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Original Article

Comparative study of release profile of sustain release carvedilol matrix tablets using Methocel K100LV CR, Methocel K100M CR and xanthum gum polymer

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ABSTRACT

In present study an attempt was made to formulate and to evaluate the sustain release Carvedilol matrix tablets by using METHOCEL K100LV CR, METHOCEL K100M CR and Xanthum Gum polymer. The tablets were prepared by direct compression method. The granules were evaluated by angle of repose, bulk density, tapped density and compressibility index, surface P^H. The formulated tablets were evaluated by weight variation, thickness, diameter, hardness, friability and drug content. Drug content in formulation was determined by UV method. The granules showed satisfactory flow properties. The in-vitro release study of matrix tablets were carried out in 0.1N HCL using USP paddle method with sinker which was conducted for 8 hours and examined. Statistically significant differences were found among the drug release profile from different classes of polymeric matrix. Higher polymer content (30%) in the matrix decreased the rate of drug release due to the increase tortuosity and decrease porosity. At lower polymeric level (5%), the rate of drug release was elevated. METHOCEL K100M CR was found to cause the strong retardation of drug. On the other hand, highest release was found from Xanthum Gum while METHOCEL K100LV CR gave an intermediate release profile of Carvedilol. The release mechanism was explored and examined by Zero order; First order, Higuchi, korsmeyer-Peppas and Hixson-Crowell equation. The release of the drug from all the formulations was found to follow Higuchi model, as the plots showed high linearity. Also high viscosity METHOCEL grades mostly followed anomalous or non-ficking transport process. Therefore, the results generated in this study showed that the formulated sustained release matrix tablets deliver the drug through a combination of both diffusion and erosion controlled mechanism.

Keywords: Carvedilol**,** METHOCEL K100LV CR**,** METHOCEL K100M CR**,** Xanthum Gum**,** Sustain release

INTRODUCTION

The oral route is the most popular route of drug administration. Physiology of Gastrointestinal track offers more flexibility in dosage form design [1].The terms Sustained release, prolonged release, modified release, extended release and depot formulation are used to identify drug delivery systems that are designed to achieve or extend therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose [2].There are several reasons for attractiveness of these dosage forms which are enhancement of bioavailability of drug, reduction in the frequency of drug administration, prolongation of duration of effective blood levels, reduction of fluctuation of blood concentration of drug and side effects and possibly improvement of the specific distribution of the drug. If one want to develop an ideal drug delivery system, two pre-requisites will have to be ensured. They are firstly single dose for the duration of treatment whether for days or weeks as with infection, diabetes or hypertension and secondly it must deliver the active entity directly to the site of action minimizing the side effects. There are some considerations for the preparation of extended release formulations. Such as If the active compound has a long half-life, it sustains for long time. If the pharmacological activity of the active is not directly related to its blood levels, If the absorption of the drug involves an active transport and If the active compound has very short half-life then it will require a large amount of drug to

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maintain a prolonged effective dose. The above factors need serious review prior to design. The advantage of administration of a single dose of a drug is to release of drug over an extended period of time. The desire of maintaining a near constant or uniform blood level of a drug often translates into better patient compliance as well as enhanced clinical efficacy of the drug for its intended use [3]. Because of increased complication and expense involved in marketing of new drug entities, it has focused greater attention on development of sustained or controlled release drug delivery systems [4].Matrix system is widely used for the purpose of sustained release. It is the release system which prolongs and controls the release of the drug that is dissolved or dispersed. In fact, a matrix is defined as a well-mixed composite of one or more drugs with gelling agent i.e. hydrophilic polymers [5].The goal of an extended release dosage form is to maintain therapeutic drug level in plasma for extended period of time.

Carvedilol is a third-generation, non-cardioselective β-blocker [6] that also possesses α_1-adrenergic-blocking, antioxidant, and calcium antagonist effects. It blocks β_1- and β_2-adrenergic receptors, improves myocardial function, and attenuates (or reverses) the detrimental ventricular remodeling that marks HF. Carvedilol lacks intrinsic sympathomimetic activity and does not demonstrate inverse agonist activity, which may contribute to its generally favorable tolerability profile [7]. A sustained-release (SR) delivery system for carvedilol has been developed with the intention of allowing once-daily dosing while maintaining favorable pharmacodynamic features. With carvedilol SR, there is an opportunity to improve patient care by increasing the probability of medication adherence. The availability of vasodilating β-blockers, such as the combined nonselective β- and α_1-blocker carvedilol, represents an opportunity to use a cardio protective agent without the concerning hemodynamic, renal and metabolic responses associated with traditional β-blocker therapy. In contrast with earlier generations of β-blockers, carvedilol effect on lowering BP which reflects on reduction of vascular resistance and preservation of cardiac output [8-9]. Furthermore, carvedilol increases insulin sensitivity and glucose disposal and has a neutral effect on lipid profiles.

