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Research Paper

Formulation and Characterization of carvedilol microspheres

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The aim of present research work was to formulate and optimize of carvedilol microspheres to improve the therapeutic efficacy in the treatment of hypertension and angina pectoris. The microspheres were prepared by water-in-oil (w/o) emulsification technique. Different polymers were used like sodium alginate, Cellulose acetate and eudrajit S 100. In the preoptimized study the different polymers and the different ratio of the polymers were studied. Different formulations of microspheres were prepared using different drug polymer ratio.Studying the shape and the surface topography, as well as the results of entrapment efficiency of the prepared formulations. The formulations of sodium alginate showed good flow property and maximum entrapment efficiency (73.82). From the results of drug release after the 12th hr. that is (72.23) of A3 (drug: sodium alginate) ratio of 1:2 was selected for further studies.

Keywords: carvedilol , microspheres , polymers, formulations.

INTRODUCTION

The objective behind the development of controlled drug delivery systems is to make a therapeutic agent to do its best when administered into the body. This means high therapeutic efficacy with minimal toxicity. Controlled drug delivery system provides drug release at a predetermined, predictable & controlled rate to achieve high therapeutic efficiency with minimal toxicity. Successful application of many therapeutic agents is hampered by multitude of problems. Drugs administered normally distribute throughout the body interacting not only with the target cells but also with the normal healthy cells which often results in toxic effects. Conventional therapy requires frequent administration of the therapeutic agents to the patients, which reduces patient compliance. Systemic administration of the drug often requires high concentration to maintain the therapeutic effect because of the dilution effect and the difficulty and the drug placement in the target site. To obtained maximum therapeutic efficacy, it become necessary to deliver the agent to the target tissue in the optimal amount for the right period of time thereby causing little toxicity and minimal side effects. A well designed controlled drug delivery system can overcome some of the problems of conventional therapy and enhanced the therapeutic efficacy of a given drug[1].

The concept of drug delivery has been revolutionized. The strides have been taken to lend patient desire maximum benefits of a drug. The drug should be delivered to specific target sites at a rate and concentration that permit optimal therapeutic efficacy while reducing side effect to minimum[2].

The most desirable and convenient method of drug administration is the oral route. The drug is formulated with a series of polymers to improve the absorption &prolong the half life in gastric region[3]The concepts of the advanced drug delivery system especially those offering a sustained and controlled action of drug desired area of effect. Between 1940 and 1960s the concept of chemical Microencapsulation technology began as an alternative means of delivering drugs. In continued quest for the more refined system, in 1980s polymer membrane technology came to be known at forefront. For researchers, the process of targeting and site specific delivery with absolute accuracy can be achieved by attaching bioactive molecules to various particulate carriers (e.g., Nanoparticles and Microspheres)[3]

However in many instances the oral administration is unstable when the drug undergoes significant degradation in the gastrointestinal tract or in metabolized to a high degree via first pass effect in the liver[4].

Microsphere therapy a tremendous attention for systemic drug delivery by many researchers within the last few decades due to its great potential utility for drug delivery. It offers alternatives for drug that have lower oral bioavailability & destroyed by gastrointestinal fluids or are highly susceptible to hepatic first pass metabolism[5].

Carvedilol is a non-selective _-adrenergic antagonist used in the treatment of hypertension and stable angina pectoris (Packer et al. 2002). It is well absorbed from the gastrointestinal tract and its absolute bioavailability is_25% (Thummel et al. 2001).

Characterization of Microspheres

The prepared microspheres were evaluated for their physico-chemical characteristics.

Tapped Density

The tapping method was used to calculate tapped densities. The volume of weighed quantity of microspheres was determined after 100 taps using tapped density apparatus.

Tapped density= Mass of microspheres/Volume of microspheres after tapping

True Density

The microspheres were immersed in 0.02% tween 80 solutions for three days in a metal mesh basket. The microspheres that are sunk after this process are used for density measurements. True density of microspheres

was determined by Liquid displacement method using relative density bottle.[6]

Flow properties

Flow properties of the prepared microspheres were evaluated by the value of Angle of repose, carr's Index and hausner's ratio, and the obtained result were compared to that of standard value.

