Original Article

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Formulation and Evaluation of Sustained Release Matrix Tablets of Cephalexin: Effects of Hydrophilic and Hydrophobic Matrix on Drug Release

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Abstract

Sustained release cephalexin tablets were prepared by using different polymers like HPMC K4M, HPMC K15M, HPMC K100M, HPMC K 100LV, Ethyl cellulose, Carbopol 971P, Carbopol 974P, Eudragit RS100, Eudragit RL100 and Eudragit L100. The tablets were prepared by wet granulation technique and were evaluated for different parameters such as thickness, hardness, weight uniformity, content uniformity, friability, *in-vitro* drug release, drug release mechanism study and stability studies. The results of the studies indicate that the polymers used have significant release-retarding effect on the formulation. The dissolution profile comparison of the prepared batches and market preparation (Nufex CR Tablet) was done by similarity and difference factor determination. The formulation K4 (5.8% HPMC K100M, 1.0% ethyl cellulose) with a similarity factor of 68.28 was found to be nearest to the marketed formulation. Formulation K4 shows first order drug release and the mechanism of drug release was found to be anomalous. The results of the accelerated stability study of best formulation K4 for two months revealed no significant changes in formulation. It is concluded that carbopol, eudragit and HPMC were found to be suitable as bases for preparing tablet matrices containing Cephalexin but only carbopol 971and HPMC K4M were able to produce release profile similar to that of marketed preparation.

Keyword: Cephalexin, Dissolution profile, Ethyl cellulose, Stability study, Sustained release

INTRODUCTION

Compressed hydrophilic matrices are commonly used as oral drug delivery systems because they easily provide a desirable drug-release profile, they are economical, compatible with most of the drug material and they are broadly accepted by the US Food and Drug Administration[1]. Hydroxypropyl methylcellulose (HPMC) represents the most frequently used polymer in the formulation of hydrogel matrices for controlled drug delivery[2]. Drug released primarily either via diffusion or erosion of matrix from such compressed matrices. Water soluble drugs are released primarily by diffusion of dissolved drug molecules across the gel layer, whereas poorly water-soluble drugs are released predominantly by erosion mechanisms[3]. The tablet erosion is thus the most critical property for such drugs in order to obtain the desired target plasma concentration profiles and clinical benefits of ER administration. On the other

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hand, carbopol, an acrylic acid derivative, has also attracted interest for its use in controlled release. HPMC provides release which is dependent on the pKa of the drug[4] whereas carbopol gels at above pH 7.3 and therefore provides a pH dependent release[5]. Eudragits are biocompatible copolymers synthesized from acrylic and methacrylic acid esters which offers a wide range of flexibility to achieve the desired drug release profile by releasing the drug at the right place and at the right time and, if necessary, over a desired period of time.

Cephalexin is a semisynthetic antibiotic derived from cephalosporin C and is almost completely absorbed from the gastrointestinal tract with a bioavailability of 95%. Cephalexin has a half life of around 1 h. To maintain the therapeutic range, the drug should be administered three to four times a day, which leads to saw tooth kinetics resulting in ineffective therapy[6]. Hence we attempted to formulate extended release tablets of cephalexin, which can provide a constant effective drug level for six hours, based on calculations considering pharmacokinetic parameters. This paper also examines the potential of combining these polymers to extend the dissolution of a drug, cephalexin and seeks to rationalize the role played by the polymers in controlling drug release.

MATERIALS AND METHODS

Materials

Cephalexin was kindly provided by Intas Pharma, Ahmadabad, India. Hydroxypropyle methylecellulose (HPMC K4M, HPMC K15M, HPMC K100M, HPMC K100 LV) and ethyl cellulose was obtained from Colorcon India. Carbopol 971P, Carbopol 974P were obtained as a gift sample from Lubrizol Advanced Materials Europe BVBA. Eudragit RS100, Eudragit RL 100 and Eudragit L100 were obtained from Evonik Degussa India Pvt. Ltd. Mumbai. All other chemicals purchased from Loba Chemi Mumbai and were of pharmaceutical grade.