MATERIALS AND METHOD

Materials: Carvedilol (received from Drug International Ltd.) Kollidon® SR (BASF Bangladesh Limited.) Microcrystalline cellulose (Ming Tai Chemical Co. Limited, Taiwan), and Hydroxypropylmethylcellulose (Colorcon, USA) and Magnesium stearate (Colorcon, USA), Potassium dihydrogen phosphate buffer (Merck, Germany) & Sodium hydroxide (Merck, Germany)

Equipment: Electronic Balance (Model: AR2140)**,** USA.**,** Perkin-Elmer Laboratory Hydraulic Press**,** UK. Digital Force Gauge (Model: EH-01P) Electrolab, India.**,** Digital pH Meter-pH210**,** Hanna Intruments, Romania., Dissolution Tester (Model: TDT-08L plus)**,** Electrolab, India., UV-1800 Spectrophotometer**,** Shimadzu, Japan., Friabilator (Model: EF2)**,** Electrolab, India., Sonicator (Model: Power Sonic505), Hwashin Technology SEOUL, Korea., Slide Caliper**,** Germany., Volumetric flask, Pipette, Beakers, Test tubes, Funnel.

METHODS

Preparation of Carvedilol matrix tablet: The active ingredient, matrix polymer, release modifiers and lubricant were blended together and made into tablets by direct compression at a fixed compression force. **Table No.1, Table No.2** and **Table No.3** summarize the formulation of carvedilol sustained release tablets. All the components required for tablets were blended for 10 minutes. The appropriate amounts of the mixture were then compressed using a hydraulic press equipped with a 13 mm flat faced punch and dies set. The compression force and compression time were 5 ton and 1 minute respectively.

Evaluation of Tablet Blends or Granules: Tablet blends or granules of proposed formulation were evaluated for Angle of Repose, Bulk Density and Tapped Density, Hausner's Ratio and Carr's Compressibility Index. Angle of repose of granules was determined by the funnel method. Angle of repose (θ) can be determined by the equation $\tan\theta = h/r$ [10-11]. An accurately weighed quantity of the granules or powder (W) was carefully poured into the graduated cylinder and volume (V) was measured. Bulk density is the ratio of weight and volume of the granules (BD= W/V) [12-13]. After tapping, note down the reduce volume of the granules and it was the volume of granules (V_f). Then calculate the tapped density. Tapped density = W/V_f. Hausner's found that this ration was related to interparticle friction and as such could be used to predict powder flow properties. Generally a value less than 1.25 indicates good flow properties. Hausner's Ratio = Tapped density/Bulk density. Carr's index of each formulation was calculated according to equation given [14] Carr's Compressibility Index (%) = [100 (TD-BD)]/TD. Where, TD is the tapped density and BD is the bulk density**.**

Evaluation of Tablets: Tablets of proposed formulation were evaluated for Diameter Size and Shape, Thickness, Uniformity of Weight, Friability, Hardness, Swelling Study, Surface pH Study, Drug-Excipients Interaction Study, Assay of formulated Carvedilo, In-Vitro Dissolution Study. The tablets of various sizes and shapes were prepared but generally they were circular with either flat or biconvex faces. The thickness of the tablets was determined by using a Digital Caliper (range 0-150 mm). The weights were determined by using an electronic balance (Adventurer TM electronic balance, Model AR2140, Capacity (Max) - 210 gm, Readability- 0.0001 gm). Then the percentage of weight variation of each tablet was determined by using following formula. Percentage of weight variation: (Average weight – Individual weight)/ Average wt.×100. The instrument used for friablility test is known as 'Friability Test Apparatus' or 'Friabilator'. The hardness of the tablets was determined by using a hand operated hardness tester apparatus (Electrolab EH-01P). The extent of swelling was measured in terms of percentage of diameter and thickness gained by the tablet. Two tablets from each formulation were exposed to pH 7.4 phosphate buffer. At the end of 2 hour, tablets were withdrawn, soaked with tissue paper and the swelling behaviors of the formulations were observed. The method for surface pH study adopted by Battenberg *et al* [15] was used to determine the surface pH of the tablet. A combined glass electrode was used for this purpose. The tablet was allowed to swell by keeping it in contact with 5 mL of distilled water (pH 6.5 ± 0.05) for 2 h at room temperature. The pH was measured by bringing the electrode in contact with the surface of the tablets and allowing it to equilibrate for 1 min.

Drug-Excipients Interaction Study: Among the various methods, UV-spectroscopy is the simplest method for the evaluation of possible incompatibilities. The UV spectra of each the four formulations were compared with the standard spectrum of Carvedilol.