Particle size analysis

Samples of microspheres were analyzed for particle size by optical microscopy. Linear diameters of 100 microspheres were measured per field for every sample.[7]

Least count of the ocular micrometer was calculated by the following formulae:

$$\text{Least Count} = \frac{\text{No. of Divisions of Stage micrometer}}{\text{No. of divisions of ocular micrometer}} \times 0.01$$

N = No. of divisions of ocular micrometer

Scanning Electron Microscopy Analysis

The shape and surface morphology of microsphere samples were studied by SEM Microspheres were dusted onto double sided carbon dust which was placed onto sample carrier (aluminum stubs having double adhesive tape) in the shape of a cylinder with 5 mm of height and 10 mm of diameter and were coated with Au–Pd (Gold- Palladium) mixture under vacuum (100mTorr) with sputter coater (Hummer VII) to thickness of 50 nm. The samples were imaged using a 5–15 kV electron beam. The microphotographs of suitable magnifications were obtained for surface topography.[7]

Drug Content

Weighed quantity of microspheres was dissolved in 10 ml of 0.1 N HCl. The solution was filtered through a 0.2μm filter, suitably diluted and assayed spectrophotometrically at 276 nm against a reagent blank. Corresponding drug concentrations in the samples were calculated from the calibration plot generated by regression of the data. The capture efficiency of the microspheres or the percent entrapment efficiency is calculated using following equation:

$$\%\,\text{Entrapment} = \frac{\text{Actual content}}{\text{Theoretical content}} \times 100$$

In-vitro Drug Release Study

Release of Carvedilol from prepared microspheres was studied in PBS 7.4 (900 ml) using an USP XXII six station dissolution rate test apparatus with a basket stirrer at 50 rpm. A sample of microspheres equivalent to 15 mg of Carvedilol filled in capsule shell were used in each test. Samples were withdrawn through a filter (0.2 micron) at different time interval and were assayed at 276 nm for Carvedilol using U.V spectrophotometer.[8]

Preparation of microsphere[8]

The emulsification method was utilized for the

preparation of microsphere followed by cross-linking with calcium chloride. Overall 15formulations were prepared using different polymer. Sodium Alginate (Code A) ,Cellulose acetate (Code B) & Eudrajit (Code C).

Firstly drug was dissolved in different proportions of 1:1,1:1.5,1:2,1:2.5 &1:3 (drug:polymer) in aqueous solution . Then this solution was dispersed in n- octanol containing 2% v/v Span80 using a mechanical stirrer at 1500 rpm. The ratio of the aqueous to n-octanol phase used was 1:20. The resultant w/o emulsion was stirred for 30 min. Calcium chloride solution was added drop-wise and the dispersion was stirred another for 5 min. The microsphere were collected by vacuum filtration, washed three times with isopropyl alcohol and dried in air at room temperature**.**

Result and Discussion

Particle size

The prepared microspheres were evaluated for various physicochemical parameters including micromeritics properties, Percentage drug content, and in vitro drug release studies. The mean Particle size analysis of different formulation was done by optical microscopy. The average particle size was found to be in the range of 320.11µm to 426.55µm. The mean Particle size for sodium alginate varied between349.82µm to 403.28 µm and for cellulose acetate it was 308.36 µm to 392.11 µm while for eudragit it was from 382.10 µm to426.55 µm as shown in table Microsphere of sodium alginate and cellulose acetate shows the least particle size.

Preliminary studies showed that as the concentration of polymer was increased, the particle size also proportionally increased. Low alginate concentration (1 % w/v) resulting in clumping of microspheres, where as high sodium alginate concentration (3% W/v) resulted in formation of discrete microspheres with size 524.21 µm. This could be attributed in relative increase in the viscosity at higher concentration of polymer and formation of large particle s during emulsification. Hence the optimized concentration of (2% w/v) was selected for preparing of different batches of microspheres. The size of microspheres was increased with an increase in drug loading.[9]

The shape and surface morphology of the microspheres were examined by scanning electron microscopy (JSM 5610 LV, jeol Datum Ltd. Japan).The samples were mounted directly on to the SEM sample holder using a double sided sticking tape and images were recorded at the required magnification at the acceleration voltage of 10 kV.

Scanning electron micrographs were indicating a spherical shape of microspheres prepared with

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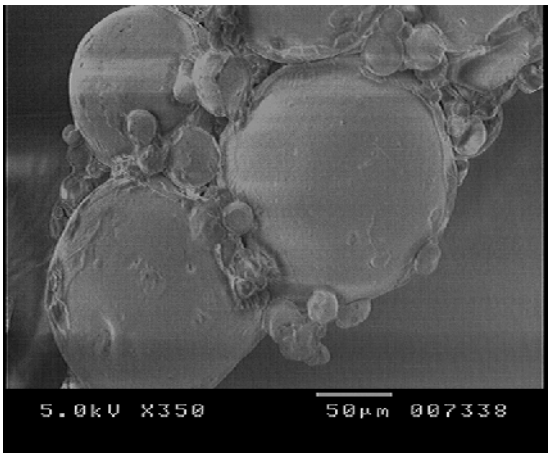