Formulation of matrix tablets

The tablets were prepared by wet granulation technique. The ingredients and quantities used are shown in Table 1, 2 and 3. Cephalexin, lactose and polymer were passed through 60# sieve and then granulated using PVP K-30 in isopropyl alcohol as granulating agent, the wet mass was passed through # 16 sieves. The granules were air dried for one hour and lubricated in poly bag using magnesium stearate. Desired quantity of granules was weighed and fed manually to compression machine. The flat faced beveled edge punch of diameter 12 mm was used for compression.

Table 1. Matrix systems containing hypromellose and ethyl cellulose

Ingredients (mg)	Formulation									
	K1	K2	K3	K4	K5	K6	K7	K8	K9	K10
Cephalexin monohydrate	395*	395*	395*	395*	395*	395*	395*	395*	395*	395*
Lactose	40	40	40	40	40	40	40	40	40	40
PVP K-30	7	7	7	7	7	7	7	7	7	7
Magnesium stearate	3	3	3	3	3	3	3	3	3	3
Ethyl cellulose	5	5	5	5	5	5	5	5	5	5
HPMC K4M	-	-	-	-	35		-		-	-
HPMC K15M	-	-	-	-		35	32	-	-	-
HPMC K100M	70	53	44	28	-	-	-	-	-	-
HPMC K100 LV	-	-	-	-	-	-	-	35	45	100
Tablet weight (mg)	520	503	494	478	485	485	482	485	495	550

* Equivalent to 375 mg of anhydrous cephalexin

Table 2. Matrix systems containing carbomer

Ingredients (mg)	Formulation						
	C1	C2	C3	C4	C5	C6	C7
Cephalexin monohydrate	395*	395*	395*	395*	395*	395*	395*
Lactose	40	40	40	40	40	40	40
PVP K-30	7	7	7	7	7	7	7
Magnesium stearate	3	3	3	3	3	3	3
Carbopol 971P	50	20	30	35	-	-	-
Carbopol 974P	-	-	-	-	45	30	35
Tablet weight (mg)	495	465	475	480	490	475	480

* Equivalent to 375 mg of anhydrous cephalexin

Table 3. Matrix systems containing eudragit

Ingredients (mg)	Formulation						
	E1	E2	E3	E4	E5	E6	E7
Cephalexin monohydrate	395*	975*	395*	395*	395*	395*	395*
Lactose	40	40	40	40	40	40	40
PVP K-30	7	7	7	7	7	7	7
Magnesium stearate	3	3	3	3	3	3	3
Eudragit RS 100	-	-	-	45	15	-	-
Eudragit RL 100	-	-	-	-	-	45	20
Eudragit L100	45	80	100	-	-	-	-
Tablet weight (mg)	490	525	545	490	460	490	465

* Equivalent to 375 mg of anhydrous cephalexin

Evaluation of physical properties of precompressed powder blend[7]

Angle of repose

The angle of repose was determined to study the flow property of powder. A funnel with 10 mm inner diameter of the stem was fixed at a height of 2 cm over the platform. About 10 g of sample was slowly passed along the wall of funnel till the tip of the pile formed touches the stem of the funnel. A rough circle was drawn around the pile base and the radius of powder cone was measured. Angle of repose was calculated from three averages using following formula.

$$\theta = \tan^{-1}(h/r)$$

Where, θ = angle of repose
h = height of powder cone
r = radius of the powder cone

Bulk density

The powder sample under test was screened through sieve No. 18 and the sample equivalent to 25 g was accurately weighed and filled in a 100 ml graduated cylinder and the powder was leveled and the unsettled volume. Vo was noted.
The bulk density was calculated in g/cm3 by the formula,

Bulk density ($\rho 0$) = M/Vo …..…….. (1)

Where, M = Mass of powder taken
V_o = Apparent unstirred volume

Tapped density

The powder sample under test was screened through sieve No. 18 and the weight of sample equivalent to 25 g was filled in 100 ml graduated cylinder. The mechanical

tapping of the cylinder was carried out using tapped density tester at a nominal rate of 300 drops per minute for 500 times initially and the tapped volume Vo was noted. The tapping was proceeding further for an additional tapping 750 times and tapped volume, Vb was noted. The difference between two tapping volumes was less than 2%, so Vb was considered as a tapped volume V_f.

The tapped density was calculated in g/cm^3 by the formula,

Tapped density (ρt) = M/V_f …….. (2)

Where, M = Weight of sample powder taken
V_f = Tapped volume

Compressibility index (%)

The bulk density and tapped density were measured and compressibility index was calculated using the formula.

