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Research Article

FORMULATION, DEVELOPMENT AND EVALUATION OF CEFACLOR EXTENDED RELEASE MATRIX TABLET

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ABSTRACT

Cefaclor is a second generation cephalosporin antibiotics chemically related to penicillins widely used in treatment of respiratory, urinary and skin infections most affective against gram negative organism. The objective of this work is to retardant polymers were employed with varying concentrations & also in combination in different ratio to get promising concentration for extended release matrix tablets. Matrix tablets of cefaclor were formulated using hydrophilic swellable polymers HPMC E-15 & HPMC K-100M with lactose as diluents. LHPC, Colliodal silicon dioxide, Talc, Mg.stearate & Crosscarmelose sodium were used as excipients. All the formulations prepared were found to comply with the weight variation, friability, drug content uniformity & in-vitro dissolution studies.

Keywords: Cefaclor matrix tablet, Extended release, Direct compression, HPMC Polymer.

INTRODUCTION

Cefaclor[1] having molecular formulae $C_{15}H_{14}ClN_3O_4S•H_2O$ and molecular weight 367.808 belongs[2,3] to the family of second-generation cephalosporin antibiotic known as the cephalosporin's and are used to treat[4] certain infections caused by bacteria such as pneumonia, ear, lung, skin, throat and urinary tract infections. Chemically cefaclor is (6*R*, 7R)-7-[[(2R) –amino-phenyl acetyl]-amino] - 3-chloro-8-oxo-5-thia 1 Azabicyclo [4.2.0] oct-2-ene- 2-carboxylic acid monohydrate, which is soluble in water, HCl and insoluble in methanol, chloroform and benzene. No drug accumulation was noted when cefaclor extended-release tablets were given twice daily. The goal of an extended release dosage form is to maintain therapeutic blood or tissue levels of drug for an extended period attempting to obtain zero-order release from the dosage form. Sustained release systems generally do not attain this type of release and provides drug is a slow first order fashion. 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. These are devices in which dissolved or dispersed drug is distributed uniformly in an inert polymeric matrix[5]. The present study aims to develop extended release matrix tablet using hydrophilic swellable polymers HPMC E-15 & HPMC K-100M with lactose as diluents. LHPC, Colloidal silicon dioxide, Talc, Mg.stearate & Crosscarmelose sodium was used as excipients along with drug in varying proportions by dry granulation method[6].

MATERIALS AND METHODS

Materials

Cefaclor HCl were obtained from Plethico Pharmaceutical limited Indore, Lactose Signet (Roquette) Mumbai, HPMC E-15,HPMC K-100M Colorcon Asia Privat Ltd Goa ,L-HPC Colorcon Asia Privat Ltd, Goa, Aerosil-200 Degussa Evonik AG, Germany , Talc,Ac-Di-Sol BASF chemicals Company Germany.

Preformulation Study

Preformulation study is the first step in the rational development of dosage form of a drug substance. It can be defined as an investigation of physical and chemical properties a drug substance alone and when combined with excipients. The solubility of drug was determined in solvents of different polarities. It freely soluble in water, slightly soluble in methanol and ethanol[7, 8]. The results show in table 1.

Table 1: Physical properties of starting material and granules [(F1- F10)

Property	Drug	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Angle of repose (°)	-	28.84	27. 501	25.019	26.57	27.29	23.80	24.14	25.11	27.29	26.95
Bulk density (gm/cm^3)	0.60	0.47	0.48	0.47	0.45	0.47	0.52	0.45	0.47	0.46	0.46
Tapped density (gm/cm^3)	0.74	0.80	0.76	0.56	0.56	0.58	0.62	0.69	0.54	0.54	0.56
Carr's compressibility ratio	18.18	41.45	36.84	16.07	19.64	18.96	16.66	16.66	12.96	14.81	17.85
Hausner's compressibility ratio	1.22	1.70	1.58	1.19	1.24	1.23	1.2	1.2	1.14	1.11	1.21
Flow property	Good	Poor	Good	Good	Good	Good	Good	Good	Good	Good	Good

Table 2: Compositions of the investigated tablet: [(F1 - F5)]