Fig. 1 : Scanning Electron Micrographs of carvedilol with Cellulose acetate

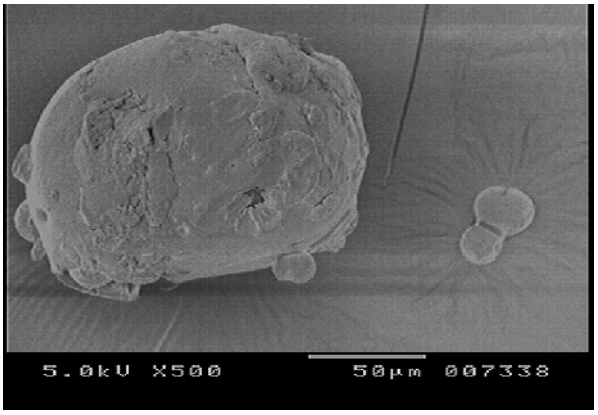

Fig. 2: Scanning Electron Micrographs of carvedilol with Eudrajit S-100

sodium alginate and cellulose acetate, while microsphere prepared with eudrajit were rough surface and irregular in shapes. micrograph were represented in Fig. No.1 to 2 of different formulations of sodium alginate, cellulose acetate and eudrajit respectively.

The flow property of prepared micro sphere was determined by various tests such as angle of repose, Carr's index and Hausner ratio.

When compared with calculated values of the Angle of Repose to that standard values it was observed that Sodium Alginate & Cellulose Acetate microspheres exhibit excellent flow properties where as microspheres of Eudragit S 100 showed good flow properties.In the case of Car's Index comparing of the observed result with standard values it was observed that the microspheres of Sodium Alginate showed excellent flow property while microspheres of cellulose Acetate and Eudragit S-100 showed good properties.So according to that test performed for flow properties it was found that microspheres of Sodium Alginate showed excellent flow property as compared to Cellulose Acetate and EudragitS- 100

Tapped density of microspheres was determined by using test density apparatus. The values of tapped density of formulations range between 0.161 to 0.196 gm/cm^3.The true densities of microspheres were determined by liquid displacement method. The true densities range between 0.682 to 0.847 g/cm^3.The density values of microspheres were found to be less than that of gastric fluid supporting the floating nature. Data presented in table

Encapsulation Efficiency

The Encapsulation Efficiency of all the formulations was established by UV Spectrophotometeric method. The Encapsulation

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Table 1: In vitro drug release data of Formulation A1 & A2

Formulation A1				Formulation A2			
Time	Cumulative %released	Log cumulative % retained	Log(Mt/M∞)	Time	Cumulative % released	Log cumulative % retained	Log(Mt/M∞)
1	6.31	1.984	1.887329	1	5.246	1.976	1.764386
2	10.39	1.952	2.103915	2	9.591	1.956	2.026421
3	19.26	1.907	2.371956	3	16.375	1.922	2.258739
4	33.26	1.824	2.52378	4	25.145	1.874	2.445009
5	35.78	1.807	2.64094	5	34.79	1.814	2.586012
6	46.35	1.729	2.75335	6	42.978	1.756	2.677804
7	50.36	1.695	2.789386	7	50.834	1.691	2.750712
8	57.72	1.629	2.848626	8	61.459	1.586	2.833143
9	65.08	1.543	2.900747	9	73.979	1.418	2.913666
10	70.32	1.472	2.934379	10	79.385	1.314	2.944296
11	78.04	1.336	2.979617	11	82.121	1.172	2.974594
12	81.79	1.26	3	12	84.249	0.989	3

Table 2: In vitro drug release data of Formulation A3 & A4

Formulation A3				Formulation A4			
Time	Cumulative %released	Log cumulative % retained	Log(Mt/M∞)	Time	Cumulative % released	Log cumulative % retained	Log(Mt/M∞)
1	4.768	1.978	1.749531	1	5.74	1.974	1.793052
2	7.675	1.965	1.956273	2	10.907	1.949	2.071845
3	13.69	1.936	2.207598	3	14.971	1.929	2.209391
4	21.14	1.896	2.3963	4	22.43	1.889	2.384969
5	30.555	1.841	2.556277	5	31.882	1.833	2.537686
6	36.613	1.802	2.63483	6	37.296	1.797	2.605802
7	46.794	1.789	2.741385	7	48.728	1.709	2.721919
8	56.708	1.727	2.824839	8	58.927	1.613	2.804454
9	66.269	1.658	2.892505	9	68.458	1.498	2.869564
10	75.696	1.577	2.950268	10	78.356	1.335	2.928212
11	84.369	1.486	2.997378	11	81.021	1.113	2.973764
12	89.88	1.486	3	12	82.44	0.878	3