C.I. = {(ρ_t - ρ_o)/ρ_t) x 100 ……..…… (3)

Where, ρ_t = Tapped density
ρ_o = Bulk density

Hausner ratio

Tapped density and bulk density were measured and the Hausner ratio was calculated using the formula,

Hausner ratio = ρ_t/ρ_o ……....…… (4)

Where, ρ_t = Tapped density
ρ_o = Bulk density

Evaluation of tablets

The thickness, diameter, hardness and friability of the tablets were determined using digital vernier calipers, Monsanto hardness tester and friabilator respectively. Weight variation test was carried out by weighing 20 tablets individually and then calculating the average weight8.

Drug content

Five tablets were weighed and powdered. The quantity of powder blend equivalent to 100 mg of anhydrous cephalexin was weighed accurately and taken in 100 ml volumetric flask. To it 50 ml of distilled water was added and sonicated for 5 minutes. The volume was made up to 100 ml with distilled water and filtered. From the above solution, 2 ml was diluted to 100 ml. The drug content was determined spectrophotometrically at 261 nm.

In-vitro drug release studies

Dissolution studies were performed using Tablet Dissolution Tester USP-24 (Electro lab TDT-06) type 2 with 900 ml, 0.1N HCl for 2 hours and continued in pH 6.8 phosphate buffer as dissolution media (degassed at 40 °C for 30 min under vacuum with constant stirring) at 37±0.1 °C and 100 rpm for 180 minute[s9]. At fixed time intervals, 5 ml of the aliquots was withdrawn, filtered through a 0.45µm syringe filter, suitably diluted (if needed) and assayed for Domperidone content by measuring the absorbance at 261 nm against the blank using a UV-visible spectrophotometer (Shimazdu-1601, UV–vis spectrophotometer, Shimadzu Corp, Kyoto, Japan). An equal volume of the fresh medium prewarmed at the same temperature was replaced in the dissolution medium after each sampling to maintain constant volume throughout the test. Each test was performed in triplicate and % cumulative release was plotted using calculated mean values of cumulative drug release.

Drug release mechanism study

The *in vitro* dissolution data was subjected to different kinetic treatments (Zero order, First order, Higuchi and Hixson-Crowell). The coefficient of determination (R^2) was considered as main parameter for interpreting the release kinetics. In order to predict the release mechanism, the data were subjected to Korsmeyer Peppas model[10].

Drug excipients compatibility studies

Drug excipient compatibility studies were done by Fourier Transform Infrared Spectroscopy. The IR spectrum of cephalexin,

HPMC, carbopol, eudragit and matrix tablet formulation were recorded using Shimadzu-8001 model using KBr pellet technique. For recording the FT-IR spectrum, compressed tablets of Cephalexin containing HPMC, carbopol, and eudragit, were crushed and passed through 60# sieve. The ratio of KBr: sample (3:1) was used.

Comparison of optimized formulation batches with marketed formulation

Optimized formulation batches were compared with marketed dosage form of cephalexin (Nufex CR Tablet, RPG Life Sciences, Mumbai) using model independent parameters like Similarity factor (f2), difference factor (f1) and mean dissolution time (MDT).

Stability studies

Stability studies of optimized formulation batches were performed as per ICH guidelines. Optimized formulation batches were kept for stability studies at 40 ^{o}C and 75% RH for two months[11].

RESULTS AND DISCUSSION

Physical properties of precompressed powder blends

Physical properties of precompressed powder blends for formulations are summarized in Table 4.

Table 4. Physical properties of precompressed powder blends of formulations.