Assay of formulated Carvedilol SR Tablets: The absorbance of standard solution and sample solution were measured at 241 nm by using UV spectrophotometer. The percentage of potency was measured by appropriated equation.

In-Vitro Release Kinetics Study: Dissolution Parameters: Medium: Phosphate buffer solution P^H 7.4, Apparatus: USP Type II (Rotating paddle method), RPM: 75, Time: 7 hours, Temperature: 37 ± 0.5˚C, Method: UV spectrophotometer. Procedure: The absorbance was measured by using UV-1800 SHIMADZU UV spectrophotometer at the wave length of 270 nm. Then the percentage of drug release was calculated by using following equation: % of drug release: CDR (cumulative drug release)/35 × 100.

Analysis of Release Data: The release data obtained were treated according to zero-order (cumulative amount of drug release versus time (hr)), first order (log cumulative percentage of drug remaining versus time (hr)), Higuchi (cumulative percentage of drug release versus square root of time (hr)), Korsmeyer-Peppas (log cumulative percentage of drug release versus log time (hr)) and Hixson-Crowell (cubic root of percentage drug release versus time (hr)) equation models.

Dissolution data were also fitted according to the well-known exponential equation, which is often used to describe the drug release behavior from polymeric systems introduced by Korsmeyer-Peppas et. al. $M_t / M_\infty = k\ t^n$. Where, M_t is the amount of drug release at time t, M_∞ is the amount of drug release after infinite time; k is a release rate constant incorporating structural and geometric characteristics of the tablet and n is the diffusional exponent indicative of the mechanism of drug release. A value of n = 0.45 indicates Fickian (case I) release, > 0.45 but < 0.89 for non-Fickian (anomalous) release and > 0.89 indicates super case II type of release. Case II generally refers to the erosion of the polymeric chain and anomalous transport (non-Fickian) refers to a combination of both diffusion and erosion controlled-drug release [16]. Mean dissolution time (MDT) was calculated from dissolution data using the following equation (Mockel and Lippold) [17].$MDT = (n / n+1)\ k^{-1/n}$. Where, n is the release exponent and k is the release rate constant.

RESULTS AND DISCUSSION

Evaluation of Tablet Blends or Granules: The granules of the different formulations were prepared and evaluated for angle of repose, bulk density, tapped density, compressibility index and Hauser's ratio. The results are presented in the **Table 4.**

Drug Content and Physical Evaluation of Carvedilol Matrix Tablets: The prepared tablets were subjected to preliminary characterization such as physical parameters (thickness, diameter, hardness and friability), weight uniformity and drug content of all the fabricated tablets. The values are indicated in **Table.5**.

Swelling Study: Swelling behaviors of the formulated Carvedilol SR were observed. Polymers, used in the formulations-Methocel

K100LV, Methocel K100M CR, Xanthum gum showed different degree of swelling ability. The diameter and thickness of the tablets increase after 5hours were shown in **Table 6**.

In-Vitro Dissolution Studies: The dissolution data (from the values of 0 to 8 hours drug release) of all formulations were fitted into various mathematical models (zero-order, first-order, Higuchi, Korysmeyer-Peppas model, Hixson-Crowell plot) to know which mathematical model will best fit the obtained release profile. The obtained dissolution data of all the formulations are presented in figure 1 to 15 respectively. The release kinetics parameters of all formulations are presented in **Table 7.**

Effect of Polymer on Drug Release Rate: Drug release is controlled by penetration of water through the gel layer produce by hydration of polymer and diffusion of drug through the swollen, hydrated matrix in addition to erosion of the gelled layer. In case of plastic polymer, the release of drug is controlled through the porous channel. High drug polymer ratios resulting formulation of which drug release is controlled by attrition [18]. The result of the effect of polymer on release of Carvedilol SR is shown in **Tables 8-10**.

Release of Drug According to Higuchi Equation: Based on highest regression coefficient value (r^2) the best-fit model for all formulations was Higuchi model. Times required for 25%, 50% and 75% of drug release which were mentioned in **Tables 11-13** were corrected using linear equation of Higuchi plot. From this study, it was observed that formulated tablets of formulation 1 were released more than 8.5 hours. So, it was concluded that more than 12 hours required for 100% release.

DISCUSSION

The result of angle of repose ranged from 32.19° to 36.07° for Methocel K100LV, 33.59° to 39.73° for Methocel K100M CR, 42.66° to 45.94° for Xanthum gum. And the result of compressibility index (%) ranged from 26.83° to 30.05° for Methocel K100LV, 27.99° to 33.01° for Methocel K100M CR, 34.50° to 38.25° for Xanthum gum respectively. The results of angle of repose value less than 30 degrees indicates good flow properties. This was further supported by the lower compressibility index. The lowest compressibility index around 21% and below are considered to have fair and excellent flow properties [19].Although the results of some formulation of angle of repose and compressibility index were not shown within the range of limit but no handling and flow properties problem occurred during the compression of tablets and the formulated tablets were shown the results within the range of limit.

