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Research Article

FORMULATION AND EVALUATION OF CLARITHROMYCIN IMMEDIATE RELEASE FILM COATED TABLETS

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ABSTRACT

The main goal of this study was to develop a stable formulation of antibiotic drug clarithromycin as an immediate- release tablet. The task of developing immediate release tablet is accomplished by using suitable diluents and superdisintegrants. Faster disintegration of the tablet administrated orally minimizes absorption time and improves its bioavailability in less time. The formulation development work was initiated with wet granulation method and a total of 8 formulations (F_1-F_8) were made. The formulated tablets were evaluated for various precompression parameters and post compression parameters like thickness, hardness, weight variation, friability, disintegration test, drug content uniformity and *in vitro* release studies. The formulation F_8 showed satisfactory physical parameters, and it was found to be stable among other formulations. Formulation F_8 was subjected to 3^2 randomized full factorial optimization studies and 9 formulations (OF_1-OF_9) were developed and evaluated for various precompression and post compression parameters. Among the entire optimized batches, formulation OF_7 has been selected for further studies; since it shows better results (i.e., faster disintegration time and rapid drug release) than other optimized batches. The drug release of clarithromycin IR tablet (OF_7) was found to be 101.62±0.48 at the end of 30 min.The tablets of OF_7 optimized batch was subjected to accelerated stability studies as per ICH guidelines and the results showed that there were no significant changes in the physical and chemical parameters studied. From this study, it was concluded that optimized clarithromycin tablet (OF_7) containing croscarmellose sodium (3.029%) and Pregelatinized starch (6.029%) showed better characteristics of immediate release tablets.

Keywords: Clarithromycin, Croscarmellose sodium, Immediate release, and Pregelatinized starch.

INTRODUCTION

Immediate release drug delivery system are based on single or multiple-unit reservoir or matrix system, which are designed to provide immediate drug levels in short period of time. Immediate release drug delivery is desirable for drugs having long biological half life, high bioavailability, lower clearance and lower elimination half life.

Clarithromycin is a macrolide antibiotic with broad spectrum of activity. It is given in the treatment of respiratory tract infections, skin and soft tissue infections. Clarithromycin may be given to eradicate *H. pylori* in treatment regimens for peptic ulcer diseases. The terminal half-life of Clarithromycin is reportedly about 3-4 hours. Clarithromycin possesses greater acid stability, improved pharmacokinetic properties, and fewer gastrointestinal side effects. The recommended dosage regimen for these types of infections in adult patients is 250 to 500 mg twice daily for 7-14 days of the immediate-release oral formulation of clarithromycin[1-3].The formulation development work was initiated with wet granulation method. Microcrystalline cellulose PH 102 was used as diluent. Povidone was used as the binder. Croscarmellose sodium and pre gelatinized starch were used as superdisintegrants. Talc and magnesium stearate were used as lubricant.

MATERIALS AND METHODS

Materials

Clarithromycin was procured as a gift sample from Anuh pharma private limited, Mumbai, India. Croscarmellose sodium and Avicel pH101 were procured from signet chemical pvt Ltd, Mumbai, India. Pregelatinised starch was procured from DMV Fonterra excipients, USA. Avicel pH102, brand name of MCC was supplied by Weiming Pharmaceuticals, Taipei, Taiwan. Povidone IP (K-30) was supplied by Nanberg, India. All other ingredients used were of Analytical grade.