Formulation code	Angle of repose (θ)	Bulk density pb (g/cm^3)	Tapped density pT (g/cm^3)	Compressibility (%)	Hausner Ratio
K1	20.2±1.6	0.533±0.87	0.690±0.29	22.75±1.53	1.29
K2	25.8±2.1	0.538±0.29	0.809±0.39	33.49±0.34	1.50
K3	21.2±1.2	0.494±0.65	0.669±0.29	26.15±0.76	1.35
K4	18.5±1.4	0.512±0.45	0.663±0.21	22.77±0.96	1.29
K5	20.6±2.6	0.498±0.47	0.673±0.32	26.00±1.53	1.35
K6	18.3±1.3	0.505±0.57	0.652±0.43	22.54±1.34	1.29
K7	16.1±1.2	0.487±0.54	0.599±0.32	18.69±0.85	1.22
K8	13.2±1.1	0.522±0.16	0.613±0.23	14.84±0.76	1.17
K9	15.9±1.1	0.460±0.15	0.602±0.18	12.61±0.54	1.11
K10	17.1±0.9	0.568±0.20	0.513±0.15	12.89±0.34	1.11
C1	28.2±0.7	0.375±0.25	0.418±0.20	12.28±0.59	1.11
C2	27.7±1.7	0.543±0.25	0.627±0.28	13.39±0.75	1.11
C3	27.9±1.4	0.549±0.25	0.631±0.26	13.99±0.77	1.14
C4	28.8±0.6	0.520±0.30	0.632±0.30	13.54±0.78	1.14
C5	28.5±0.3	0.358±0.22	0.419±0.16	15.12±0.71	1.17
C6	27.6±0.4	0.361±0.24	0.420±0.14	15.32±0.36	1.16
C7	28.6±1.8	0.362±0.21	0.422±0.12	14.22±0.38	1.16
E1	28.1±1.6	0.360±0.23	0.430±0.17	14.36±0.78	1.17
E2	28.8±1.2	0.361±0.18	0.445±0.15	14.79±0.76	1.15
E2	28.9±1.1	0.360±0.15	0.402±0.18	12.61±0.54	1.11
E3	28.1±0.9	0.368±0.20	0.413±0.15	12.89±0.34	1.11
E4	28.2±0.7	0.375±0.25	0.418±0.20	12.28±0.59	1.11
E5	27.7±1.7	0.543±0.25	0.627±0.28	13.39±0.61	1.11
E7	27.9±1.4	0.549±0.25	0.631±0.26	13.99±0.67	1.14

Percent drug content of optimized formulation batches

The % drug content of optimized formulation batches is shown in Table 5. The drug content varied from 98.23 to 100.03%.

Table 5. Physical parameters for formulation batches of Cephalexin Tablets and its marketed dosage form.

Formulation Code	Thickness (mm)	Hardness (Kg/cm2)	Weight variation Average Weight (mg)	Friability (%)	Drug Content (%)
K1	3.1	5.0	518.2	0.21	99.71
K2	3.0	4.9	502.5	0.43	98.88
K3	2.9	4.9	493.0	0.28	100.1
K4	2.9	5.0	477.0	0.30	99.38
K5	3.0	5.5	484.3	0.47	98.77
K6	3.0	5.0	484.5	0.49	99.73
K7	3.0	5.0	481.0	0.51	98.23
K8	3.0	4.9	485.3	0.16	99.37
K9	3.0	4.9	496.0	0.21	98.97
K10	3.1	5.0	549.3	0.19	99.18
C1	3.0	5.0	494.8	0.24	99.92
C2	2.9	5.0	464.2	0.18	99.74
C3	2.9	5.0	477.0	0.25	100.03
C4	2.9	5.0	479.3	0.16	99.25
C5	3.9	5.0	489.2	0.14	98.58
C6	2.9	5.0	476.8	0.22	99.47
C7	2.9	5.0	482.2	0.19	98.95
E1	2.9	5.0	470.6	0.71	100.08
E2	3.0	4.9	504.6	0.21	99.22
E2	3.1	5.0	525.6	0.62	98.81
E3	2.9	4.9	470.0	0.26	99.18
E4	2.9	5.0	445.2	0.58	99.66
E5	2.9	5.0	470.0	0.65	98.22
E7	2.9	5.0	439.2	0.53	98.73
M1	4.0	5.5	543.0	0.16	100.03

Physical parameters of cephalexin tablets.

The tablets passed the weight variation test as per USP8. The hardness of matrix tablets was found to be in the range of 4 to 5 Kg/cm2. Friability values were found to be within acceptable limits, ranged from 0.14 to 0.71%. Drug content in the tablets was found to be in the range of 98.22 to 100.08%.

