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Research Article

Formulation and Evaluation of Cefaclor Extended-Release Tablet

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Abstract

Over past 30 years as the expanse and complication involved in marketing new drug entities have increased, with concomitant recognition of the therapeutic advantages of controlled drug delivery, greater attention has been focused on development of extended or controlled release drug delivery systems.

In the present research work an attempt has been made to optimize, formulate and characterize extended-release tablet of Cefaclor. The preformulation studies were performed for the drug (e.g., physico-chemical properties, melting point, solubility etc.). The drug had shown the results under standard specifications. UV spectroscopic analytical method was also performed for quantitative determinations by plotting standard curve. Before this the pure drug was also scanned for the λ max value at different concentrations.

The pre-compressions parameters and the post compression parameters for the nine formulated tablets were performed. The drug release study of the selected formulations EF3, EF6 and EF9 was performed as those formulations has shown the results within pharmacopoeia limits. The Formulation EF9 was then taken for release kinetic study as it has shown best results among the other three formulations. So, it confirms the drug release by Higuchi diffusion mechanism. From the results, conclusion can be drawn that the formulation consisting 10-12% concentration of hydroxypropyl methyl cellulose K4-M with 1% microcrystalline cellulose and 25% of lactose are considered as ideal for the optimized extended-release tablet formulation for Cefaclor.

Keywords: Extended release, Cefaclor, Higuchi diffusion mechanism, PBP, bacterial cell wall synthesis.

INTRODUCTION:

In recent year Extended Release (ER) dosage forms continue to draw attention in the search for improved patient compliance and decreased incidence of adverse drug reactions. Extended release, prolonged action-controlled release, sustained action, timed release, depot and repository dosage forms are terms used to identify drug delivery system that are designed to achieve or prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose.¹

The main objective of the present research work was to optimize, formulate and characterize extended-release tablet of Cefaclor. This drug has low half-life of 0.5 to 1 hr and which is rapidly eliminated. So, cefaclor is lacking to maintain its concentration at site of action. Conventionally so we found it as excellent candidate for extended-release oral drug delivery system. Hence extended-release oral drug delivery of cefaclor will be able to maintain therapeutic concentration at the site of action.

MATERIAL AND METHOD:

Material: Cefaclor was received as a gift sample from Plethico Pharmaceuticals Limited, Indore(M.P.).

Hydroxy propyl methyl cellulose HPMC K-100M, Hydroxy propyl methyl cellulose HPMC E-5, Hydroxy propyl methyl cellulose HPMC K-4M and Microcrystalline cellulose were received from Finar Scientific. Further chemicals used were of analytical grade.

Methods: The Cefaclor ER tablet was prepared by using direct compression method. All the ingredients except Magnesium Stearate and Aerosil were passed through sieve No: 40 Cefaclor ER Tablets weighed and mixed for 15 min. and finally blended well in ascending order of their weights. Magnesium Stearate and Aerosil were passed through sieve No: 60 and mixed it to the above blend and compressed in a 16-station automatic punching machine with a punch size of 6 mm.

Table 1: Composition of Extended-Release Tablet of Cefaclor

S. No.	Ingredients	Formulations								
		EF1	EF2	EF3	EF4	EF5	EF6	EF7	EF8	EF9
1	Cefaclor	375	375	375	375	375	375	375	375	375
2	HPMC K-100M	45	55	65	-	-	-	-	-	-
3	HPMC E-5	-	-	-	45	55	65	-	-	-
4	HPMC K4-M	-	-	-	-	-	-	45	55	65
5	Lactose	170	160	150	170	160	150	170	160	150
6	Magnesium Stearate	2	2	2	2	2	2	2	2	2
7	Microcrystalline cellulose	6	6	6	6	6	6	6	6	6
8	Aerosil	2	2	2	2	2	2	2	2	2
	Total	600	600	600	600	600	600	600	600	600

Evaluation of prepared tablets:**Weight variation:**

It was carried out to ensure the proper amount of drug in each tablet. 20 tablets were weighed individually with the help of analytical balance. The average weight was calculated and the percent weight variation was calculated with the help formula.

% Weight Variation = (Individual weight - Average weight) / Average weight x 100

The hardness of the tablet was determined with the help of Monsanto hardness tester and expressed in kg/cm².

Thickness variation:

Ten tablets from each formulation were taken randomly and their thickness was measured with a micrometer screw gauge.

Friability:

Tablets equivalent to 6.5 gm were weighed and placed into the apparatus. They were exposed to rolling and repeated shocks as they fall from six inches in each turn within the apparatus. After 4 minutes or 100 revolutions, the tablets were reweighed and the loss due to abrasion was measured. Not more than 1% of the weight of the tablets is acceptable.