The results of loose bulk density ranged from (0.512 to 0.531) for Methocel K100LV, (0.503 to 0.531) for Methocel K100M CR, (0.472 to 0.495) for Xanthum gum and tapped bulk density ranged from (0.712 to 0.741) for Methocel K100LV, (0.7111 to 0.76) for Methocel K100M CR, (0.745 to 0.781) for Xanthum gum. Carvedilol SR tablets of all the formulations showed surface pH values ranged from 6.68 to 6.90 which indicates no risk of mucosal damage or irritation.

All the batches showed uniform thickness and diameter. The average percentage deviation of 10 tablets of each formulation was less than 5%, and hence all formulations passed the test for uniformity of weight as per official requirements. The hardness of all the formulations is within the range of limit. The usage of Methocel K100LV, Methocel K100M CR, Xanthum gum has facilitated the compression of the tablets and made it possible to impart proper hardness settings. It is possible to have better control in a larger production control. Tablets hardness is, however, not an absolute indicator of strength. The percentage of friability of the tablets of all the formulations was also within the range. In the present study, the percentage of friability for all formulations was below 1% w/w, indicating that the friability is within the prescribed limits. So, all the tablet formulations showed acceptable pharmacopoeia properties and complied with pharmacopoeia specifications for weight variation and friability. All the formulations showed good uniformity in drug content.

Based on highest regression coefficient value (r^2) the best-fit model for all formulations was Higuchi model. When the data where plotted according to a Higuchi equation, the formulations M100LV-F1, M100LV-F2, M100LV-F3, M100LV-F4, M100LV-F5, M100LV-F6, M100M-F1, M100M-F2, M100M-F3, M100M-F4, M100M-F5, M100M-F6 and Xa.G-F2, Xa.G-F3, Xa.G-F4, Xa.G-F5, Xa.G-F6 showed a fair linearity, but Xa.G-F1 don't showed a fair linearity, while the data were plotted according to a first-order equation, all the formulations except M100M-F1 showed a fair linearity. Based on the 'n' values ranging from $0.45 < n < 0.89$ the drug release was found to follow anomalous or non-Fickian release. This value indicates a coupling of the diffusion and erosion mechanism and indicates that the drug release was controlled by more than one process. This finding was in accordance with other reported works [20-21].

Carvedilol SR loaded on Methocel K100LV shows drug release after 8 hours 97% when Polymer is 5% of total weight, 92.55% when Polymer is 10% of total weight, 71.43% when Polymer is 15% of total weight, 63.28% when Polymer is 20% of total weight, 51.44% when Polymer is 25% of total weight, 45.39% when Polymer is 30% of total weight. Carvedilol SR loaded on Methocel K100M CR shows drug release after 8 hours 75.54% when Polymer is 5% of total weight, 64.88% when Polymer is 10% of total weight, 58.69% when Polymer is 15% of total weight, 53.56% when Polymer is 20% of total weight, 38.61% when Polymer is 25% of total weight, 31.23% when Polymer is 30% of total weight. Carvedilol SR loaded on Xanthum Gum shows drug release after 8 hours 105.40% (after 6hrs) when Polymer is 5% of total weight, 102.5% when Polymer is 10% of total weight, 84.09% when Polymer is 15% of total weight, 78.81% when Polymer is 20% of total weight, 60.13% when Polymer is 25% of total weight, 49.56% when Polymer is 30% of total weight.

Based on highest regression coefficient value (r^2) the best-fit model for all formulations was Higuchi model. Time required for 25%, 50% and 75% of drug release was correlated using linear equation of Higuchi plot. From this study, it was observed that formulated tables of formulation 1 were released more than 8.5 hours. So, it was concluded that more than 12 hours required for 100% release.

CONCLUSION

METHOCEL K100M CR was found to cause the strong retardation of drug. On the other hand, highest release was found from Xanthum Gum while METHOCEL K100LV CR gave an intermediate release profile of Carvedilol. The release of the drug from all the formulations were found to be followed Higuchi model, as the plots showed high linearity and also showed that high viscosity METHOCEL grades mostly followed anomalous or non-ficking transport process. Therefore, the results generated in this study showed that the formulated sustained release matrix tablets deliver the drug through a combination of both diffusion and erosion controlled mechanism.