Methods

Preparation of Clarithromycin Immediate Release Tablets

Clarithromycin 500 mg sifted through 30# was mixed with required quantities of 2.0% croscarmellose sodium sifted through 60# for 3-5 minutes, the blend was granulated by Kneading method or in FBP, using Povidone in isopropyl alcohol as binder, the wet coherent mass was dried in hot air oven at 60oC until the moisture content of granules is NMT 1% and passed through sieve # 20 to get the uniform particle size. The granules were mixed with Croscarmellose sodium, Pregelatinized starch and microcrystalline cellulose of required grade sifted through # 60 for 4-5 minutes. The above granules was lubricated with specified quantity of talc, aerosil for 2-3 minutes and finally mixed with Magnesium stearate manually using polyethylene bag for1-2 minutes. Precompression parameters (Angle of repose, Bulk density, Tapped density, Compressibility index, and Hausner's ratio) of the granules were evaluated before compression into tablets. The granules were compressed on 8 station rotary tablet press using 19.5 X 9.5 caplet punches. The weights of the tablets were kept constant, which were 850 mg for all formulations. The formulation of Clarithromycin tablets were presented in Table 1.

Film coating of Clarithromycin Tablets

Ethyl cellulose was dissolved in isopropyl alcohol in a stainless steel vessel and HPMC15 cps was dispersed in the ethyl cellulose solution. Dichloromethane was added to ethyl cellulose- HPMC solution and mixed well for 10 minutes. Quinoline yellow lake, titanium dioxide and talc were accurately weighed, passed through # 60, triturated in a mortar and transferred to above stirred solution and mixed well. Propylene glycol and ethyl vanillin was added to the above mixture and mixed well. The tablets were loaded in coating pan with baffles fixed and coated according to the standard parameters. Clarithromycin tablet was coated using the following ingredients mentioned in the Table 2.

Table 2: Formula of coating solution

Ingredients	Qty/500 Tablet (gm)
Hydroxy propyl methyl cellulose 15 cps	7.20
Ethyl cellulose	2.40
Titanium dioxide	2.20
Talc	1.175
Quinoline yellow (lake)	0.250
Ethyl vanillin	1.2
Propylene glycol	1.65
Dichloro methane	144ml
Iso propyl alcohol	144ml

Table 1: Formulation of Clarithromycin trial batches

Ingredients	F_1 (mg)	F_2 (mg)	F_3 (mg)	F_4 (mg)	F_5 (mg)	F_6 (mg)	F_7 (mg)	F_8 (mg)
Clarithromycin	500.00	500.00	500.00	500.00	500.00	500.00	500.00	500.00
Croscarmellose sodium	17.00	17.00	17.00	17.00	17.00	17.00	17.00	17.00
Povidone	-	-	21.00	34.25	35.00	35.00	35.00	35.00
Colloidal silicon dioxide	-	-	-	-	6.00	8.50	8.50	-
Hydroxy propyl cellulose	15.00	20.00	-	-	-	-	-	-
Microcrystalline cellulose PH101	235.70	229.30	230.00	220.00	-	-	-	-
Croscarmellose sodium	25.50	25.50	-	25.50	25.50	25.50	25.50	25.50
Microcrystalline cellulose PH112	-	-	39.45	-	-	-	-	-
Microcrystalline cellulose PH102	50.00	48.00	-	36.00	251.50	249.00	199.00	196.00
Pregelatinised starch	-	-	-	-	-	-	50.00	50.00
Talc	-	-	8.50	4.25	10.0	8.65	8.65	9.50
Colloidal silicon dioxide	2.55	3.82	4.30	4.50	-	-	-	9.50
Magnesium stearate	4.25	6.38	4.75	8.5	5.00	6.35	6.35	7.50
Isopropyl Alcohol	-	-	-	q.s	q.s	q.s	q.s	q.s
Purified water	q.s	q.s	q.s	-	-	-	-	-
Weight of each tablet	**850**	**850**	**850**	**850**	**850**	**850**	**850**	**850**

Optimization of trial batch (F_8) by full factorial design [4, 5]

In order to obtain "best" or an "optimized product" nine different formulations were generated using a 3^2 randomized full factorial. Based on preformulation study the amounts of croscarmellose sodium (X_1) and microcrystalline cellulose PH102 (X_2) were selected as the independent factors, studied at 3 levels each (-1, 0, +1). The percentage drug release (y_1) and disintegration time (y_2) were taken as dependent factors. Experimental trials were performed at all 9 possible combinations of X_1 and X_2. The formulations of all batches for factorial design are shown in Table 3.The Formulation of optimized trial batches was presented in Table 4.