In vitro dissolution studies

The cumulative % drug release of formulation batches containing HPMC and ethyl cellulose in 0.1N HCl for 2 hours and pH 6.8 phosphate buffer from 3 to 6 hours is shown in Fig. 1A & 1B. The proportion of ethyl cellulose was kept at 0.9 to 1% in formulation batches K1 to K10. The proportion of HPMC K 100M

in formulation batches K1, K2, K3 and K4 was kept at 13.46, 10.50, 8.90 and 5.85 %. The cumulative drug release after 6 h was found to be 52.60, 56.44, 64.11, 94.91% respectively. It was expected from formulation batch to show complete drug release after 6 hours. The decrease in drug release was due to the high viscosity of the HPMC K100M. Hence in formulation batches K5, HPMC K 4M was used in 7.21 % to have the expected drug release. In K5 the drug release was found to be 99.90% respectively. In K6 and K7 the proportion of HPMC K15M was kept at 7.21 and 6.63% respectively which showed the drug release of 97.81 and 100.03% respectively. In formulation batches K8, K9, and K10, the proportion of HPMC K100 LV was kept at 7.21, 9.09 and 18.18% respectively. In K8, the complete drug release was found at 4 h, whereas K9 and K10, the complete drug release was observed after 5 and 6 h respectively. As expected the release rate was slower with higher quantities and higher viscosities of HPMC. The molecular weight variations in HPMC are commonly expressed as viscosity grades. Larger viscosity grades correspond to the greater polymer molecular weight. The drug release rate was found in the rank HPMC K100 LV <K4M <K15M <K100M. From the above results, formulation batch K4, K5, K7 and K10 were selected for further studies since these batches showed the desirable drug release for 6 h.

As shown in Table 2, the proportion of carbopol 971P in formulation batches C1 to C4 was kept at 10.10, 4.30, 6.31, 7.29% respectively. The proportion of carbopol 974P in formulation batches C5 to C7 was kept at 9.18, 6.31, and 7.29 % respectively. In the formulation batches C1 to C7, the cumulative drug release after 6 hours was found to be 79.67, 99.97, 100, 100.98, 84.48, 99.04, 99.26 % respectively(Figure1C).Althoughboth carbopols sustained the drug release, the rate of drug release was slower in case of carbopol 974P, which may be attributed to its viscosity, which is greater than that of carbopol 971P. From the above results, formulation batches C4 and C7 showed drug release of 100.98 and 99.26% after 6 hours. Hence formulation batches C4 and C7 were selected for further studies. In order to study the effect of Eudragit on the release of Cephalexin, eudragit L100 (pH dependent) and eudragits RL100 & RS100 (pH independent) were used. As shown in Figure 1D, The complete drug release of formulation batch E1 was observed after 4 h, whereas the formulation batches E2 and E3 showed 99.45% drug release after 5 h and 100.09 after 6 h respectively. The proportion of eudragit RS100 in formulation batches E4 and E5 was kept at 9.18 and 3.26% respectively. The cumulative drug release of formulation batch E4 and E5 after 6 h was found to be 79.14 and 99.58% respectively. The proportion of eudragit RL100 in formulation batches E6 and E7 was kept at 9.18 and 4.30% respectively. The cumulative drug release of formulation batch E6 and E7 after 6 h was found to be 73.80 and 99.93% respectively. An inverse relation was observed between the release of cephalexin and quantity of eudragit. Eudragit L100 being pH dependent, solubilise above pH 6. It showed a release retardant effect in acidic pH for initial 2 h and faster release was observed in alkaline pH up to 6 h. The release rate with eudragit RS100 was slower as compared to eudragit RL100 due to lower permeability of eudragit RS100 as compared to eudragit RL100. Hence formulation batches E3, E5 and E7 were selected for further studies since the complete drug release was observed up to 6 h.