Table 3: In vitro drug release data of Formulation A5 & B1

Formulation A5				Formulation B1			
Time	Cumulative %released	Log cumulative % retained	Log(Mt/M∞)	Time	Cumulative % released	Log cumulative % retained	Log(Mt/M∞)
1	4.315	1.98	1.665509	1	4.991	1.977	1.815726
2	9.751	1.955	2.019577	2	9.152	1.958	2.079054
3	16.552	1.921	2.249379	3	16.009	1.924	2.321902
4	24.72	1.876	2.423577	4	23.709	1.882	2.492451
5	35.099	1.812	2.575823	5	29.614	1.847	2.589035
6	40.876	1.771	2.641997	6	39.817	1.779	2.717607
7	49.385	1.704	2.724123	7	46.522	1.728	2.785196
8	59.218	1.61	2.802982	8	54.652	1.656	2.855144
9	66.047	1.53	2.850381	9	58.454	1.618	2.884352
10	77.383	1.354	2.919174	10	64.496	1.55	2.927071
11	82.277	1.168	2.96136	11	69.473	1.484	2.959354
12	83.212	0.831	3	12	76.289	1.375	3

Encapsulation Efficiency of microspheres was found in the range of 55.40% to 73.82%. The %EE showed a dependence on drug loading, amount of cross linking agent and time of cross linking. The formulations loaded with higher amount of drug exhibit higher encapsulation efficiency, however shows an inverse with increasing calcium chloride concentration and cross linking time. The highest encapsulation efficiency was found for formulation A3 containing sodium alginate . The encapsulation efficiency of cellulose acetate was found comparatively lesser. The rank order of encapsulation efficiency observed as follows sodium alginate ≥ eudragit s100 ≥ cellulose acetate

In vitro drug release

In vitro release studies of all the formulation were performed in phosphate buffer pH 7.4 at 242 nm using USP XXII basket apparatus. It was found that the release behavior of the drug varies significantly with the types and amount of polymer used. The release behavior was also found to vary with the method of preparation of microsphere. The study was performed for 12 hrs. and cumulative drug released was calculated at specific tie intervals .the result of in vitro drug release of carvedilol is shown in table.The perfect sink condition was maintained during the drug dissolution study period by replacing an equivalent volume of dissolution medium.

The in vitro drug release data were fitted to Zero order and first order kinetics. Higuchi model and The results of in-vitro dissolution studies obtained in these formulations were plotted in four models of data treatment as follows.

(i) Cumulative percentage of drug released v/s time.
(ii) Log cumulative percentage of drug remained v/s time.
(iii) Cumulative percentage of drug released v/s Square root of time (Higuchi's plot).
(iv) Log cumulative percentage of drug released v/s Log time (Peppa's plot).

The drug release data and profile were found to be dependent on the nature of polymer. It was found that the drug release from different formulations was distinguishly different for the different polymer used as well as for different ratios of drug and polymer in the formulations. At the end of 12 hrs. the percentage cumulative release of Carvedilol from Sodium Alginate microspheres were found to be in range of 81.79, 84.24, 89.88, 82.44 & 83.21 for formulation the percentage cumulative amount of drug release decreased as the concentration A1,A2,A3,A4 &A5 respectively. The percentage cumulative release of Carvedilol from Cellulose Acetate microspheres was found to be in the range of 76.28, 82.04, 86.94, 83.19 & 86.94 for formulation B1, B2, B3, B4 &B5 respectively.

The percentage cumulative release of

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Table 4: In vitro drug release data of Formulation B2 & B3

Formulation B2				Formulation B3			
Time	Cumulative %released	Log cumulative % retained	Log(Mt/M∞)	Time	Cumulative % released	Log cumulative % retained	Log(Mt/M∞)
1	5.571	1.975	1.806204	1	6.245	1.972	1.818074
2	8.949	1.959	2.012046	2	11.028	1.949	2.065038
3	14.129	1.933	2.210383	3	16.938	1.919	2.251404
4	23.632	1.882	2.433772	4	26.245	1.867	2.441588
5	32.728	1.827	2.575191	5	33.693	1.821	2.550081
6	41.781	1.765	2.68125	6	43.457	1.752	2.660601
7	54.08	1.662	2.793308	7	55.323	1.65	2.765447
8	61.845	1.581	2.851576	8	63.396	1.563	2.824603
9	71.263	1.458	2.913135	9	73.267	1.427	2.88745
10	74.978	1.398	2.935205	10	83.214	1.225	2.942738
11	81.114	1.252	2.974688	11	83.038	0.998	2.976967
12	82.042	1.112	3	12	86.942	0.704	3

