

Preparation and Evaluation of Carbamazepine Sustained Release Tablets

Shib Sankar Saha¹, Mehrina Nazmi², Nandini Saha² and Md. Selim Reza¹

¹Department of Pharmaceutical Technology, Faculty of Pharmacy, University of Dhaka, Dhaka-1000, Bangladesh.

²Department of Pharmacy, University of Asia Pacific, Dhanmondi, Dhaka-1209, Bangladesh

ABSTRACT: The purpose of the present studies was to develop and characterize sustained release tablets of Carbamazepine, an antiepileptic drug. Tablets were prepared by direct compression method. In the formulation, the active drug was taken 200 mg in every formulation. Methocel K4M, Methocel K15M CR, Methocel K100LV CR, Eudragit RSPO and Eudragit RLPO polymers were used as rate retarding agents in twenty four formulations (F-1 to F-24). The effect of hydrophilic polymer PEG 6000 as channeling agent with Methocel K4M was observed in four formulations (F-5 to F-8). The granules were evaluated for angle of repose, bulk density, tapped density. The tablets were subjected to average weight, diameter, thickness, weight variation, hardness, friability and *in vitro* dissolution studies. The granules showed satisfactory flow properties, compressibility and drug content. The *in vitro* dissolution study was carried using USP Apparatus-I (Rotating basket method apparatus) for 6 to 12 hours in distilled water with 1% sodium lauryl sulphate as the dissolution medium. The release mechanisms were explored and explained by Zero order, First order, Higuchi, Korsmeyer-Peppas and Hixson-Crowell equations. Primarily twelve formulations were prepared by using four variable amount of three polymers; Methocel K4M (50, 100, 150 and 200 mg) in the formulations from F-1 to F-4, Methocel K15M CR (50, 100, 150 and 200 mg) in the formulations from F-9 to F-12 and Methocel K100LV CR (50, 100, 150 and 200 mg) in the formulations from F-13 to F-16. Then four formulations were prepared where Methocel K4M amount was same but using variable amount of hydrophilic polymer PEG 6000 (50, 100, 150 and 200 mg). After that another eight formulations were prepared by using polymer Eudragit RSPO and Eudragit RLPO by using variable amount. In F-17 to F-20 the use of Eudragit RSPO was in variable amount (50, 100, 150 and 200 mg) and in F-21 to F-24 the use of Eudragit RLPO was in variable amount (50, 100, 150 and 200 mg). Other excipients remained same in the formulations. Among these twenty four formulations' sustainability was studied and compared with three market product of 200 mg tablet. It was found that effect of PEG 6000 as channeling agent subsequently decreased the sustaining action (Formulation F5-F8).

Key words: Anti epileptic, channeling agents, sustained release, direct compression.

INTRDOUCTION

Carbamazepine sustained release matrix tablets was prepared by direct compression method utilizing different grades of Hydroxylpropylmethyl cellulose (HPMC) that were Methocel K4M, Methocel K15M CR, Methocel K100LV CR and acrylic acid polymer Eudragit RSPO and Eudragit RLPO. Different grades of Methocel polymer are hydrophilic in nature and eudragit polymer are pH independent in nature. Oral sustained release dosage form by direct compression technique is a very simple approach of drug delivery systems which is very rational in the pharmaceutical

arena for its ease, compliance, faster production, avoid hydrolytic or oxidative reactions occurred during processing of dosage forms.¹ Sustained or controlled drug delivery occurs while embedded within a polymer that may be natural or semi-synthetic or synthetic in nature. The polymer is judiciously combined with the drug or other active ingredients in such a way that the active agent is released from the material in a predetermined fashion and released the drug at constant rate for desired time period.²

There are number of techniques applied in the formulation and manufacturing of sustained release dosage form. However, matrix tablet prepared by direct compression method has attracted much