Table 3: Formulation trials as per experimental design

Trial No.	Coded factor levels	
	X_1	X_2
I	-1	-1
II	-1	0
III	-1	1
IV	0	-1
V	0	0
VI	0	1
VII	1	-1
VIII	1	0
IX	1	1

Translation of coded levels in actual units			
Coded level	**-1**	**0**	**1**
X_1: CCS (%)	2	3	4
X_2:MCC102 (%)	21	23	25

Table 4: Formulation of optimized batches

Ingredients	Formulation code Qty/Tab (mg)								
	OF_1	OF_2	OF_3	OF_4	OF_5	OF_6	OF_7	OF_8	OF_9
Clarithromycin	500	500	500	500	500	500	500	500	500
Croscarmellose sodium	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0
Povidone	35.00	35.00	35.00	35.00	35.00	35.00	35.00	35.00	35.00
Croscarmellose sodium	25.25	25.25	25.25	25.50	25.50	25.50	25.75	25.75	25.75
Microcrystalline cellulose PH102	194.5	196.5	198.5	194.5	196.5	198.5	194.5	196.5	198.5
Pregelatinised starch	51.75	49.75	47.75	51.5	49.5	47.50	51.25	49.25	47.25
Talc	9.50	9.50	9.50	9.50	9.50	9.50	9.50	9.50	9.50
Colloidal silicon dioxide	9.50	9.50	9.50	9.50	9.50	9.50	9.50	9.50	9.50
Magnesium stearate	7.50	7.50	7.50	7.50	7.50	7.50	7.50	7.50	7.50
Isopropyl alcohol	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Weight of each tablet	**850**	**850**	**850**	**850**	**850**	**850**	**850**	**850**	**850**

Chemical compatibility studies by FT-IR

The crude drug sample, drug-excipient mixtures of the formulation were chosen for the study. Samples were compressed with potassium chloride and transformed into disk[6]. The disk was scanned between 4000-400 cm^{-1} in a SHIMADZU FT-IR (IR Affinity-1) spectrophotometer.

Pre-compression parameters

The granules were evaluated for pre compression parameters like angle of repose, bulk density, tapped density, compressibility index and Hausner's ratio. The angle of repose was determined by funnel method[7].Bulk and tapped density was determined using digital bulk density apparatus[8, 9] .The compressibility index of the granules was

determined by Carr's compressibility index and the Hausner's ratio was calculated by using the formula:

Hausner's Ratio = Tapped density/ Bulk density.

Carr's index (%) = [(TD-BD) / TD] ×100.

TD = Tapped density, BD = bulk density.

Moisture content

Initially 5g of weighed granules were taken and kept for drying at 105º C for a required time in an oven. Then the granules were removed and again reweighed and the final weight is noted. The difference in the weights was noted as moisture content.

Evaluation of Clarithromycin tablets

The dimensions of the tablet like thickness, length were measured using Vernier-caliper. Ten tablets were selected randomly for this test and the average value was reported. Hardness of tablet was determined by Monsanto hardness tester. In the weight variation test, twenty tablets were selected at random and average weight was calculated. Then individual tablets were compared with the average weight**.** Disintegration test was carried out by using Disintegration test apparatus. The time taken for the tablet to disintegrate completely was noted. Friability test was done by Roche friabilator. Ten tablets were weighed and were subjected to the combined effect of attrition and shock by utilizing a plastic chamber that revolve at 25 rpm dropping the tablets at distance of 6 inch with each revolution. After 100 revolutions, the tablets were de dusted and reweighed. The percentage friability was calculated[10-12]

Assay (By HPLC) [13, 14]

Preparation of standard stock solution

62.50 mg of clarithromycin USP working standard was accurately weighed and transferred in a 100ml volumetric flask and dissolved using methanol, and made up to the volume using mobile phase.