Table 5: In vitro drug release data of Formulation B4 & B

Formulation B4				Formulation B5			
Time	Cumulative %released	Log cumulative % retained	Log(Mt/M∞)	Time	Cumulative % released	Log cumulative % retained	Log(Mt/M∞)
1	6.414	1.971	1.837732	1	5.431	1.975	1.858545
2	11.676	1.946	2.097897	2	13.285	1.938	2.136859
3	18.885	1.902	2.30672	3	21.465	1.895	2.345228
4	29.332	1.849	2.497944	4	26.423	1.866	2.435479
5	39.311	1.783	2.625117	5	36.91	1.799	2.580641
6	46.987	1.724	2.70258	6	45.531	1.728	2.671804
7	57.901	1.624	2.793289	7	54.957	1.653	2.75352
8	65.981	1.531	2.850022	8	77.879	1.344	2.904917
9	76.444	1.372	2.913946	9	81.109	1.142	2.948546
10	83.076	1.228	2.950078	10	83.653	0.866	2.980356
11	81.914	1.044	2.979573	11	84.048	0.9	2.977511
12	83.196	0.833	3	12	86.94	0.485	3

Table 6: In vitro drug release data of Formulation C1 & C2

Formulation C1				Formulation C2			
Time	Cumulative %released	Log cumulative % retained	Log(Mt/M∞)	Time	Cumulative % released	Log cumulative % retained	Log(Mt/M∞)
1	4.495	1.98	1.739647	1	4.971	1.977	1.739647
2	8.559	1.961	2.019341	2	11.223	1.948	2.019341
3	14.102	1.933	2.236198	3	17.113	1.918	2.236198
4	23.122	1.885	2.450943	4	24.525	1.877	2.450943
5	31.373	1.838	2.583474	5	35.658	1.808	2.583474
6	39.542	1.781	2.683976	6	45.676	1.735	2.683976
7	49.022	1.707	2.777309	7	55.408	1.649	2.777309
8	58.363	1.619	2.853055	8	64.642	1.548	2.853055
9	65.107	1.542	2.900545	9	71.226	1.459	2.900545
10	67.201	1.515	2.914293	10	75.308	1.392	2.914293
11	73.624	1.421	2.953937	11	82.344	1.246	2.953937
12	81.862	1.258	3	12	85.357	1.165	3

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Table 7: In vitro drug release data of Formulation C3 & C4

Formulation C3				Formulation C4			
Time	Cumulative %released	Log cumulative % retained	Log(Mt/M∞)	Time	Cumulative % released	Log cumulative % retained	Log(Mt/M∞)
1	5.853	1.973	1.840887	1	5.742	1.974	1.795686
2	11.044	1.949	2.116635	2	10.416	1.952	2.054324
3	14.745	1.93	2.242153	3	16.642	1.92	2.257829
4	22.914	1.886	2.433609	4	27.541	1.86	2.476603
5	33.062	1.825	2.592837	5	38.382	1.789	2.620751
6	41.645	1.766	2.693071	6	46.689	1.726	2.705838
7	53.914	1.663	2.80521	7	56.006	1.643	2.784858
8	65.983	1.531	2.89294	8	61.822	1.581	2.827766
9	70.908	1.463	2.924204	9	68.121	1.503	2.869904
10	75.645	1.386	2.952289	10	76.589	1.369	2.920789
11	80.33	1.293	2.978386	11	85.496	1.161	2.968569
12	84.429	1.192	3	12	86.913	0.907	3

Caarvedilol from Eudragit microspheres was found to be in the range of 53.28, 56.63, 60.12, 62.12 &59.85 for formulation C1, C2, C3, C4 & C5 respectively.It was observed that percentage cumulative amount of drug release decrease as the concentration of polymer increased. The cumulative percentage drug release for Sodium Alginate microspheres was found to be maximum followed by Cellulose Acetate and followed by Eudrajit S 100 microspheres.

The sequence for cumulative percentage drug release was found as follows

A1>A2>A3>A4>A5>B1>B2>B3>B4>B5>C1>C2>C3>C4>C5

The data obtained from in vitro drug release studies are shown graphically according to various modes of data treatment to assess the release mechanism from microspheres. The graphical presentation of data of all the formulations is shown in Fig.1-14.