Correspondence to: Md. Selim Reza
Tel: 880-2-8612069; Fax: 880-2-8615583
Email: selim.du@gmail.com

attention due to its technological simplicity in comparison with other controlled release systems. Direct compression method had been applied for preparation of matrix tablet that involved simple blending of all ingredients used in the formulations and then underwent direct compression. It required fewer unit operations, less machinery, reduced number of personnel and reduced processing time, increased product stability and faster production rate.³

There are three primary mechanisms by which active agents can be released from a delivery system: diffusion, degradation, and swelling followed by diffusion. The release of drug from the matrix tablet depends on the nature of polymer. Methocel K4M, Methocel K15M CR and Methocel K100LV CR are hydrophilic polymers that become hydrated, swollen and facilitates to diffuse the drug.⁴ The effect of hydrophilic polymer PEG 6000 which act as a channeling agent was evaluated on the matrix tablet with combination of Methocel K4M. Here pH independent swelling of Eudragit RSPO and Eudragit RLPO released the drug from the matrix. In the present study an attempt had been made to formulate carbamazepine as sustained release matrix tablet with the addition of release retarding polymers Methocel K4M, Methocel K15M CR, Methocel K100LV CR, Eudragit RSPO and Eudragit RLPO. Three market products were also evaluated.

MATERIALS AND METHODS

Drug. Carbamazepine was obtained from Beximco Pharmaceutical Ltd., Dhaka.

Polymers. Hydroxypropyl methylcellulose Methocel K4M Premium (Colorcon USA), Hydroxypropyl methylcellulose Methocel K15M Premium (Colorcon USA), Hydroxypropyl methylcellulose Methocel K100LV CR, Premium (Colorcon USA), Eudragit RSPO (EVONIK, Germany) Eudragit RLPO (EVONIK, Germany).⁸

Other excipients. Microcrystalline Cellulose (Avicel PH 102) (Hanau chemicals ltd), Poly ethylene glycol (PEG), Ludipress (BASF), Aerosil,

Talc, Magnesium Stearate were procured from local market.

Solvents and reagents. Methanol (Merck, Germany) and Distilled water were obtained from our laboratory.

Equipments. Single punch tablet press; Simadzu UV spectrophotometer, Digital pH meter, Electrolab tablet dissolution test machine (XXII), Sartorius electronic balance were available in the departmental laboratory.

Preparation of matrix tablet. Drug, polymer and other excipients were weighed separately for 30 tablets per formulation as per proposed formulations. The proposed formulations were coded as F-1, F-2, F-3, F-4, F-5, F-6, F-7, F-8, F-9, F-10, F-11, F-12, F-13, F-14, F-15, F-16, F-17, F-18, F-19, F-20, F-21, F-22, F-23, F-24. The amounts of drug and excipients were expressed in milligram unit. Then active ingredient, microcrystalline cellulose, polymer and aerosil were blended for 15 minutes and then magnesium stearate, talc were added and further blended for another 1 minute. Blended mass was taken in the hopper and then die and punch were adjusted to get the desired weight of the tablet. The tablets were prepared by direct compression, the types and amounts of polymers used are shown in Table 1.

Physical evaluation of powders. The powders were evaluated for angle of repose, loose bulk density, tapped bulk density, compressibility index, total porosity etc.

Bulk density. LBD (Loose Bulk Density) and TBD (Tapped Bulk Density) were determined by 2 g of powder from each formula. The powder was previously lightly shaken to break any agglomerates formed and then it was placed into a 10 ml measuring cylinder. After the initial volume was observed, the cylinder was allowed to tap under its own weight onto a hard surface from the height of 2.5 cm at 2 second intervals. The reading of tapping was continued until no further change in volume was noted. Using the following equation LBD and TBD was calculated:

LBD = Weight of the powder / bulk volume of the packing. TBD = Weight of the powder / Tapped volume of the packing.

Compressibility index. The compressibility index of the granules was determined by Carr's compressibility index:

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

Angle of repose. The angle of repose of granules was determined by the funnel method.