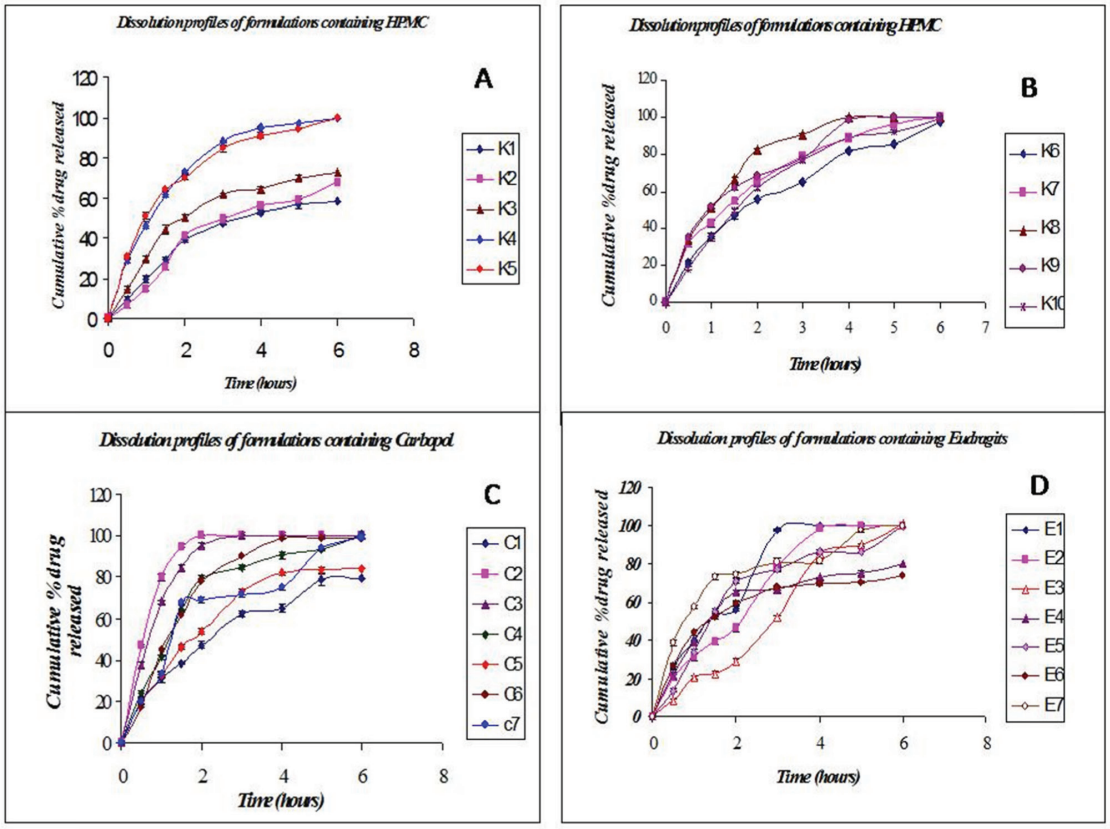

Figure 1. Influence of type and quantity of (A & B). HPMC on *in vitro* release of cephalexin from the matrix tablets. (C). Carbopol on *in vitro* release of cephalexin from matrix tablets. (D). Eudragit on *in vitro* release of cephalexin from matrix tablets.

Comparison of optimized formulation batches with marketed formulation

The optimized formulation batches were compared with the marketed dosage form of cephalexin Nufex CR tablets containing 375 mg Cephalexin anhydrous (RPG Life Sciences, Mumbai) for *in vitro* release profiles. The cumulative release profiles are shown in Figure 2 & 3. As shown in table 6, the comparison of *in vitro* release profiles of optimized formulation batches and marketed dosage form was done using similarity factor (f2) and difference factor (f1).

The time required for cumulative release of 50, 70 and 90% of optimized formulation batches and marketed dosage form is shown in Table 7.

Similarity factor and difference factor were calculated for all formulations (showing sustained effect for six hours) considering the marketed formulation as the reference standard (MI). The values for the same are shown in Table 7. It can be seen that formulations C7 and E3 have lowest values of f2 i.e. 48.85 &31.01 respectively and higher values of f1 i.e. 12.39 & 18.80 suggesting that these formulations show greatest deviation from marketed formulation as compared to other formulated products. Other formulations show f2 values between 50-100 and f1 values between 0-15 indicating similarities of dissolution profiles with that of marketed formulation.