The data obtained from the in vitro drug release studies were fitted to various Kinetics models to determine the Kinetic and mechanism of drug release like Zero order kinetics, First order kinetics, Higuchi model and Korsemeyer model,

Table 8: In vitro drug release data of Formulation C5

Formulation C5			
Time	Cumulative %released	Log cumulative % retained	Log(Mt/M∞)
1	4.588	1.979	1.735235
2	8.707	1.96	2.01348
3	14.222	1.933	2.226572
4	21.732	1.893	2.410711
5	31.751	1.834	2.575369
6	40.131	1.777	2.677091
7	49.693	1.701	2.769906
8	68.547	1.497	2.9096
9	64.871	1.545	2.885662
10	74.248	1.41	2.944296
11	78.922	1.323	2.970809
12	84.09	1.193	3.000

The coefficient of regression and release rate constant values for Zero, first Higuchi and Korsemeyers models were computed and showed in Table No. 9 to 11 From the correlation coefficient values obtained it is conclude that

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Table 9:Release kinetic model for Sodium Alginate microspheres, Formulation (A1to A5)

Code	Zero order		First order		Higuchi model		Korsemeyer model	
	R^2	K (mg/hr)	R^2	K (hr^{-1})	R^2	K ($mg.hr^{-1/2}$)	R^2	n
A1	0.992	7.24	0.972	0.064	0.979	32.61	0.991	1.089
A2	0.991	8.26	0.932	0.088	0.959	37.98	0.994	1.218
A3	0.984	7.95	0.967	0.048	0.943	36.65	0.988	1.268
A4	0.984	8.10	0.879	0.092	0.937	37.85	0.990	1.172
A5	0.993	7.98	0.868	0.091	0.957	37.59	0.998	1.255

Table 10 :Release kinetic model for Cellulose acetate microspheres , Formulation (B1to B5)

Code	Zero order		First order		Higuchi model		Korsemeyer model	
	R^2	K (mg/hr)	R^2	K (hr^{-1})	R^2	K ($mg.hr^{-1/2}$)	R^2	n
B1	0.994	6.63	0.977	0.054	0.971	30.74	0.994	1.145
B2	0.988	7.90	0.954	0.078	0.958	36.92	0.984	1.217
B3	0.992	8.47	0.883	0.106	0.952	39.38	0.992	1.169
B4	0.994	8.36	0.928	0.10	0.971	38.80	0.994	1.143
B5	0.993	8.64	0.896	0.095	0.958	40.08	0.992	1.199

Table 11:Release kinetic model for Eudrajit s-100 microspheres,Formulation (C1to C5)

Code	Zero order		First order		Higuchi model		Korsemeyer model	
	R^2	K (mg/hr)	R^2	K (hr^{-1})	R^2	K ($mg.hr^{-1/2}$)	R^2	n
C1	0.991	7.2	0.963	0.063	0.965	33.68	0.992	1.231
C2	0.988	7.78	0.970	0.076	0.972	37.19	0.993	1.194
C3	0.983	7.76	0.967	0.074	0.954	36.16	0.985	1.164
C4	0.995	7.99	0.988	0.091	0.972	37.19	0.991	1.174
C5	0.992	7.58	0.952	0.073	0.959	35.48	0.989	1.258

the drug release from microspheres followed Zero order kinetics. A lower variation was also obtained for Zero order release rate constants indicating a Zero order release pattern from the microspheres. Higuchi model explained the matrix diffusion mechanism of drug release for all the formulation of microspheres. The coefficient of determination of R^2 values were much closer to 1 for Higuchi model that indicating that drug release followed matrix diffusion mechanism or Higuchi pattern release from prepared microspheres. In order to understand the mechanism and kinetics of drug release, the data was analyzed by as Korsemeyers equation (Ritger and Peppas 1987), $Mt/M\infty = tn$, where Mt is the amount of drug released at time t, $M\infty$ is the amount released at time∞, $Mt/M\infty$ is the fraction of drug released at time t, k is a constant characteristic of the drug-polymer system and n is the diffusional exponent, a measure of the primary mechanism of drug release. Using the least squares procedure, the values of n, k and correlation coefficient(r) were estimated (Table 9-11). In spherical matrices, if $n \leq 0.43$, a Fickian diffusion (case-I), $0.43 \leq n \leq 0.85$, anomalous or non-

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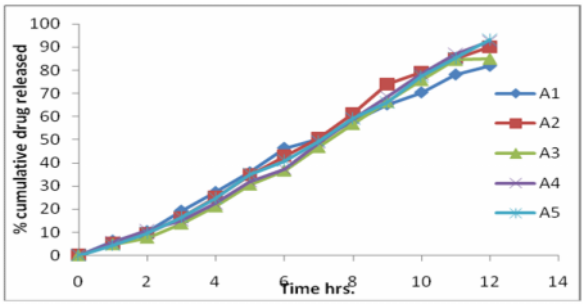