Preparation of standard solution

10 ml of standard stock solution was taken in a 50ml volumetric flask and made up to a volume with mobile phase. This solution contains about 125µg of clarithromycin per ml.

Preparation of resolution solution

62.5 mg of clarithromycin USP related compound A was weighed in a 50ml volumetric flask and dissolved using methanol. Then 10 ml of this solution and 10 ml of standard stock solution was transferred to a 50 ml volumetric flask and made up to the volume with mobile phase.

Preparation of sample solution

20 tablets were weighed and crushed to a fine powder, then weighed 438.0 mg of tablet powder (i.e., equivalent to about 250 mg of clarithromycin) and transferred to 200 ml volumetric flask. To this 75 ml of methanol was added, sonicated for 30 minutes and diluted with methanol to volume, mixed well, and the solution is allowed to settle insoluble matter. Then 5ml of supernatant solution is transferred to a 50 ml volumetric flask and made up to volume with mobile phase and mixed well. The solution is passed through filter paper and used.

Chromatographic conditions: Column: Stainless steel column (250×4.6mm) packed with Octa decyl silane (C18) bonded to porous silica, Flow rate: 1.0 ml/min, Column oven temperature: 50^{o}C, Injection volume: 50µL, Wave length: 210 nm

Procedure:

50 microlitres of filtered portion of the resolution solution, standard solution and sample solution were separately injected into the HPLC system. The chromatogram was recorded and the responses were measured for the major peaks. The content per tablet was calculated using the following expression

Content of tablet=(AT/AS) ×(WS/100) ×(10/50)×(200/WT)×(5/50) ×(P/100)× Avg.wt ×100

Where, AS is average area of the clarithromycin peak in standard solution, AT is Area of the clarithromycin peak in sample solution, WS is Weight of clarithromycin taken for standard in g, WT is Weight of clarithromycin taken for sample in g, P is Percent purity of clarithromycin on as such basis respectively.

***In Vitro* dissolution studies[13, 14]**

Dissolution parameters

Apparatus: Dissolution Apparatus USP Type – II (Paddle), Speed: 50 RPM, Medium: 900 ml of Acetate buffer pH 5.0, Temperature: 37°C ± 0.5°C, Time: 30 Minutes

Preparation of standard solution

62.50 mg of clarithromycin USP working Standard was accurately weighed and transferred in a 100ml volumetric flask and dissolved using methanol, and made up to the volume using dissolution medium. From the above solution, 10 ml was taken in a 50 ml volumetric flask and made up to a volume with mobile phase.

Preparation of sample solution

Apparatus was set as per above conditions, one tablet was placed in each of the six dissolution vessel and the dissolution test was started. After completion of 30 minutes, 20 ml of the solution was withdrawn from dissolution bowl. The filtrate was collected after discarding first few ml of the filtrate**.** From this 5 ml of the filtrate was diluted to 25 ml with mobile phase.

Chromatographic conditions

Apparatus: HPLC, Column: Stainless steel column (250×4.6mm) packed with Octa decyl silane (C18) bonded to porous silica, Flow rate: 1.0 ml/min, Column oven temperature: 50^{o}C, Injection volume: 50µL, Wave length: 210 nm

Procedure

50 microlitres of filtered portion of the standard solution and sample solution were separately injected into the HPLC system. The chromatogram was recorded and the responses were measured for the major peaks. The amount of drug released was calculated in percentage with respect to label claim by using the following expression.

% Drug released = (AT/AS)×(WS/100)×(10/50)×(900/1)×(25/5) ×(P/100)

Stability studies[15]

As per ICH guidelines, tablets were packed in Alu-Alu blister and required blisters were placed into the stability chamber by storing at 40±2°C/75±5%RH over a period of 3 months. The samples were analyzed at 0, 1, 2 and 3 months for Physical parameters (Description, Hardness, Thickness, DT), Physiochemical parameter (*In vitro* Dissolution Study) and Chemical parameter (Assay).