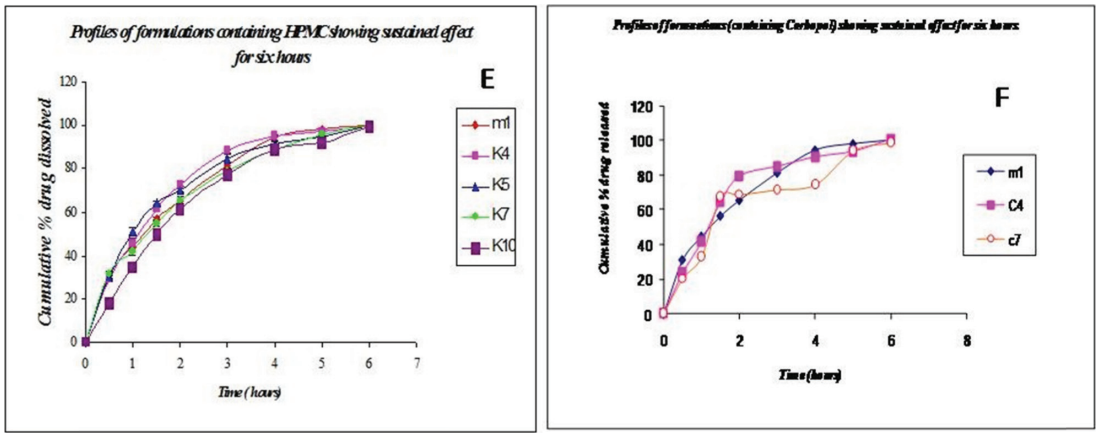

Figure 2. (E). *In vitro* release profiles of formulations (containing HPMC) showing sustained effect for 6 h, (F). *In vitro* release profiles of formulations (containing carbopol) showing sustained effect for 6 hours.

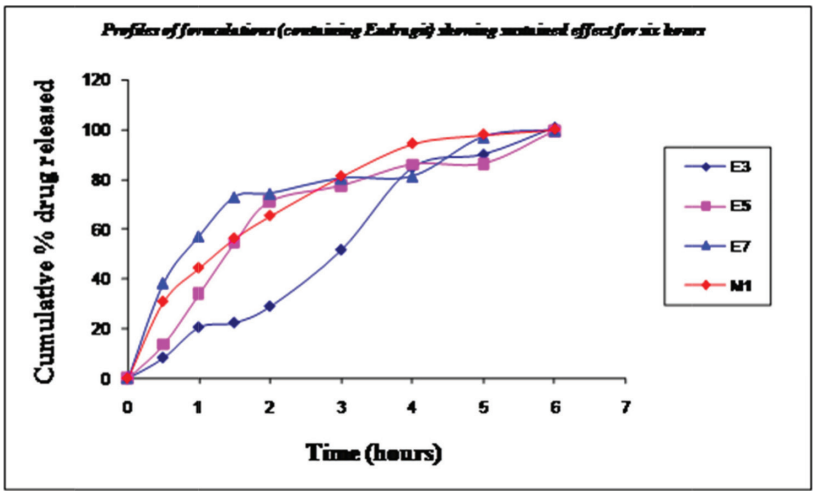

Figure 3. *In vitro* release profiles of formulations (containing eudragit) showing sustained effect for 6 hours.

Table 6. Comparison of *in vitro* profiles of optimized formulations with marketed formulation.

Formulation code	Similarity factor (f2)	Difference factor (f1)
K4	68.28	4.4
K5	66.73	5.23
K7	57.46	8.51
K10	53.74	8.78
C4	57.81	7.96
C7	48.85	12.39
E3	31.01	18.80
E5	51.81	10.47
E7	50.53	10.67

Table 7. Comparison of $t_{50\%}$, $t_{70\%}$, $t_{90\%}$ of optimized formulations with marketed formulation.

Formulation code	$t_{50\%}$ (Hour)	$t_{70\%}$ (Hour)	$t_{90\%}$ (Hour)	Mean dissolution time(Hour)
K4	1.48	2.82	4.18	1.46
K5	1.64	3.03	4.56	1.54
K7	2.05	3.30	4.56	1.93
K10	1.07	2.53	4.00	1.34
C4	1.60	2.93	4.26	1.60
C7	1.94	3.31	4.67	1.94
E3	2.81	3.93	5.04	2.78
E5	2.03	3.33	4.63	1.94
E7	1.24	2.79	4.34	1.50
M1	1.67	2.98	4.30	1.61

Best fit model

The *in vitro* release data thus obtained was subjected to different kinetic treatments (Zero order, First order, Higuchi and Hixson-Crowell). The results are shown in Tables 8 .The coefficient of determination (R^2) was considered as main parameter for interpreting the release kinetics. For Zero order treatment the R^2 values ranged from 0.804-0.90, which indicates that, the formulations do not follow zero order kinetics. The R^2 values of first order treatment range from 0.820-0.997. Mainly the formulations containing HPMC show fair linearity in release of drug from the matrices as the R^2 values are 0.996, 0.997, 0.974, 0.994, and 0.962 for the formulations K4, K5, K7, K10 and C4 respectively. When the data was subjected to Higuchi treatment the R^2 values ranged from 0.88-0.97. The formulations containing HPMC as well as eudragit produce fair linearity, R^2 values ranging from 0.914-0.987 further strengthen the statement.