Total porosity. Total porosity was determined by measuring the volume occupied by a selected

weighed granules were taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the heap of the granules. The granules were allowed to flow through the funnel freely onto the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation. Angle of Repose $\theta = \tan^{-1} h/r$, where, h = Height of the powder cone, r = Radius of the powder cone.

Table 1. Formulation design of Carbamazepine sustained release tablets containing Methocel K4M, Methocel K15M CR, Methocel K100LV CR, PEG 6000, Eudragit RSPO. and Eudragit RLPO.

Formulation	Carbamazepine (mg)	Avicell PH 102 (mg)	Ludipress (mg)	Methocel K4M (mg)	PEG 6000 (mg)	Methocel K15M CR (mg)	Methocel K100LV CR (mg)	Eudragit RSPO (mg)	Eudragit RLPO (mg)	Aerosil (mg)	Magnesium Stearate (mg)	Talc (mg)	Total weight (mg)
F1	200	100	100	50						2	1	1	454
F2	200	100	100	100						2	1	1	504
F3	200	100	100	150						2	1	1	554
F4	200	100	100	200						2	1	1	604
F5	200	100	100	100	50					2	1	1	554
F6	200	100	100	100	100					2	1	1	604
F7	200	100	100	100	150					2	1	1	654
F8	200	100	100	100	200					2	1	1	704
F9	200	100	100			50				2	1	1	454
F10	200	100	100			100				2	1	1	504
F11	200	100	100			150				2	1	1	554
F12	200	100	100			200				2	1	1	604
F13	200	100	100				50			2	1	1	454
F14	200	100	100				100			2	1	1	504
F15	200	100	100				150			2	1	1	554
F16	200	100	100				200			2	1	1	604
F17	200	100	100					50		2	1	1	454
F18	200	100	100					100		2	1	1	504
F19	200	100	100					150		2	1	1	554
F20	200	100	100					200		2	1	1	604
F21	200	100	100						50	2	1	1	454
F22	200	100	100						100	2	1	1	504
F23	200	100	100						150	2	1	1	554
F24	200	100	100						200	2	1	1	604

In vitro dissolution studies. Dissolution testing was performed in an "Electrolab Dissolution Tester, Germany" using Apparatus 1 (Basket method) at 100 rpm. Six tablets were evaluated per formulation in this study. The dissolution medium was 900ml distilled water with 1% sodium lauryl sulphate (USP method) in $37.0 \pm 0.5^\circ\text{C}$. The amount of drug present was determined according to the USP monograph for carbamazepine tablets using UV spectrophotometer

testing at 284nm.⁶ In the USP monograph it is said that 65-90% drug should be released in 6-12 hours. Dissolution studies were carried over 7-12 hours in the medium.

Kinetic analysis of release data. The release of drug from sustained release dosage form was regulated by several process. These are extraction or diffusion of matrix or erosion of matrix alternatively.

The drug dissolved in the matrix material and then released by diffusion through membrane.⁷ In some cases, drug may be released by osmotic process. Different kinetic equations (Zero order, First order, Higuchi release, Korsmeyer-peppas, Hixon-crowell) were applied to interpret the release rate from the tablet. The best fitted models were zero order kinetics, Korsmeyer-peppas and Hixon crowell, as these plots showed the highest linearity.

Statistical Analysis. Data from the experiments were analyzed using the Statistical Package for Social Science (SPSS) software for windows version 17 (SPSS Inc., Chicago, Illinois, USA). Statistical analysis of the results was performed by using oneway analysis of variance (ANOVA) followed by Dennett's t-test for comparisons. The limit of significance was set at $p < 0.05$.

Mechanism of drug release. Korsmeyer *et al* (1983) derived a simple relationship which described drug release from a polymeric system Equation (1). To find out the mechanism of drug release, first 60%

drug release data was fitted in Korsmeyer–Peppas model:

$$M_t / M_\infty = Kt^n \dots \dots \dots (1)$$

Where, M_t / M_∞ is the fraction of drug released at time t , k is the rate constant and n is the release exponent. The n value is used to characterize different release mechanisms as given in the following for cylindrical shaped matrices:

Value of diffusion exponent (n)	Release mechanisms
0.45	Fickian diffusion
$0.45 < n < 0.89$	Anomalous (non-Fickian) diffusion
0.89	Case-II transport
$n > 0.89$	Super case-II transport

RESULTS AND DISCUSSION

Different physical properties like angle of repose, LBD, TBD, carr's index, total porosity and *in vitro* dissolution studies were observed. The results are given in the following tables.