RESULTS AND DISCUSSION

The present study of clarithromycin film coated tablets were developed with a view to deliver the drug immediately. The formulation development work was initiated with wet granulation method and a total of 8 formulations (F_1-F_8) were made. The formulated tablets were evaluated for various precompression parameters and post compression parameters like thickness, hardness, weight variation, friability, disintegration test, drug content uniformity and *in vitro* release studies. All the formulations except F_8 failed in either precompression or post compression parameters. The formulation F_8 showed satisfactory physical parameters, and it was found to be stable among other formulations. Hence formulation F_8 was subjected to 3^2 randomized full factorial optimization studies and 9 formulations (OF_1-OF_9) were developed from that. Based on preformulation studies, the amounts of croscarmellose sodium (X_1) and microcrystalline cellulose PH102 (X_2) were selected as the independent factors, studied at 3 levels each (-1, 0, +1). The percentage drug release (y_1) and disintegration time (y_2) were taken as dependent factors.

The prepared clarithromycin granules were evaluated for the following parameters, which includes Angle of repose, bulk density, tapped density, compressibity Index and hausner's ratio. The values of compressibility index, hausner's ratio and angle of repose of all the batches indicate a good flow property of the granules. The results are presented in Table 5.

Table 5: Precompression parameters for optimized formulations

Formulationcode	Angle of repose(θ)	Bulkdensity(g/cc)	Tappeddensity(g/cc)	Compressibilityindex (%)	Hausner'sratio	Moisture content (%)
OF_1	30.10±0.60	0.483±0.015	0.568±0.011	14.96±0.01	1.17±0.01	0.85±0.01
OF_2	32.43±0.68	0.487±0.005	0.554±0.007	12.09±0.05	1.13±0.04	0.88±0.03
OF_3	32.33±0.27	0.510±0.015	0.585±0.015	12.82±0.10	1.14±0.02	0.82±0.05
OF_4	31.40±0.73	0.532±0.015	0.610±0.035	14.66±0.02	1.14±0.01	0.77±0.01
OF_5	30.44±0.51	0.532±0.001	0.595±0.013	10.58±0.02	1.11±0.01	0.83±0.05
OF_6	30.33±.34	0.534±0.012	0.603±0.011	11.44±0.03	1.12±0.10	0.88±0.05
OF_7	34.54±0.29	0.577±0.025	0.647±0.062	12.17±0.02	1.12±0.08	0.87±0.05
OF_8	33.61±0.15	0.575±0.013	0.662±0.023	13.14±0.01	1.15±0.06	0.79±0.02
OF_9	32.51±0.11	0.576±0.014	0.656±0.016	12.19±0.01	1.13±0.03	0.86±0.01

All the values are expressed as mean ± SD (n=3)

The spectra of the crude drug sample and drug-excipient mixtures were compared to check the incompatibility problems. When the characteristic peak of drug was compared with the drug-excipient mixture, it was found that the same fundamental peaks were also present in the drug-excipient combinations indicating there was no interaction between drug and excipient used.

The tablets of different formulation were subjected to various evaluation tests such as thickness, disintegration and drug content. All the tablets possessed uniform thickness, hardness and weight. The disintegration of all batches (OF_1 to OF_9) of clarithromycin are found within limits (2.08-3.06 min).The drug content of clarithromycin coated tablets was found to be uniform among all the formulations which ranges from 99.99% – 104.54%. The values of optimized tablet parameters in above all batches are within the limits. The evaluation results of clarithromycin IR tablets were given in Table 6.