% Friability = (W1 - W2) / W1 x 100

Here, W 1 is the initial weight of tablet and W 2 is the final weight of tablet.

Content of Active Ingredients:

Ten tablets were powdered and weighed by pestle in a mortar, a quantity of powder equivalent to 375 mg of Cefaclor was taken in to a volumetric flask with the solvent. The content of the flask was sonicated for 10 min. The Cefaclor content was estimated by UV method at 264 nm after appropriate dilutions. The mean percent drug content was calculated as an average of three determinations.

In Vitro Dissolution or Drug Release Studies:

The *in vitro* dissolution of extended-release formulations was determined using USP XXIII (basket method) dissolution apparatus. The basket was allowed to rotate at a speed of 100 rpm and temperature of 37 ± 0.5°C was maintained. The dissolution medium used was 900 ml of 0.1N HCl (pH 1.2) for the initial 2 hours followed by study in simulated intestinal fluid Phosphate buffer solution (pH 6.8). Aliquots (5 ml) of sample were collected at predetermined time intervals (0.5, 1, 1.5, 2, 2.5, 3, 4, 5, 6 and 8 hrs) from the dissolution apparatus and it was replaced with equal volume of fresh dissolution medium. The aliquots withdrawn were filtered through 0.45µm Millipore filters. The concentration

of Cefaclor in the dissolution media was estimated by UV method at 264 nm. Drug concentration was calculated from the standard calibration curve and expressed as cumulative percent drug dissolved. The release studies were performed in replicates of three.

Release kinetics studies:

To study the release kinetics and mechanism of release *in-vitro* release data was applied to kinetic models such as zero order (Cumulative % drug release vs. time), first order (Log Mean % drug unreleased vs. time), Higuchi (Mean % cumulative drug release vs. square root of time) and Korsemeyer-Peppas (Log mean % cumulative drug release vs. Log time) using Microsoft Excel software and the regression values (R²) were calculated.

Stability Studies:

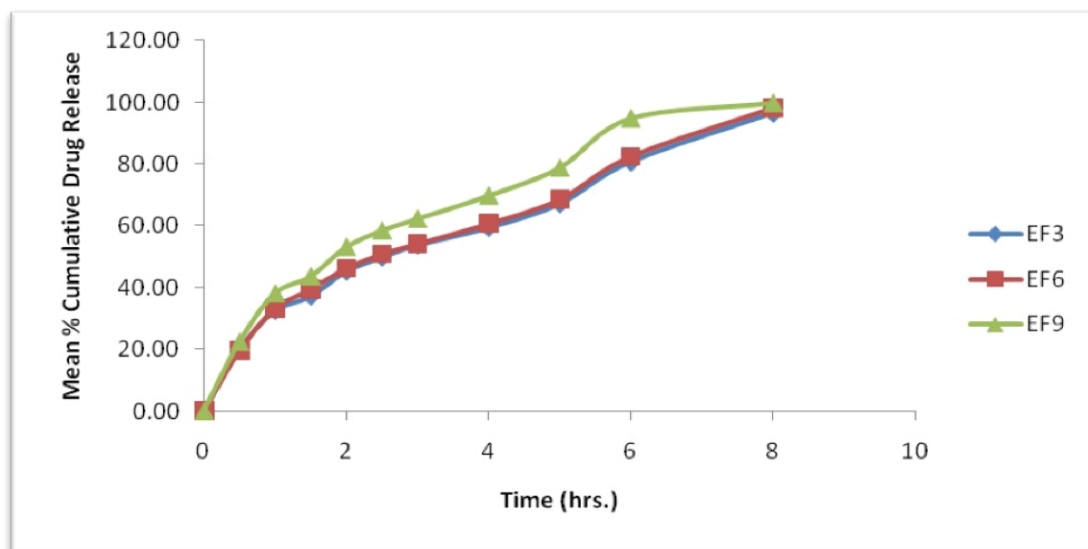
Stability is defined as the capacity of the drug product to remain within specifications established to ensure its identity, strength, quality and purity. Most recently a guideline issued by the International Conference on Harmonization indicates that the purpose of stability testing is to provide evidence on how the quality of a drug substance or the drug product varies with time under the influence of variety of environmental factors, such as temperature, humidity and light, and enables recommended storage conditions, retest periods, and shelf life to be established.