Table 2. Properties of granules of carbamazepine and excipients containing Methocel K4M, Methocell K15M CR, Methocell K100LV CR, PEG 6000, Eudragit RSPO and Eudragit RLPO.

Formulations	Angle of repose (°)	Loose bulk density (LBD) (g/ml)	Tapped bulk density (TBD) (g/ml)	Carr's index (%)	Hausner ratio	Total porosity (%)
F-1	28.07±0.02	0.418±0.01	0.505±0.02	17.22±0.08	1.20±0.01	17.14±0.01
F-2	26.57±0.05	0.405±0.06	0.5±0.04	19±0.02	1.23±0.03	18.96±0.04
F-3	28.1±0.03	0.461±0.08	0.539±0.09	14.47±0.01	1.16±0.04	14.29±0.03
F-4	23.75 ±0.01	0.446±0.05	0.539±0.09	17.25±0.07	1.20±0.02	17.14±0.04
F-5	29.98±0.01	0.458±0.01	0.54±0.011	15.18±0.02	1.17±0.03	15.15±0.02
F-6	25.17±0.03	0.459±0.02	0.57±0.02	19.47±0.02	1.24±0.01	19.44±0.02
F-7	27.07±0.02	0.471±0.04	0.569±0.02	17.22±0.02	1.20±0.04	17.24±0.02
F-8	26.32 0.06	0.45±0.08	0.548±0.02	17.88±0.03	1.21±0.02	17.86±0.06
F-9	28.01± 0.04	0.469±0.04	0.525±0.08	10.66±0.02	1.11±0.03	10.71±0.05
F-10	32.01±0.04	0.409±0.04	0.478±0.07	14.43±0.02	1.16±0.02	12.5±0.04
F-11	30.96±0.06	0.405±0.05	0.468±0.06	13.46±0.01	1.15±0.04	9.756±0.04
F-12	29.73±0.02	0.449±0.05	0.518±0.06	13.32±0.02	1.15±0.03	13.33±0.04
F-13	31.05± 0.01	0.423±0.05	0.497±0.04	14.88±0.01	1.17±0.02	11.11±0.02
F-14	28.92±0.05	0.416±0.01	0.493±0.03	15.61±0.05	1.18±0.02	15.38±0.07
F-15	26.32 0.07	0.409±0.01	0.57±0.01	28.24±0.05	1.39±0.03	14.29±0.07
F-16	28.01± 0.05	0.405±0.01	0.569±0.03	28.82±0.05	1.40±0.03	17.14±0.01
F-17	32.08±0.05	0.449±0.01	0.548±0.03	18.06±0.08	1.22±0.03	15.15±0.02
F-18	30.96±0.07	0.423±0.03	0.525±0.05	19.42±0.04	1.24±0.04	19.44±0.03
F-19	29.73±0.03	0.416±0.04	0.478±0.05	12.97±0.03	1.14±0.03	17.24±0.04
F-20	31.05± 0.02	0.409±0.05	0.46±0.08	11.08±0.02	1.12±0.01	17.86±0.04
F-21	25.92±0.06	0.405±0.04	0.518±0.07	21.81±0.02	1.27±0.03	10.71±0.05
F-22	26.32 0.08	0.449±0.04	0.497±0.06	9.65±0.04	1.10±0.01	12.5±0.07
F-23	29.01± 0.06	0.423±0.06	0.493±0.08	14.19±0.05	1.16±0.02	9.756±0.01
F-24	33.01±0.06	0.448±0.08	0.497±0.04	9.65±0.02	1.37±0.03	12.5±0.06

Table 3. Percentage of release of twenty four formulations and market product of Carbamazepine sustained release tablets against time.