Table 6: Post compression parameters for optimized formulations

Formulationcode	Thickness (mm)*	Hardness (kg/cm²)*	Weight variation test* (mg)	Disintegration test*(min)	Assay#(%)
OF_1	6.12±0.026	9.3±0.67	876.10±0.94	3.12±0.04	100.04±0.07
OF_2	6.17±0.031	9.5±0.35	876.56±1.44	3.06±0.06	99.99±0.01
OF_3	6.13±0.025	10.0±0.61	876.03±1.23	3.27±0.05	102.99±0.01
OF_4	6.19±0.065	10.0±0.5	874.75±1.35	2.53±0.023	101.99±0.01
OF_5	6.16±0.031	9.5±0.5	875.03±0.08	2.25±0.018	104.54±0.02
OF_6	6.11±0.053	9.5±0.35	874.0±1.12	2.24±0.01	103.30±0.63
OF_7	6.17±0.064	9.5±0.612	876.06±1.05	2.16±0.02	101.69±0.01
OF_8	6.13±0.039	9.5±0.35	875.89±1.08	2.08±0.04	103.01±0.04
OF_9	6.14±0.037	9.5±0.35	876.55±0.64	1.55±0.05	103.68±0.01

All the values are expressed as * mean ± SD (n=6); # Mean ± SD (n=3)

Dissolution profile of optimized coated tablets were found to be similar with innovator drug dissolution profile. The results are presented in Table 7. Among the entire optimized batches, formulation OF_7 has been selected as best formulation for calculating similarity factor since it shows faster disintegration time and rapid drug release. The drug release of clarithromycin IR tablet(OF_7) was found to be 70.83%, 84.96%, 95.45%, 98.46%, and 101.62% at 5^{th}, 10^{th}, 15^{th}, 20^{th}, 30^{th} min respectively. The drug release of innovator product was found to be 80.88%, 95.46%, 97.55%, 99.34% and 102.56% at 5^{th},10^{th},15^{th},20^{th} ,30^{th} minute respectively.

Table 7: Comparative dissolution study of clarithromycin optimized coated tablets with innovator product

Formulation code	Cumulative percentage drug release(min)				
	5	**10**	**15**	**20**	**30**
OF_1	70.28±0.62	83.61±0.65	95.91±0.96	97.56±0.21	99.38±0.23
OF_2	69.04±0.613	83.19±0.64	94.67±0.64	96.73±0.36	98.21±0.56
OF_3	68.65±0.649	82.59±0.63	94.76±0.54	96.91±0.15	98.57±0.18
OF_4	70.59±0.651	84.68±0.54	95.03±0.48	98.21±0.65	100.46±0.35
OF_5	69.19±0.16	83.31±0.25	95.27±0.76	97.36±0.65	101.15±0.27
OF_6	68.59±0.621	82.11±0.46	94.98±0.56	96.02±0.64	99.83±0.74
OF_7	70.83±0.354	84.96±0.57	95.45±0.54	98.46±0.66	101.62±0.48
OF_8	69.54±0.633	83.63±0.56	94.86±0.64	96.08±0.67	100.28±0.13
OF_9	68.73±0.458	82.77±0.68	93.88±0.26	96.46±0.64	101.14±0.25
Innovator	80.88±0.04	95.46±0.14	97.55±0.41	99.34±0.23	102.56±0.34

All the values are expressed as * mean± SD (n=6)

The dissimilarity factor f_1 value of 5.147 and similarity factor f_2 value of 59.658 indicates that the two products were similar in *in-vitro* drug release. The formulation OF_7 shows the dissimilarity factor f_1 and similarity factor f_2 values within the specified limits (i.e., 5.147 and 59.658) when compared with the innovator product. Hence, formulation OF_7 was selected for stability studies. The comparative release profiles of formulation OF_7 and the innovator was presented in Fig.1.