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Table 1: Formulation of Carvedilol loaded Methocel K100LV Based Matrix Tablet

Ingredients	Formulation code					
	F1	**F2**	**F3**	**F4**	**F5**	**F6**
Carvedilol	12.5	12.5	12.5	12.5	12.5	12.5
Methocel K100LV	12.5	25	37.5	50	62.5	75
Avicel PH101	100	100	100	100	100	100
Lactose	120	107.5	95	82.5	70	57.5
Magnesium Stearate	5	5	5	5	5	5
Total weight	250	250	250	250	250	250

Table 2: Formulation of Carvedilol loaded Methocel K100MCR Based Matrix Tablet

Ingredient	Formulation code					
	F1	F2	F3	F4	F5	F6
Carvedilol	12.5	12.5	12.5	12.5	12.5	12.5
Methocel K100MCR	12.5	25	37.5	50	62.5	75
Avicel PH101	100	100	100	100	100	100
Lactose	120	107.5	95	82.5	70	57.5
Magnesium Stearate	5	5	5	5	5	5
Total Weight	250	250	250	250	250	250

Table 3: Formulation of Carvedilol loaded Xanthum Gum Based Matrix Tablet

Ingredient	Formulation code					
	F1	F2	F3	F4	F5	F6
Carvedilol	12.5	12.5	12.5	12.5	12.5	12.5
Xanthum Gum	12.5	25	37.5	50	62.5	75
Avicel PH101	100	100	100	100	100	100
Lactose	120	107.5	95	82.5	70	57.5
Magnesium	5	5	5	5	5	5
Total weight	250	250	250	250	250	250

Table 4: **Granule properties of the different formulations of Carvedilol sustained release matrix tablets**.

	Parameters					
Formulation code	Angle of repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Hausner's Ratio	Compressibility index (%)	Surface P^H
M100LV-F1	35.30^0	0.523	0.741	1.42	29.42	6.68
M100LV-F2	33.19^0	0.531	0.734	1.38	27.66	6.74
M100LV-F3	32.19^0	0.521	0.712	1.37	26.83	6.80
M100LV-F4	36.07^0	0.512	0.732	1.43	30.05	6.78
M100LV-F5	33.12^0	0.522	0.721	1.38	27.60	6.74
M100LV-F6	32.64^0	0.53	0.728	1.37	27.20	6.72
M100M-F1	33.59^0	0.512	0.711	1.39	27.99	6.81
M100M-F2	39.73^0	0.503	0.752	1.50	33.11	6.74
M100M-F3	38.02^0	0.511	0.748	1.46	31.68	6.82
M100M-F4	36.63^0	0.528	0.76	1.44	30.53	6.89
M100M-F5	37.55^0	0.516	0.751	1.46	31.29	6.72
M100M-F6	34.93^0	0.531	0.749	1.41	29.11	6.76
Xa.G-F1	45.94^0	0.482	0.781	1.62	38.28	6.84
Xa.G-F2	45.08^0	0.472	0.756	1.60	37.57	6.90
Xa.G-F3	42.66^0	0.495	0.768	1.55	35.55	6.82
Xa.G-F4	44.36^0	0.486	0.771	1.59	36.96	6.77
Xa.G-F5	43.36^0	0.479	0.75	1.57	36.13	6.78
Xa.G-F6	41.40^0	0.488	0.745	1.53	34.50	6.68

Table 5: Tablet properties of the different formulations of Carvedilol sustained release matrix tablets

	Parameters					
Formulation code	Thickness (mm) n=5	Diameter (mm) n=5	Hardness (kgf) n=5	Friability %	Average Wt.(mg) n=10	Drug content %
M100LV-F1	5.00±0.01	8.00±0.01	4.93±0.03	0.21	248.01±0.52	97.80
M100LV-F2	5.00±0.01	8.00±0.01	5.01±0.07	0.18	246.08±0.42	98.22
M100LV-F3	5.01±0.01	8.01±0.01	4.88±0.05	0.15	247.56±0.18	101.30
M100LV-F4	5.00±0.01	8.00±0.01	4.87±0.03	0.17	245.80±0.48	96.46
M100LV-F5	5.01±0.01	8.00±0.01	5.34±0.12	0.8	246.05±0.23	97.20
M100LV-F6	5.00±0.01	8.00±0.01	5.02±0.08	0.5	247.03±0.93	98.30
M100M-F1	5.00±0.01	8.01±0.01	4.21±0.04	0.18	245.90±0.38	97
M100M-F2	5.00±0.01	8.00±0.01	4.30±0.04	0.15	247.18±0.53	97.60
M100M-F3	5.01±0.01	8.00±0.01	4.21±0.03	0.18	246.18±0.03	96.50
M100M-F4	5.00±0.01	8.00±0.01	4.12±0.10	0.8	246.10±0.58	96.82