RESULTS:**Table 2: Pre-compression Parameters for Extended-Release Tablets**

S. No.	Formulations	Bulk Density($\pm$ sd)	Tapped Density($\pm$ sd)	Carr's Index($\pm$ sd)	Hauser's Ratio($\pm$ sd)	Angle of Repose($\pm$ sd)
1.	EF1	0.48 $\pm$ 0.12	0.56 $\pm$ 0.04	13.82 $\pm$ 0.19	1.16 $\pm$ 0.04	25.97 $\pm$ 0.43
2.	EF2	0.48 $\pm$ 0.10	0.55 $\pm$ 0.07	12.25 $\pm$ 0.16	1.14 $\pm$ 0.02	25.89 $\pm$ 0.37
3.	EF3	0.47 $\pm$ 0.11	0.55 $\pm$ 0.13	14.08 $\pm$ 0.08	1.16 $\pm$ 0.07	25.44 $\pm$ 0.29
4.	EF4	0.46 $\pm$ 0.13	0.53 $\pm$ 0.06	12.71 $\pm$ 0.14	1.15 $\pm$ 0.03	25.84 $\pm$ 0.47
5.	EF5	0.48 $\pm$ 0.08	0.56 $\pm$ 0.16	13.82 $\pm$ 0.22	1.16 $\pm$ 0.05	25.92 $\pm$ 0.51
6.	EF6	0.47 $\pm$ 0.14	0.54 $\pm$ 0.12	12.48 $\pm$ 0.18	1.14 $\pm$ 0.02	24.40 $\pm$ 0.27
7.	EF7	0.44 $\pm$ 0.07	0.51 $\pm$ 0.11	13.21 $\pm$ 0.07	1.15 $\pm$ 0.01	24.72 $\pm$ 0.19
8.	EF8	0.42 $\pm$ 0.12	0.48 $\pm$ 0.08	11.95 $\pm$ 0.17	1.14 $\pm$ 0.06	23.60 $\pm$ 0.42
9.	EF9	0.40 $\pm$ 0.16	0.47 $\pm$ 0.14	14.35 $\pm$ 0.26	1.17 $\pm$ 0.03	24.52 $\pm$ 0.23

Data wear expressed as Mean $\pm$ sdSD=Standard derivation All values are average of three determinations (n=3)**Table 3: Evaluation of Formulated Tablets (Post Compression Parameters)**

S. No.	Formulations	Average Weight Variation (mg) $\pm$ sd	Hardness (Kg/Cm ²) $\pm$ sd	Friability (%) $\pm$ sd	Content Uniformity(% $\pm$ sd)	Thickness(mm) $\pm$ sd
1.	EF1	605 $\pm$ 0.12	7.8 $\pm$ 0.45	1.13 $\pm$ 0.05	99.64 $\pm$ 0.14	5.59 $\pm$ 0.04
2.	EF2	602 $\pm$ 0.10	8.7 $\pm$ 0.37	0.16 $\pm$ 0.06	99.82 $\pm$ 0.09	5.65 $\pm$ 0.02
3.	EF3	601 $\pm$ 0.11	9.8 $\pm$ 0.32	0.17 $\pm$ 0.02	99.56 $\pm$ 0.27	5.72 $\pm$ 0.07
4.	EF4	601 $\pm$ 0.16	7.6 $\pm$ 0.41	1.18 $\pm$ 0.04	99.97 $\pm$ 0.07	5.61 $\pm$ 0.03
5.	EF5	599 $\pm$ 0.18	8.2 $\pm$ 0.53	0.38 $\pm$ 0.08	99.42 $\pm$ 0.31	6.17 $\pm$ 0.5
6.	EF6	602 $\pm$ 0.21	9.2 $\pm$ 0.36	0.41 $\pm$ 0.05	99.39 $\pm$ 0.28	5.64 $\pm$ 0.02
7.	EF7	605 $\pm$ 0.12	8.1 $\pm$ 0.24	1.25 $\pm$ 0.04	99.12 $\pm$ 0.43	5.59 $\pm$ 0.01
8.	EF8	600 $\pm$ 0.22	8.9 $\pm$ 0.34	0.37 $\pm$ 0.07	99.46 $\pm$ 0.60	5.60 $\pm$ 0.04
9.	EF9	603 $\pm$ 0.11	9.6 $\pm$ 0.23	0.28 $\pm$ 0.03	99.95 $\pm$ 0.04	5.71 $\pm$ 0.06

**Figure 1: In Vitro Drug Release from Extended-Release Layer of Tablet****Table 4: Drug Release studies for Extended-Release Layer of tablet**