Fig.3 Zero order kinetics plots of different formulations (A1to A5)

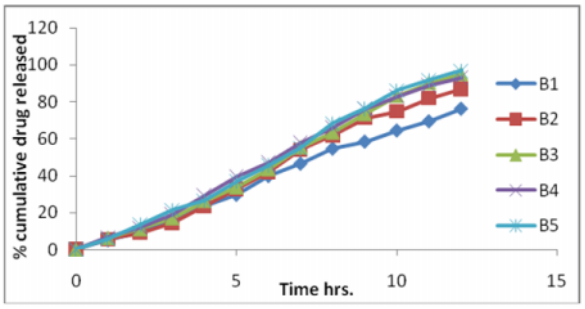

Fig. 4 Zero order kinetics plots of different Formulation (B1to B5)

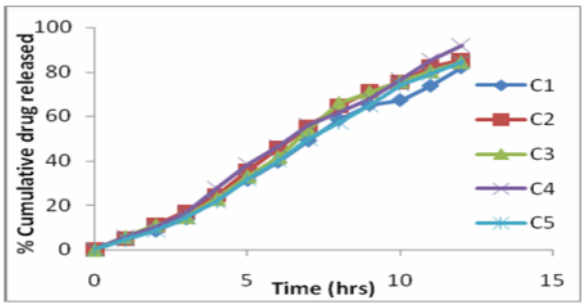

Fig. 5 Zero order kinetics plots of different Formulation (C1to C5)

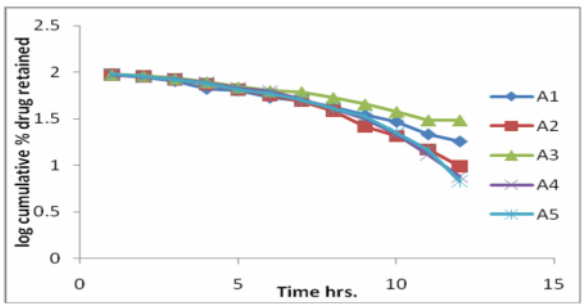

Fig. 6 First order kinetics plots of different Formulation (A1to A5)

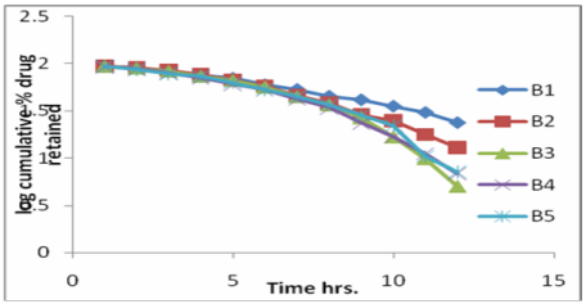

Fig. 7 First order kinetics plots of different Formulation (B1to B5)

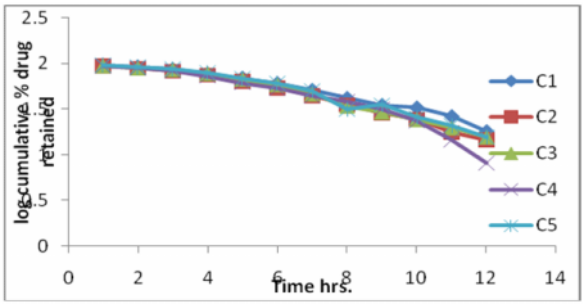

Fig. 8 First order kinetics plots of different Formulation (C1to C5)

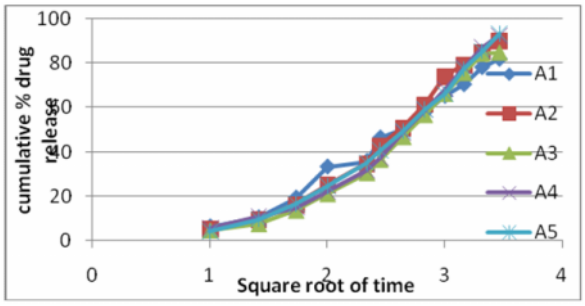

Fig. 9 Higuchi plots of different Formulation (A1to A5)

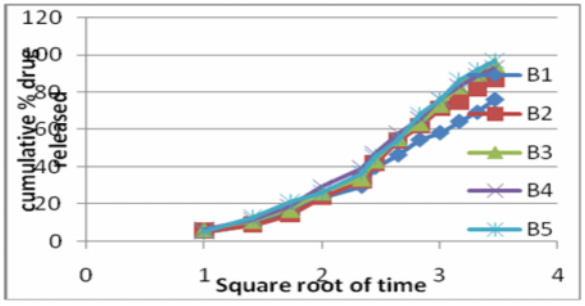

Fig. 10 Higuchi plots of different Formulation (B1to B5)

