.242
38	2974.33	62.827	5.867	3051.49	2953.12	15.549	1.009
39	3423.76	63.711	0.53	3439.19	3063.42	58.843	0.108
40	3470.06	62.615	2.374	3618.58	3441.12	32.068	1.527
41	3622.44	70.986	0.136	3641.73	3620.51	3.112	0.02

Fig 7: FTIR of F_7 tablet (post-study).

CONCLUSION

Preformulation studies, identification of API and drug excipient compatibility study by using FTIR did not show any interaction between API and excipients. Final formulation was developed based on trial and error basis and evaluated. From all the parameters studied, it can be concluded that formulation F_7 was found to be best regarding all the properties evaluated. The drug release was found to be within the limit as per USP at the end of 24th hour. The stability study indicated that the formulation F_7 was stable even after storing at 40±2^{0}C/75±5% RH for 1 month and have passed stability study. Thus the results of the present study clearly indicated a promising potential of extended release Clarithromycin tablets containing guar gum as rate controlling polymers (F_7) demonstrated slow release when compared with other formulations and could be used for effectively therapeutic action. Extended drug release following Korsmeyer-Peppas model kinetics and first order model kinetics of clarithromycin matrix tablets prepared from the guar gum can be successfully employed as a once daily oral extended drug delivery dosage form. From the above experimental data it can be concluded that a successful extended release drug delivery system for clarithromycin have been developed by using the polymer such as guar gum.

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