S No.	Ingredients (mg)	F (1)	F (2)	F (3)	F (4)	F (5)	F (6)	F (7)	F (8)	F (9)	F(10)
1	Cefaclor HCl	403.4	403.4	403.4	403.4	403.4	403.4	403.4	403.4	403.4	403.4
2	Lactose	54.5	39.5	60	65	61.6	66	66.6	65	66.6	66.6
3	HPMC E-15	25	30	30	30	-	28	-	27.50	28	-
4	HPMC K-100M	50	60	55	60	-	56	80	57.5	-	-
5	HPMC E-50	-	-	-	-	150	-	-	-	-	20
6	LHPC	50	50	44.6	44.6	20	44.6	50	44.6	44.68	50
7	Aerosil	6	6	6	8	5	8	10	8	8	10
8	Talc	5	5	5	5	2	5	5	5	5	5
9	Mg. Stearate	6	6	6	6	3	6	5	6	6	5
10	Ac-di-sol	-	-	-	10	-	5	15	20	15	20
11	SSG	-	-	10	-	-	-	-	-	-	-
	Total	600	600	620	632	650	632	640	632	632	640

Cefaclor HCl 403.418 is equivalent to 375mg pure drug

Preparation of extended release matrix tablets of cefaclor HCl by direct compression

Cefaclor HCl were prepared by the various drug polymer ratio and optimized for percentage drug content. Optimized cefaclor HCl was utilized for the formulation of matrix tablet. Excipient such as HPMC in different grades, LHPC, LACTOSE DCL- 21 and other exipient are use for the preparation of the Cefaclor HCl ER tablet compositions are given in table 2. The Talc, Magnesium Stearate and Aerosil are use for the lubrication purpose. After preparation of the tablet go for the coating on the prepared formulation. First prepared coating solution containing HPMC, TIO_2, TEC and other ingredient. (Film coating)

Table 3: Thickness, Hardness and Friability of Cefaclor HCl ER matrix tablet [(F_3-F_{10})]

Product code	Thickness (mm)	Hardness(Kg)	Friability (%)	Weight (mg)
F_3	5.6±0.03	8.2±1	1.52	639.558±31.97
F_4	5.7±0.04	8.0±1	1.38	651.992±32.59
F_5	5.9±0.05	7.8±1	0.56	669.088±32.49
F_6	5.8±.04	9.8±2	0.19	650.912±32.54
F_7	5.6±0.02	8.6±1	0.42	653.297±32.66
F_8	5.5±0.02	10.6±2	2.59	650.119±32.50
F_9	5.7±0.04	9.4±2	0.69	645.112±33.4

Evaluation of Prepared Tablet

Physico-chemical characterization (Table 3)

***In-Vitro* Release Study of Cefaclor HCl Matrix Extended Release Tablet**

In vitro release study of Cefaclor HCl has been carried out in 0.1N HCl at 100 rpm. We are using a six tablet in each tube and fill up a 900 ml of medium in it. We are withdrawing a sample in different time interval (5 ml) and transfer into a 100 ml of volumetric flask volume make up with 0.1N HCl. As per U.S.P I have seen that. They have given the limit like that Table 4.

In vitro release study of Cefaclor HCl has been carried out in 0.1N HCl at 100 rpm using paddle type of apparatus. Show the % drug release of formulation (F5, F6, and F7) in 0.1 N HCl in different time interval (Table. 5). We were found that the formulation (F5, F6 and F7) having the good release property but optimized formulation F6 those complies the USP limit and remaining formulation (F5 and F6) does not complies the USP limit. Optimized formulation F6 show the % drug release in those shown in below and formulation F6 also follow the zero order release. *In vitro* release study of Cefaclor HCl has been carried out in 0.1N HCl at 100 rpm using paddle type of apparatus. Show the % drug release of formulation (F5, F6, and F7) in 0.1 N HCl in different time interval (Table. 5). We were found that the formulation (F5, F6 and F7) having the good release property but optimized formulation F6 those complies the USP limit and remaining formulation (F5 and F6) does not complies the USP limit. Optimized formulation F6 show the % drug release in those shown in below and formulation F6 also follow the zero order release[9-11].

Table 4: % Drug release rate as per USP

S. No.	Minute	% Drug release
1	In 30 Min	0 - 30
2	In 60 Min	20 - 50
3	In 240 Min	More than 80%

Table 5: In-vitro release study of extended release matrix tablet (F5, F6 and F7) in 0.1 N HCl

Time (in hours)	Cumulative % drug release		
	F5	F6	F7
0.5	23.80	14.23	22.24
1	35.15	25.34	30.26
1.5	46.94	35.87	39.15
2	53.84	45.98	46.04
2.5	58.29	54.78	48.95
3	63.85	65.78	51.84
4	72.53	88.59	60.52
5	85.66	98.67	66.08

Stability study of formulation

Stability studies were carried out at 25^0 C / 60 % RH and 40^0 C / 75 % RH for the selected formulation for the period of 3 months result show in table 6.The selected formulations were packed in strip. They were then stored at 30^0 C / 65% RH and 40^0 C / 75 % RH for 6 months and evaluated for their physical appearance, drug content and drug release at specified intervals of time[12,13].