S. No.	Formulations	Mean Percent Cumulative Drug Released in Time (Hrs.) Mean= $\pm$ sd (n=3)										
		0	0.5	1	1.5	2	2.5	3	4	5	6	8
1	EF3	0	19.86 $\pm$ 0.04	32.46 $\pm$ 0.11	37.15 $\pm$ 0.42	45.19 $\pm$ 0.31	49.76 $\pm$ 0.26	53.69 $\pm$ 0.18	59.36 $\pm$ 0.08	67.06 $\pm$ 0.45	80.63 $\pm$ 0.21	96.45 $\pm$ 0.24
2	EF6	0	19.51 $\pm$ 0.14	33.23 $\pm$ 0.24	39.53 $\pm$ 0.18	46.25 $\pm$ 0.27	50.93 $\pm$ 0.42	54.24 $\pm$ 0.27	60.76 $\pm$ 0.34	68.63 $\pm$ 0.29	82.53 $\pm$ 0.18	98.34 $\pm$ 0.14
3	EF9	0	22.43 $\pm$ 0.07	38.19 $\pm$ 0.14	43.71 $\pm$ 0.17	53.16 $\pm$ 0.22	58.54 $\pm$ 0.31	62.34 $\pm$ 0.12	69.84 $\pm$ 0.28	78.89 $\pm$ 0.34	94.86 $\pm$ 0.09	99.72 $\pm$ 0.07

Table 5: Results of Release Kinetic Studies

Formulation	Zero order(R ²)	First order(R ²)	Higuchi's plot(R ²)	Korsemeyer's Peppas's (n)	Hixson Crowell
EF9	0.895	0.839	0.991	0.38	0.96

Figure 2: Higuchi Model for Formulation EF9

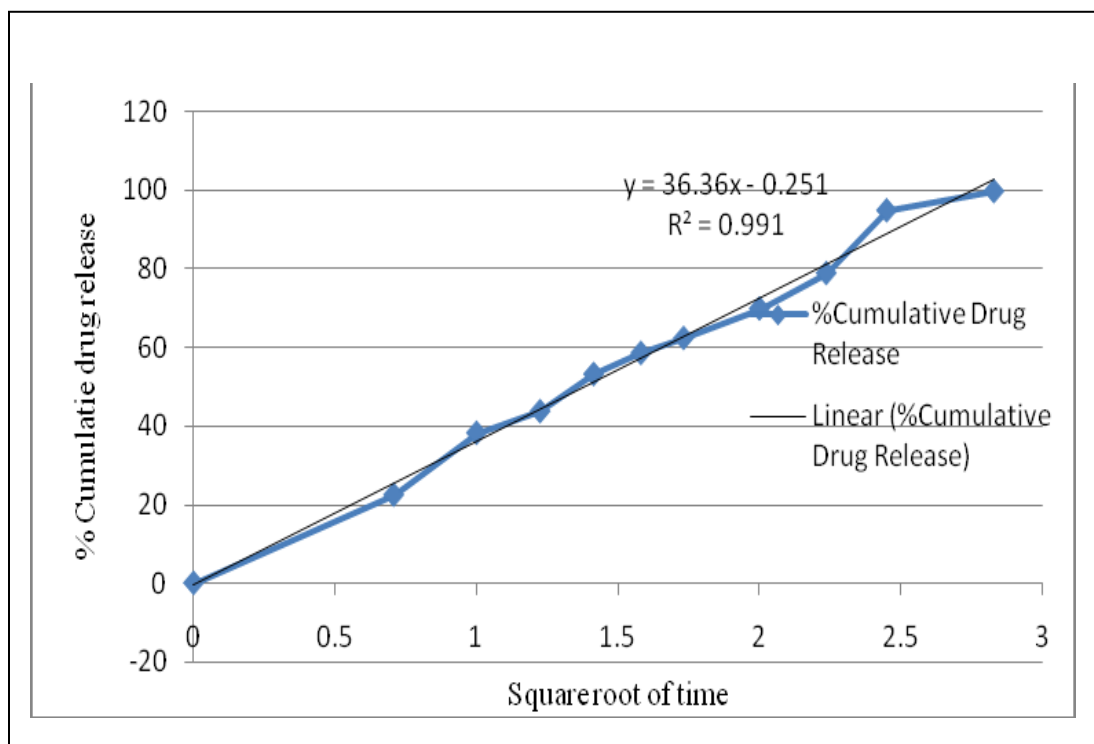


Table 6: Percent Drug Content of Extended-Release Formulation EF9

Optimized Formulation	Drug content (%)		
	Initially (0 days) (±sd)	After 15 days(±sd)	After 30 days(±sd)
EF9	98.33 ± 0.67	97.55 ± 0.89	97.10 ± 0.48

DISCUSSION:

In the present research work extended-release tablet of Cefaclor were successfully formulated and characterized. The drug had shown the results under standard specifications. From the results, conclusion can be drawn that the formulation consisting 10-12% concentration of hydroxy propyl methyl cellulose K4-M with 1% microcrystalline cellulose and 25% of lactose are considered as ideal for the optimized extended-release tablet for Cefaclor.

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