In order to predict the release mechanism, the data was subjected to Korsmeyer's treatment. The release exponent values (n) were determined. The values ranged from 0.45-1.0. For the formulations containing HPMC i.e. K4, K5, K7& K10 the values ranged from 0.5 - 0.67 indicating that the dominant mechanism of drug release through HPMC based matrix systems may be anomalous transport. For formulations containing carbopol namely C3 and C7, exponent values were 0.56 and 0.60 respectively indicating that the drug may be released by anomalous transport. On the other hand eudragit L100 containing formulation (E3) has an exponent value equal to 1.02, indicating that Super case II transport may be the release mechanism of this matrix system. For formulation E5 and E7 the (n) values were found to be 0.73 and 0.34, which denote anomalous transport. The marketed preparation shows exponent value of 0.50 indicating Fickian diffusion as a release mechanism.

Stability Studies

The release profiles of optimized formulations of cephalexin after stability studies for 2 months are shown in figure 4. From the results of stability studies, no significant change in *in vitro* dissolution profile was observed. Hence the optimized formulations proved to be stable.

Table 8. Correlation coefficient (R^2) and n values of optimized formulation batches.

Formulation Code	Correlation coefficient (R^2) values				n values
	Zero order	First order	Higuchi model	Hixson-Crowell model	
K4	0.8115	0.9964	0.9344	0.9860	0.50
K5	0.8044	0.9969	0.9490	0.9680	0.45
K7	0.8745	0.9745	0.9869	0.9510	0.48
K10	0.9001	0.9940	0.9744	0.9770	0.67
C4	0.7887	0.9626	0.8890	0.8570	0.56
C7	0.8209	0.8279	0.8810	0.9020	0.60
E3	0.9747	0.9162	0.9523	0.8390	1.02
E5	0.8419	0.9310	0.9159	0.9140	0.73
E7	0.7362	0.8199	0.9141	0.9060	0.34
M1	0.8636	0.9643	0.9747	0.9630	0.49

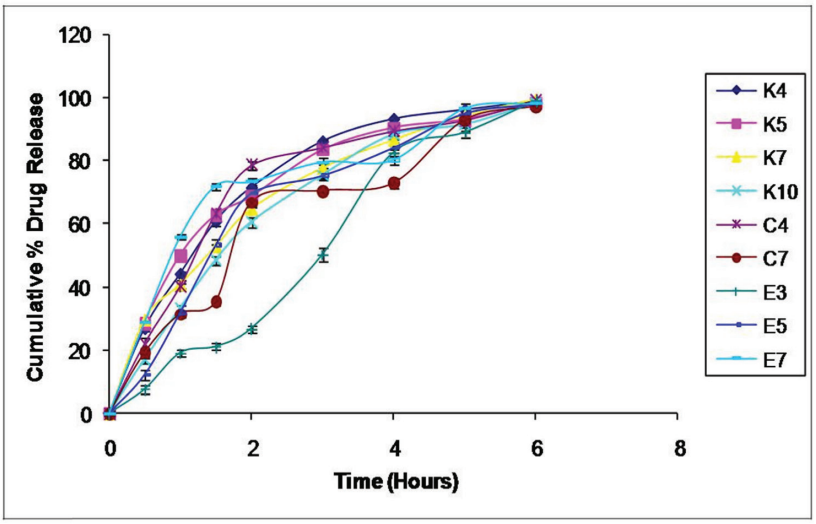

Figure 4. Cumulative % drug release of optimized formulation after stability studies for 2 months

CONCLUSION

Sustained release matrix tablets of Cephalexin were prepared successfully using hypromellose, carbomers and polymethacrylates as release retarding polymers by the wet granulation method. Various evaluation parameters like thickness, hardness, friability and drug content of all formulations were found to be satisfactory. Thus carbopol, eudragit and HPMC were found to be suitable as bases for preparing tablet matrices containing cephalexin but only carbopol 971 and HPMC K4M were able to produce release profile similar to that of marketed preparation.

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