Time(hr)	0	0.25	0.5	1	2	3	4	5	6	7	8	9	10	11	12	
Percent Release of Drugs	F1	0	6.35	8.37	16.00	32.26	53.90	70.11	83.52	97.85	99.09	-	-	-	-	-
	F2	0	6.26	8.74	15.26	30.11	49.88	64.83	79.30	84.25	87.30	93.18	-	-	-	-
	F3	0	5.51	7.62	11.42	23.45	43.79	54.03	61.32	69.98	77.98	85.79	96.30	-	-	-
	F4	0	5.89	8.55	10.79	19.83	27.30	35.87	48.07	59.10	69.78	80.01	88.79	94.01	97.79	98.81
	F5	0	6.16	8.93	15.07	31.23	50.35	65.22	80.53	84.57	88.54	95.65	-	-	-	-
	F6	0	5.98	9.11	16.09	33.38	53.73	67.25	80.72	86.52	90.61	97.09	-	-	-	-
	F7	0	6.26	9.58	16.75	35.35	54.52	68.50	83.75	87.26	91.36	98.12	-	-	-	-
	F8	0	6.72	10.14	17.51	35.74	57.05	69.76	84.10	87.61	93.76	98.59	-	-	-	-
	F9	0	4.72	7.52	13.46	28.20	50.36	64.77	73.01	80.80	87.99	93.39	98.66	-	-	-
	F10	0	4.61	7.15	12.24	27.53	41.78	52.84	61.88	72.62	81.95	87.10	93.79	97.01	-	-
	F11	0	4.58	7.14	11.41	24.92	38.68	51.84	62.07	70.49	77.20	82.86	88.39	92.48	98.84	99.12
	F12	0	4.68	6.59	10.84	23.05	38.27	48.36	57.07	64.41	71.61	75.91	80.99	84.45	89.79	94.07
	F13	0	6.26	9.02	16.75	34.13	56.45	71.57	84.07	98.49	99.92	-	-	-	-	-
	F14	0	6.72	9.03	16.75	32.28	50.85	66.47	80.31	86.38	92.61	97.62	-	-	-	-
	F15	0	5.42	7.43	12.54	24.95	44.28	56.76	64.07	73.51	81.55	88.65	99.85	-	-	-
	F16	0	5.79	8.92	11.53	21.89	29.66	37.88	50.10	61.90	72.70	82.40	91.59	93.49	96.89	98.20
	F17	0	1.89	3.86	6.60	12.44	15.64	20.46	26.73	34.92	39.39	45.67	52.76	57.50	62.11	67.69
	F18	0	1.98	4.05	6.23	11.41	13.58	18.01	24.25	28.88	36.16	42.04	49.28	56.12	60.90	65.36
	F19	0	1.79	3.77	5.19	9.35	12.34	16.38	21.20	26.82	32.97	39.56	45.00	52.36	57.19	59.19
	F20	0	1.79	3.58	4.09	7.48	10.35	14.27	19.08	24.58	30.80	34.20	40.42	45.78	51.01	56.10
	F21	0	6.07	8.46	15.62	30.11	52.20	66.81	74.98	85.21	89.10	95.44	98.49	-	-	-
	F22	0	6.16	8.28	14.51	28.15	51.33	63.98	73.04	81.76	85.80	93.04	96.26	98.57	-	-
	F23	0	6.26	7.26	11.43	25.03	37.67	47.29	60.27	70.06	77.69	86.71	89.49	94.52	95.88	97.06
	F24	0	5.79	6.51	9.46	20.81	34.15	44.85	56.40	64.29	70.75	74.48	77.69	80.92	84.74	87.29
Carbazin CR(SK+F)	0	3.75	6.39	10.18	24.43	38.64	47.53	62.27	74.38	82.62	86.48	89.20	92.37	95.19	96.54	
Tegretol CR(Novartis)	0	8.77	18.91	39.66	51.35	62.05	65.60	70.40	70.88	75.34	77.44	80.04	81.23	85.78	86.84	
Epilep CR (Beximco)	0	2.07	5.44	9.69	26.25	40.67	51.44	65.11	76.51	82.73	89.19	91.38	93.64	97.96	98.98	