M100M-F5	5.00±0.01	8.01±0.01	4.03±0.09	0.10	246.50±0.82	98
M100M-F6	5.00±0.01	8.00±0.01	4.03±0.06	0.15	249.01±0.54	103.50
Xa.G-F1	5.00±0.01	8.00±0.01	5.18±0.06	0.28	248.70±0.50	102.50
Xa.G-F2	5.00±0.01	8.00±0.01	5.12±0.04	0.32	248.20±0.80	99.20
Xa.G-F3	5.00±0.01	8.00±0.01	5.17±0.03	0.16	246.70±0.30	99
Xa.G-F4	5.00±0.01	8.00±0.01	5.11±0.12	0.21	247.50±0.13	98
Xa.G-F5	5.00±0.01	8.00±0.01	5.40±0.11	0.12	248.10±0.57	97.80
Xa.G-F6	5.01±0.01	8.00±0.01	5.21±0.02	0.14	248.10±0.65	97

*The values are expressed as mean ± SEM; n is specified in each column head

Table 6: Swelling properties of the different formulations of Carvedilol sustained release matrix tablets.

Formulation code	Thickness (%)	Diameter (%)
M100LV-F1	148	133
M100LV-F2	148	131
M100LV-F3	152	130
M100LV-F4	158	136
M100LV-F5	165	138
M100LV-F6	168	137
M100M-F1	152	122
M100M-F2	154	126
M100M-F3	157	128
M100M-F4	167	129
M100M-F5	168	130
M100M-F6	172	137
Xa.G-F1	123	107
Xa.G-F2	133	112
Xa.G-F3	134	115
Xa.G-F4	136	116
Xa.G-F5	138	120
Xa.G-F6	145	122

Table 7: Kinetic parameters of formulated Carvedilol SR matrix tablets

Code	Zero order regression coefficient (r^2)	First order regression coefficient (r^2)	Higuchi regression coefficient (r^2)	Korsmeyer's regression coefficient (r^2)	Slope of Korsmeyer-Peppas plot (n)	Hixson-Crowell regression coefficient (r^2)
M100LV-F1	0.962	0.831	0.966	0.406	0.712	0.641
M100LV-F2	0.959	0.963	0.993	0.4447	0.734	0.635
M100LV-F3	0.914	0.975	0.971	0.5105	0.804	0.605
M100LV-F4	0.919	0.970	0.993	0.3926	0.624	0.540
M100LV-F5	0.947	0.967	0.949	0.428	0.675	0.617
M100LV-F6	0.981	0.986	0.966	0.5901	0.731	0.681
M100M-F1	0.967	0.586	0.987	0.451	0.7	0.631
M100M-F2	0.952	0.987	0.991	0.438	0.668	0.599
M100M-F3	0.951	0.981	0.990	0.494	0.704	0.518
M100M-F4	0.951	0.979	0.986	0.480	0.675	0.505

M100M-F5	0.948	0.953	0.959	0.459	0.575	0.575
M100M-F6	0.949	0.958	0.971	0.566	0.629	0.601
Xa.G-F1	0.951	0.922	0.107	0.011	0.171	0.031
Xa.G-F2	0.939	0.951	0.979	0.33	0.628	0.557
Xa.G-F3	0.875	0.945	0.971	0.253	0.521	0.454
Xa.G-F4	0.846	0.948	0.972	0.274	0.542	0.450
Xa.G-F5	0.954	0.958	0.957	0.455	0.653	0.513
Xa.G-F6	0.975	0.990	0.979	0.468	0.643	0.632

Table 8: Effect Of Methocel K100LV on release of Carvedilol SR from matrices

Code	Polymer	%Drug Release
M100LV-F1	5	115.17
M100LV-F2	10	92.55
M100LV-F3	15	71.43
M100LV-F4	20	63.28
M100LV-F5	25	51.44
M100LV-F6	30	45.39

Table 9: Effect Of Methocel K100M CR on release of Carvedilol SR from matrices

Code	Polymer	%Drug Release
M100M-F1	5	75.44
M100M-F2	10	64.88
M100M-F3	15	58.69
M100M-F4	20	53.56
M100M-F5	25	38.61
M100M-F6	30	31.23

Table 10: Effect of Xanthum Gum on release of Carvedilol SR from matrices.

Code	Polymer	%Drug Release
Xa.G-F1	5	105.40
Xa.G-F2	10	102.85
Xa.G-F3	15	84.09
Xa.G-F4	20	78.81
Xa.G-F5	25	60.13
Xa.G-F6	30	49.56

Table 11: Required time for 25, 50 and 75 percentage of drug release from Methocel K100LV

Code	Time 25% (hr)	Time 50% (hr)	Time 75% (hr)
M100LV-F1	0.81	1.47	2.12
M100LV-F2	0.90	1.64	2.39
M100LV-F3	1.03	1.94	2.86
M100LV-F4	1.11	2.29	3.47
M100LV-F5	1.55	2.97	4.40
M100LV-F6	1.81	3.38	4.95

Table 12: Required time for 25, 50 and 75 percentage of drug release from Methocel K100M CR