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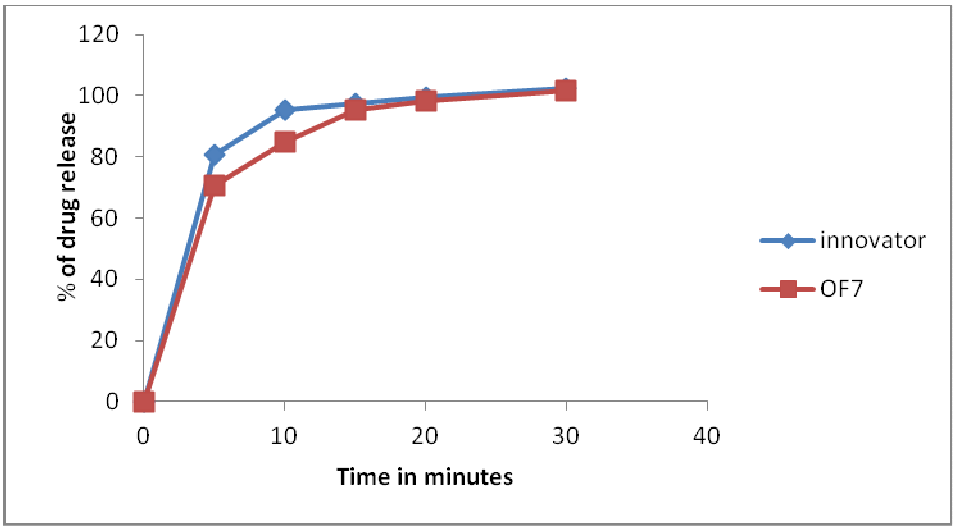

Fig. 1: Comparative *in vitro* release profile of Clarithromycin optimized coated tablet (OF_7) with innovator product

The clarithromycin immediate release tablets (OF_7) was subjected for stability studies at 40˚±2˚C/ 75 %±5%RH for three months. The results were found to be satisfactory. The stability study data's were presented in Table 8.

Table 8: Stability study data of OF_7 formulation

Post compression parameters	Storage condition40˚C ± 2˚C / 75% RH ± 5% RH			
Description	Initial *	1st month *	2nd month *	3rd month *
Thickness(mm)	6.17±0.037	6.17±0.12	6.16±0.34	6.16±0.02
Hardness(Kg/cm²)	10.0±0.09	9.5±0.77	9.5±0.44	9.5±0.09
Disintegration time (sec)	2.16±0.046	2.20±0.06	2.14±0.08	2.06±0.05
Assay (%)	101.69	100.27	99.74	96.88
Percentage drug release at 30 min (%)	101.62±0.48	101.03±0.06	100.67±0.62	99.73±0.12

*yellow coloured film-coated tablet.

CONCLUSION

Clarithromycin immediate release film coated tablets were formulated by wet granulation method using the selected excipient quantities. The formulated tablets were tested for both pre-compression parameters, post compression parameters as per requirements of standards performed and found to be within the limits. The formulated trial batch F_8 was taken for optimization by full factorial design. i.e., croscarmellose sodium (X_1) and microcrystalline cellulose sodium (X_2) as 2 independent variables at 3 levels -1, 0 and +1. Optimized batches were coded as OF_1, OF_2, OF_3, OF_4, OF_5, OF_6, OF_7, OF_8 and OF_9. Similarity was found in the results of *in vitro* dissolution study for all the optimized formulations with innovator product.

During the optimization of formulation it was observed in dissolution study that by decreasing the concentration of diluent and by increasing the concentration of disintegrant an increasing release profile was achieved. Simultaneously, pre gelatinized starch was increased by decreasing the concentration of diluent in OF_7 formulation. Among the entire optimized batches, formulation OF_7 has been selected for calculating similarity factor with the innovator, since it shows better results (i.e., faster disintegration time and rapid drug release) than other optimized batches. The dissimilarity factor f_1 value of 5.147 and similarity factor f_2 value of 59.658 indicates that the two products were similar in *in vitro* drug release. The tablets of OF_7 optimized batch subjected to accelerated stability studies revealed that there were no significant changes in the physical and chemical parameters even after storing at 40±2°C/75±5%RH for 3 months.

From this study, it was concluded that optimized clarithromycin tablet (OF_7) containing croscarmellose sodium (3.029%) and Pregelatinized starch (6.029%) could be successfully manufactured in developing clarithromycin immediate release tablets for the effective treatment of respiratory tract infections.

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