Reducing the dose frequency of Carbamazepine increases patient compliance. Patients prefer to take the drug once or twice daily. Sustained release Carbamazepine prepared by the hydrophilic matrix of HPMC and pH independent polymer Eudragit RSPO, Eudragit RLPO controlled the Carbamazepine release effectively for 7-12 hour.⁸ Hence, these formulations can be considered as twice daily sustained release tablet of Carbamazepine. The formulation showed acceptable pharmacotechnical properties. *In vitro* dissolution studies indicated a steady state sustained release pattern throughout 7-12 hour of the study which was comparable to theoretical release profile. Drug release kinetics indicated that the drug release was best explained by zero order kinetics, Korsmeyer-peppas and Hixon crowell, as these plots showed the highest linearity. In the present study Twenty four formulations were formulated primarily

by using four variable content of five polymers; Methocel K4M CR from formulation F1-F4 (variable content are 50mg, 100mg, 150mg, 200mg), Methocel K15M CR from formulation F9-F12 (variable content are 50mg, 100mg, 150mg, 200mg), Methocel K100LV CR from formulation F13-F16 (variable content are 50mg, 100mg, 150mg, 200mg), Eudragit RSPO from formulation F17-F20 (variable content are 50mg, 100mg, 150mg, 200mg) and Eudragit RLPO from formulation F21-F24 (variable content are 50mg, 100mg, 150mg, 200mg). To see the effect of Channeling agent PEG 6000 with polymer Methocel K4M, four variable amount of PEG 6000 were prepared, F-5-F-8 (50mg, 100mg, 150mg, 200 mg) where polymer Methocel K4M content remained same (100 mg). Three market products were also studied. Only six formulations F-4, F-11, F-12, F-16, F-23 and F-24 met the release profile comparable

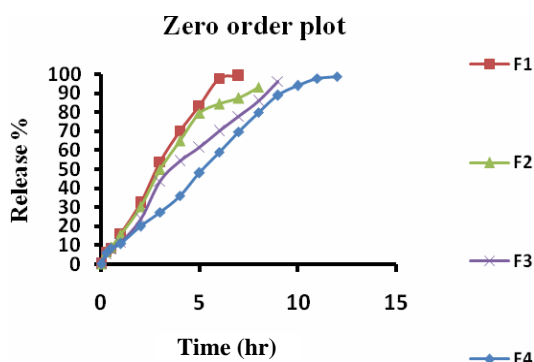


Figure 1. Zero order release kinetics of Carbamazepine sustained release tablets (F1-F4)

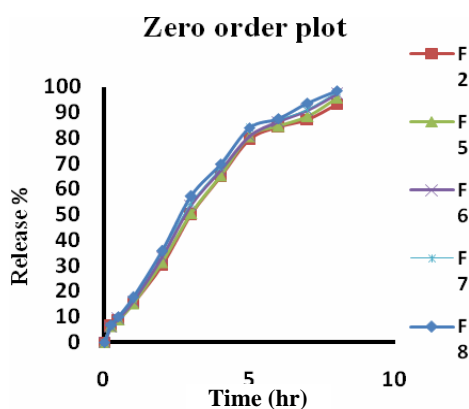


Figure 2. Zero order release kinetics of Carbamazepine sustained release tablets (F2 and F5-F8).