Code	Time 25% (hr)	Time 50% (hr)	Time 75% (hr)
M100M-F1	1.08	2.02	2.96
M100M-F2	1.16	2.25	3.33
M100M-F3	1.33	2.53	3.74
M100M-F4	1.42	2.75	4.08
M100M-F5	2.12	4.22	6.32
M100M-F6	2.59	5.10	7.61

Table 13: Required time for 25, 50 and 75 percentage of drug release from Xanthum Gum

Code	Time 25% (hr)	Time 50% (hr)	Time 75% (hr)
Xa.G-F1	0.17	2.12	4.06
Xa.G-F2	0.49	1.21	1.93
Xa.G-F3	0.65	1.61	2.58
Xa.G-F4	0.68	1.67	2.66
Xa.G-F5	1.40	2.69	3.98
Xa.G-F6	1.56	2.99	4.41

FIGURE:

Different release model of Carvedilol sustained release formulations containing Methocel K100LV.

Fig 1 : Zero-Order (Methocel K100LV)

Fig 2: Hixson-Crowell release model (Methocel K100LV)

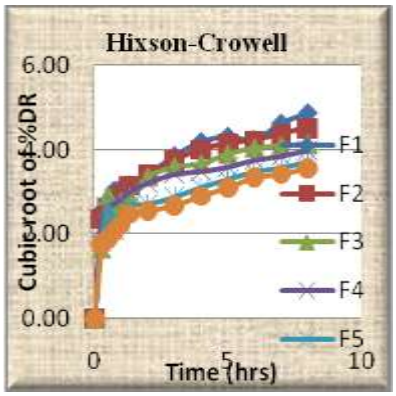


Fig3: First-Order (Methocel K100LV)

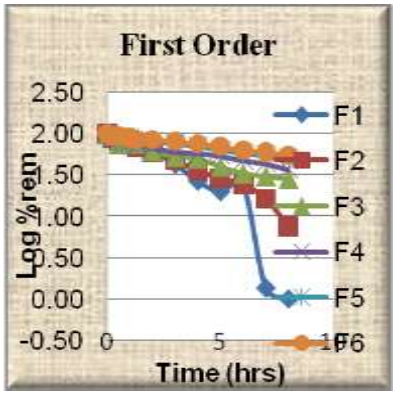


Fig 4: Higuchi RM (Methocel K100LV)

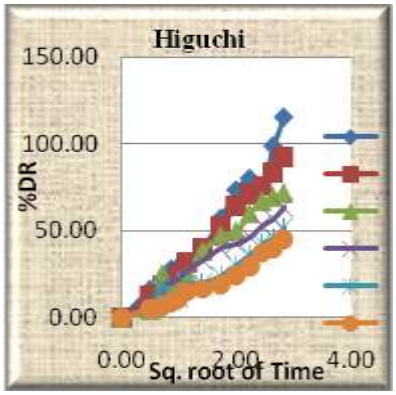
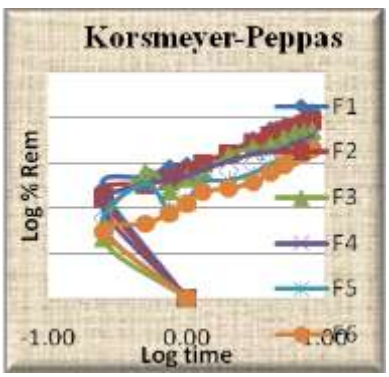


Fig5:korsmeyer-Peppasrelease(Methocel K100LV)



Different release model of Carvedilol sustained release formulations containing Methocel K100M CR.