Table 6: Third Month Stability studies data

S. No.	Test	Observation/Result [25^0C/60%RH]	[30^0C/65%RH]	[40^0C/75%RH]
1	Description	Orange color elongated biconvex Tablet with break line on one side.	Orange color elongated biconvex Tablet with break line on one side.	Orange color elongated biconvex Tablet with break line on one side.
2	Average weight	649.36	648.47	647.15
3	Dissolution			
	In 0.1 N HCl 30 min.	22.09%	20.43%	22.67%
	In 0.1 N HCl 60 min.	29.04%	31.25%	32.44%
	In 0.1 N HCl 240 min.	91.77%	92.21%	92.65%
4	Assay	99.87%	99.24%	98.66%

RESULTS & DISCUSSION

The Physical properties of prepared formulation such as hardness, friability, thickness, and weight variation and percentage drug content of prepared matrix tablets were presented in Table 3. The hardness of tablet range from 7.8 to 9.8 kg/cm^2. It was also observed that the variation of thickness was minimal. In friability test batch F3, F4 and F8 shows poor result as compared to other batches table were presented in Table 3, So that remaining batch were used for further evaluation study. Data of friability of tablet are shown so that

further study was carried out on remaining batches. Such F5, F6, F7, F9, F10. In Assay the test batch F9 and F10 was found very less those are not complies the USP limit, so that further study was carried out on remaining batches Such F5, F6, F7. The stability data of extended release tablet evaluate on different storage condition initial and 1 & 3 months on 25^{0}C/60%RH & 40^{0}C/75%RH. There were no any changes found so drug was stable.

CONCLUSION

Prepared extended release tablet of cefaclor HCl powder and the prepared granules were evaluated for poured density, tapped density and compressibility index. The physical properties of prepared extended release tablet was determined such as hardness, friability, thickness and weight and % drug content of prepared matrix tablets and it show good result.

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REFERENCES

1. The Merck Index, 13th edition, Merck and company, INC, White House station, NJ, 324 **(2001)**
2. Hebert A, Sigman E, Levy M Serum sickness reactions from cefaclor in children. Dermatol, 1991; 25:805-8.
3. Parra F, Igea J, Martín J, Alonso M Sainz T, Serum sickness-like syndrome associated with cefaclor therapy, Allergy, J. Am. Acad,1992; 47: 439–440.
4. King BA, Geelhoed GC Adverse skin and joint reactions associated with oral antibiotics in children the role of cefaclor in serum sickness like reactions, J Paediatr Child Health, 2003;39 (9): 677–681.
5. Banker GS, Rhodes CT Modern pharmaceutics, 4th ed. Marcel Dekker Inc, New York: 1992: p.501-502.
6. Rowe RC, Sheskey PJ, Weller PJ. Handbook of Pharmaceutical Excipients, 4th ed. Pharmaceutical press and the American Pharmaceutical association. 2006: p. 108-111, 161-164, 297-300, 354-357.
7. Wadke DA, Serajuddin TM and Jacobson H. Preformulation Testing. *In*: Lieberman HA, Lachman L, Pharmaceutical Dosage Form; Tablets; Vol-1, Marcel Dekker, New York: 1990: p. 1, 13,54.
8. Niazi SK, Hand book of Preformulation. Characterization of Biopharmaceutical Drugs, informa healthcare, New York, London 2007: p. 329-390.
9. Mutalik S, Naha A, Usha AN, Ranjith AK, Musmade PK Manoj, Anju P and Prasanna S Preparation, in vitro, preclinical and clinical evaluations of once daily sustained release tablets of aceclofenac. Arch Pharm Res, 2007; 30 (2): 222-234.
10. Wadke DA, Serajuddin TM and Jacobson H. Preformulation Testing. *In*: Lieberman HA, Lachman L, Pharmaceutical Dosage Form; Tablets; Vol-1, Marcel Dekker, New York: 1990: p. 1, 13,54.
11. Pillay V, Fassihi R Evaluation and comparison of dissolution data derived from different modified release dosage forms: an alternative method. Journal of Controlled Release, 1998; 55: 45–55.
12. International Conference on Harmonization (ICH), Harmonized Tripartite guideline for stability testing of new drugs substances and products Q1A(R2) 2003 Feb 6.
13. Grimm W Extension of The international conference on harmonization tripartite guideline for stability testing of new drug substances and products to countries of climatic zones iii and iv. Drug Dev Ind Pharm, 1998; 24: 313-325.