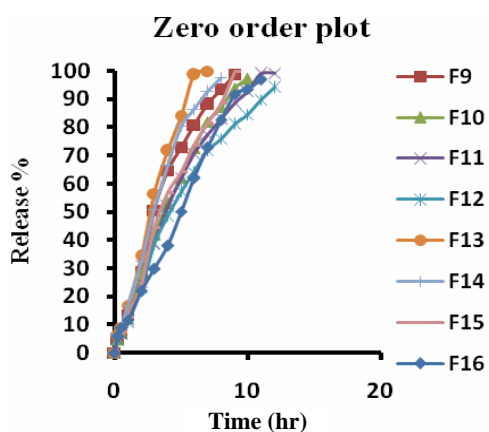


Figure 3. Zero order release kinetics of Carbamazepine sustained release tablets (F9-F16).

with market product and three formulations F-17, F-18 and F-24 met the official USP release guideline of carbamazepine sustained release tablet. The drug release followed mainly super case II transport ($n > 0.85$) in F-1, F-2, F-3, F-5, F-6, F-7, F-9, F-10, F-

11, F-13, F-15, F-17, F-18, F-19, F-20, anomalous or non-fickian transport ($n > 0.43$ and $n < 0.85$) in formulations F-4, F-8, F-12, F-14, F-16, F-21, F22, F-23, F-24.

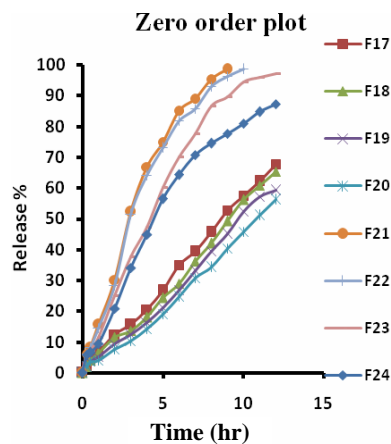


Figure 4. Zero order release kinetics of Carbamazepine sustained release tablets (F17-F24).

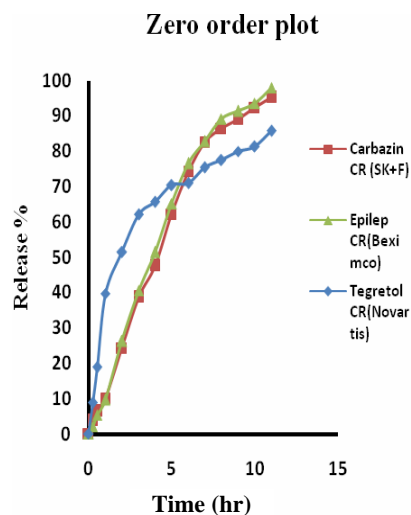


Figure 5. Zero order release kinetics of Market products of Carbamazepine sustained release tablets.

Impact of channeling agent (PEG 6000) on drug release from matrix tablet of Carbamazepine. Poly ethylene glycol (PEG) is a hydrophilic molecule. It is used in different formulation of poorly water soluble drugs to increase solubility.⁹ In formulations F-5 to F-8 variable amount of PEG 6000 was used with Methocel K4M. For formulations F-5, F-6, F-7 and F-8, the PEG 6000 content were 50mg, 100mg, 150mg and 200mg, respectively. Whereas in this formulations the Methocel K4M content remained same, which was

100mg. If we compare formulations F-5 to F-8 with F-2 (where methocel K4M content was same 100mg, but here there was no use of PEG 6000) it was found that the release of drugs from the matrix tablet carbamazepine increased due to increase content of PEG 6000. It was seen that in 8 hours, from

formulation F-2 (PEG 6000 was not used), the release was 93.18%. In Formulations F-5 (50mg PEG 6000 is used) it was 95.64%, in F-6 (100mg PEG 6000 is used) it was 97.08%, in F-7 (150mg PEG 6000 is used) it was 98.12% and in F-8 (200mg PEG 6000 is used) it was 98.59% in 8 hours.

Table 4. Release rate constants and R² values for different release kinetics of twenty four formulations and market product of Carbamazepine sustained release tablets.