Figure 6: Zero-Order release model

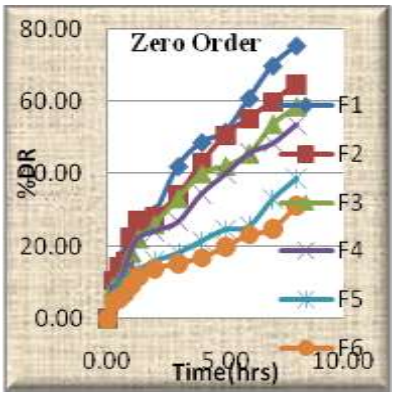


Fig7: Hixson-Crowell release model

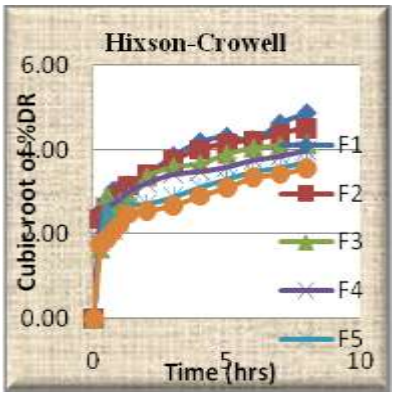


Fig 8: Korsmeye-Peppas release model

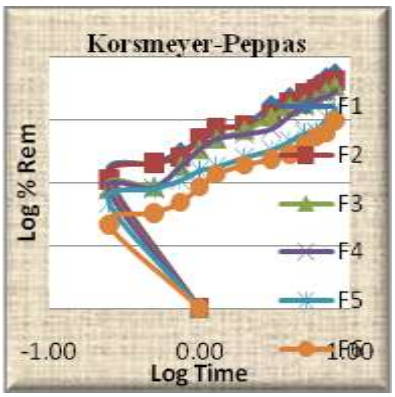


Fig 9: First-Order release model

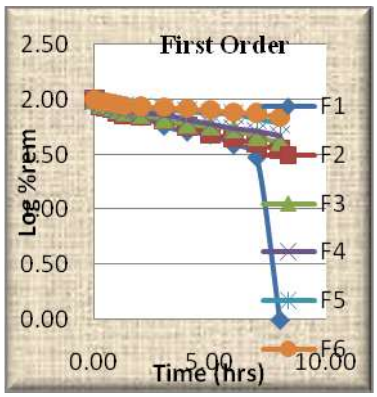
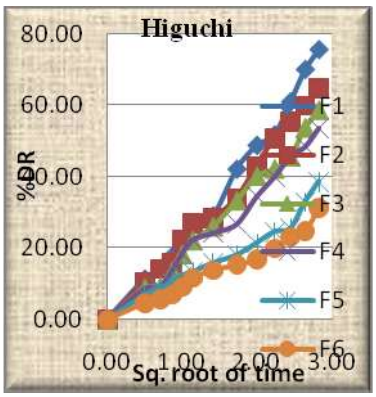


Fig 10: Higuchi release model



Different release model of Carvedilol sustained release formulations containing Xanthum gum.

Fig 11: Zero-Order release model

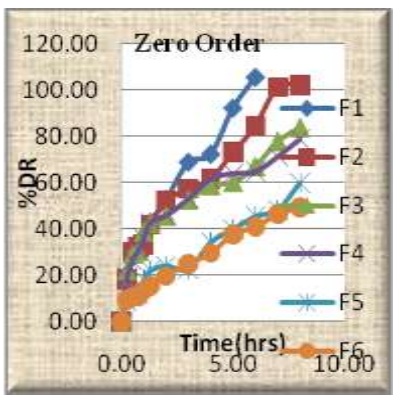


Fig 12: First-Order release model

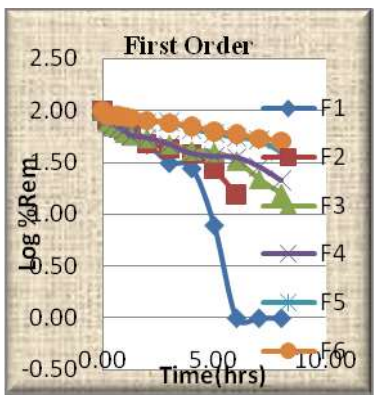


Fig 13: Hixson-Crowell release model

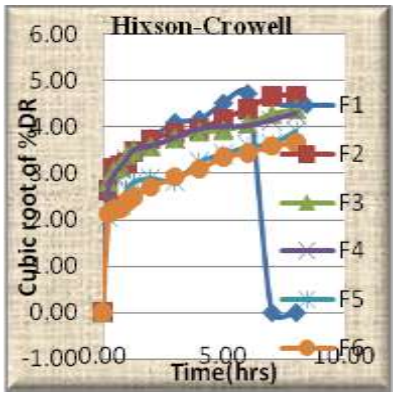


Fig 14: Korsmeyer-Peppas release model

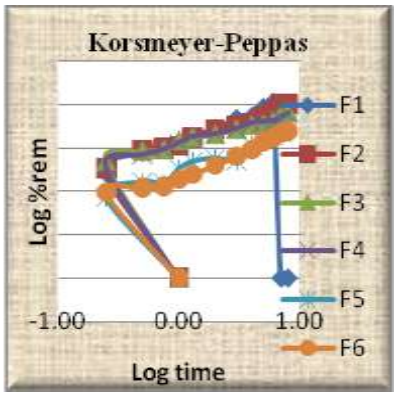
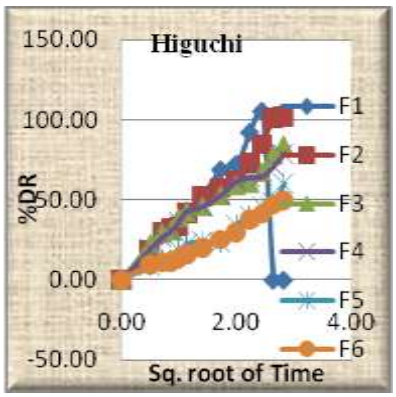


Fig 15: Higuchi release model



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