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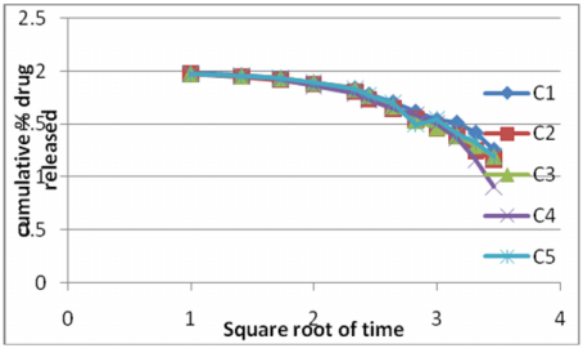

Fig. 11 Higuchi plots of different Formulation (C1to C5)

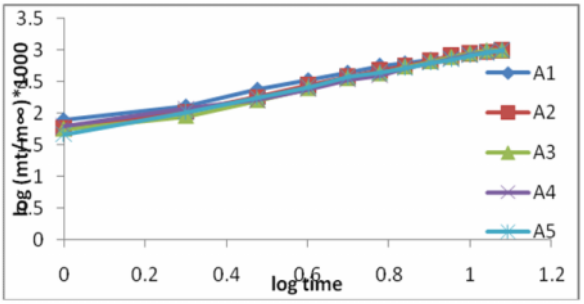

Fig. 12 Korsemeyer plots of different Formulation (A1to A5)

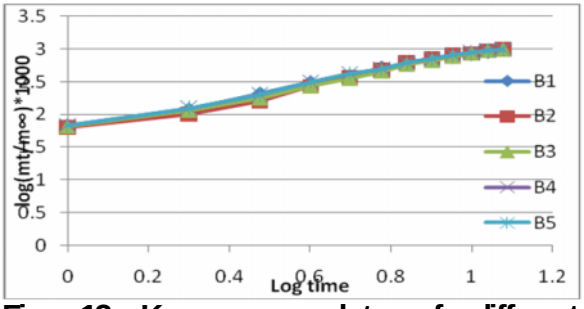

Fig. 13 Korsemeyer plots of different Formulation (B1to B5)

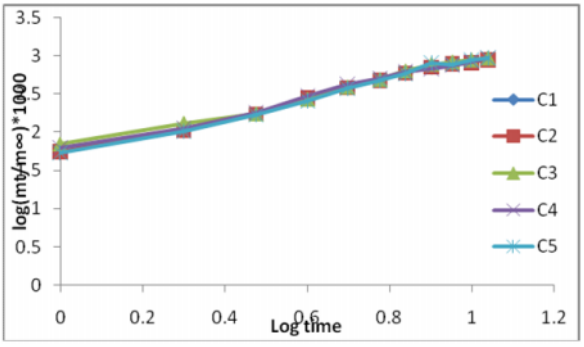

Fig. 14 : Korsemeyer plots of different Formulation (C1to C5)

Fickian transport and n ≥ 0.85,a case-II transport (zero order) drug release mechanism dominates. The values of n for all the formulations ranged from more than 1with correlation coefficient close to 0.99, indicating a non- Fickian or anomalous type of transport.

Conclusion

In the present study microspheres of Carvedilol were prepared by using different polymers like sodium alginate, cellulose acetate and eudrajit s-100, and performed various characterizations of the prepared microspheres. On the basis of micromeritics properties like flow property, particle size and density of the various microspheres it was found that microsphere prepared by sodium alginate showed very good flow property. Drug content of microspheres prepared by different polymers, the microspheres prepared by sodium alginate showed the maximum value.

It was observed that percentage cumulative amount of drug release decrease as the concentration of polymer increased. The cumulative percentage drug release for Sodium Alginate microspheres was found to be maximum followed by Cellulose Acetate and followed by Eudrajit S 100 microspheres. From the correlation coefficient values obtained it is concluded that the drug release from microspheres followed Zero order kinetics.

Higuchi model explained the matrix diffusion mechanism of drug release for all the formulation of microspheres. The coefficient of determination of R^2 values were much closer to 1 for Higuchi model that indicating that drug release followed matrix diffusion mechanism or Higuchi pattern release from prepared microspheres. The values of n for all the formulations ranged from more than 1with correlation coefficient close to 0.99, indicating a non- Fickian or anomalous type of transport.

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