Formulation	Zero order		First order		Higuchi		Korsmeyer-Peppas			Hixson- Crowell	
	K ₀	R ²	K ₁	R ²	K _n	R ²	n	K _{Km}	R ²	K _{HC}	R ²
F1	15.31	0.983	-0.617	0.869	42.64	0.95	0.906	0.184	0.987	0.663	0.958
F2	12.44	0.961	0.327	0.982	37.77	0.963	0.852	0.177	0.987	0.442	0.992
F3	10.71	0.984	-0.29	0.881	34.13	0.963	0.856	0.148	0.984	0.382	0.965
F4	9.258	0.993	-0.287	0.876	32.06	0.937	0.796	0.137	0.976	0.349	0.959
F5	12.66	0.964	-0.359	0.963	38.39	0.964	0.858	0.178	0.988	0.467	0.991
F6	12.84	0.961	-0.393	0.952	39.08	0.968	0.864	0.182	0.99	0.494	0.993
F7	12.95	0.957	-0.428	0.931	39.51	0.969	0.852	0.19	0.99	0.515	0.989
F8	13.03	0.955	-0.46	0.927	39.84	0.97	0.834	0.198	0.989	0.535	0.991
F9	11.6	0.96	-0.393	0.902	37.55	0.969	0.907	0.155	0.988	0.465	0.986
F10	10.2	0.977	-0.31	0.934	34.64	0.973	0.878	0.143	0.993	0.391	0.989
F11	9.273	0.969	-0.306	0.865	33.28	0.976	0.862	0.138	0.991	0.366	0.977
F12	8.029	0.96	-0.209	0.972	30.37	0.98	0.834	0.133	0.988	0.285	0.996
F13	15.38	0.981	-0.81	0.782	43.01	0.956	0.902	0.19	0.991	0.722	0.947
F14	12.93	0.969	-0.416	0.94	39.16	0.967	0.842	0.187	0.989	0.509	0.991
F15	11.14	0.984	-0.453	0.648	35.54	0.964	0.869	0.151	0.988	0.459	0.902
F16	9.291	0.989	-0.283	0.909	32.49	0.953	0.79	0.143	0.985	0.359	0.974
F17	5.665	0.997	-0.088	0.975	20.47	0.93	0.916	0.0662	0.995	0.148	0.991
F18	5.451	0.992	-0.083	0.96	19.5	0.906	0.891	0.0639	0.987	0.141	0.975
F19	5.064	0.991	-0.074	0.965	18.07	0.901	0.902	0.057	0.984	0.126	0.976
F20	4.617	0.991	-0.064	0.964	16.42	0.894	0.896	0.051	0.972	0.112	0.976
F21	11.65	0.953	-0.409	0.935	37.87	0.97	0.848	0.176	0.987	0.479	0.993
F22	10.48	0.942	-0.379	0.946	36.24	0.972	0.829	0.171	0.982	0.439	0.996
F23	8.916	0.954	-0.29	0.965	32.87	0.973	0.805	0.149	0.982	0.353	0.994
F24	7.845	0.945	-0.172	0.996	29.03	0.973	0.804	0.133	0.974	0.251	0.991
Carbazin CR (SK+F)	9.406	0.955	-0.278	0.982	33.14	0.956	0.901	0.126	0.986	0.34	0.991
Tegretol CR (Novartis)	6.639	0.787	-0.156	0.938	25.13	0.94	0.553	0.278	0.909	0.215	0.901
Epilep CR (Beximco)	9.665	0.951	-0.313	0.954	34.62	0.96	1.03	0.106	0.983	0.386	0.995

CONCLUSION

The experiment revealed that Methocel K4M, Methocel K15M CR, Methocel K100LV CR, Eudragit RSPO and Eudragit RLPO in varying proportions controlled the carbamazepine release effectively for 7-12 hours. The effect of wetting agent PEG 6000 was also evaluated with Methocel K4M.¹⁰ In most of the cases, the release kinetics of carbamazepine depended on the content of polymers

in the tablets. It was seen that from the above formulations only six formulations were comparable with market products and three formulations met the USP guidelines. The use of channeling agent PEG 6000 decreased the sustaining action of the tablets.

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