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Research Paper

Formulation and Evaluation of Nifedipine Microspheres

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Nifedipine is a calcium channel blocker which is used in the treatment of hypertension, angina pectoris. The aim of this study was to formulate and evaluate Nifedipine microspheres for sustained release delivery system by using different polymers. Drug loaded microspheres were prepared using different polymers like Ethyl Cellulose, Cellulose Acetate, sodium Alginate, Chitosan & Eudragit L 100 by solvent evaporation method. Prepared microspheres were evaluated for different parameters like flow property, particle size analysis, densities of microspheres, drug encapsulation efficiency and in vitro drug release and comparison of results of microspheres prepared by different polymers were analyzed. Results revealed that microspheres obtained from Eudragit L 100 shows good flow property on the basis of result obtained from Caars Index and Hassuners ratio. Particle size was low enough and shows maximum Encapsulation Efficiency of microspheres prepared by Eudragit L 100. In vitro drug release studies of microspheres prepared by different polymers were carried out and it was found that microspheres of Eudragit L 100 show maximum drug release.

Keywords: Nifedipine, calcium channel blocker, microspheres, sustained release delivery system, polymers

INTRODUCTION

Drug delivery systems that can control the release very precisely and target drug, to a specific body site have an enormous impact on health care system. The last two decades there has been a remarkable improvement in the field of Novel Drug Delivery System. The controlled release oral drug delivery system offers several advantages over conventional oral drug delivery system. This dosage form provides drug release at a predetermined, predictable & controlled rate to achieve high therapeutic efficiency with minimal toxicity. Conventional therapy requires frequent administration of drug to the patients, and also requires high concentration to maintain therapeutic effect because of the dilution effect which enhances patient compliance. To obtain maximum therapeutic efficacy it became necessary to deliver the agent at the target tissue in the optimal amount for the right period of time, thereby causing little toxicity and minimal side effects.[1]

A well design Controlled drug delivery system can overcome some of these problems of conventional therapy and enhance the

therapeutic efficacy of the drug product. There are various approaches in delivering a therapeutic substance to the target site in a sustained controlled release fashion. One such approach is using microspheres as carriers for drugs.[2] Microspheres are characteristically free flowing powders consisting of proteins or synthetic polymers which are biodegradable in nature and ideally having a particle size less than 200µm.

Method of Preparation:

Microspheres were prepared by solvent evaporation method. 100 mg nifedipine and 1.5 gm of different polymers (Cellulose acetate, Ethyl cellulose, Chitosan, Sodium Alginate and Eudragit L100) were dissolved completely in chloroform (10 ml.) using mechanical stirrer at 800 rpm as the internal phase. The solution was then added drop wise to a solution of PVA (1% w/v), which acts as the external phase. The mixture was stirred for 5 hrs. until all chloroform was evaporated and microspheres were obtained. The formed microspheres were separated with paper filter, then rinsed three times with normal hexane and dried in room temperature[3]

Characterization of Microspheres

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

1. Total weight

Total weight of formulations was determined by accurately weighing individually each formulation on digital balance.

2. Production Yield

The total amount of microspheres obtained was weighed and the percentage yield was calculated taking into consideration the weight of drug and polymer[4].

% yield= (Practical yield/Theoretical yield) x100

3. 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[5].

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

4. 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.

5. Flow properties

a. Angle of repose: Weighed quantity of microspheres (5 gm) was passed through a funnel fixed on a stand at a specific height upon the graph paper. A static heap of powder with

only gravity acting upon it was tending to flow form a conical mouth. The height of the heap (h) and the radius of the lower part of the conical were measured.[6]

The angle of repose was calculated using the following formula:

$$\tan \theta = h/r$$

b. Carr's index: It is a simple test that has been evaluate the flow ability of a powder by comparing the poured (fluff) density (ρ_{Bmin}) and tapped density (ρ_{Bmax}) of a powder and the rate at which it packed down. It was determined by taking small quantity of microsphere samples in 10 ml measuring cylinder. The height of the sample was measured before and after tapping indicates poured and tapped density respectively. The Carr's index was calculated using following formula:

$$\text{Carr's index} = \frac{\text{Tapped-density} \quad \text{Poured}}{\text{Tapped density}} \text{ X100}$$

c. Hausner ratio: A similar index has been defined by Hausner (1967). Same method was employed for determination of poured and tapped density as incase of Carr's index. Hausner ratio was calculated using following formula[7].

$$\text{Hausner ratio} = \frac{\text{Tapped density } (\rho_{B\,max})}{\text{Tapped density}} \text{ X100}$$

3. 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.

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

$$\text{Least Count} = \frac{\text{No. of divisions of stage micrometer}}{\text{No. of divisions of ocular micrometer}} \text{ x 0.01}$$

4. 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[8].

8. 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[9].

The capture efficiency of the microspheres or the percent entrapment efficiency is calculated using following equation:

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

9. In-vitro Drug Release Study

Release of Nifedipine from prepared microspheres was studied in phosphate buffer pH 7.4 (900 ml) using an USP XXII six station dissolution test apparatus with a basket stirrer at 50 rpm at the temperature of 37°C. Samples of microspheres of Nifedipine 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 236 nm for Nifedipine using U.V spectrophotometer[10].

The *in vitro* drug release data were fitted to these models to determine the kinetics and mechanism of drug release from the microspheres.

10. Stability Studies.

Stability testing of drug products begins as a part of drug discovery and ends with the demise of the compound or commercial product. FDA and ICH specifies the guidelines for stability testing of new drug products, as a technical requirement for the registration of pharmaceuticals for human use. Stability of a pharmaceutical preparation can be defined as "the capability of a particular formulation (dosage form or drug product) in a specific container/closure system to remain within its physical, chemical, microbiological, therapeutic and toxicological specifications thorough out its shelf life. The purpose of stability testing is to assess the effects of temperature, humidity, light and other environment factors on the quality of a drug substance or product[11].

The objective of stability study is to determine the shelf life, namely the time period of storage at a specified condition with in which the drug product still meets its established specifications. Stability studies on the optimized formulations were carried out to determine the effect of the presence of formulation additives on the stability of the drug and also to determine the physical stability of the formulations under accelerated storage conditions of temperature.[12]

Protocol for Stability Study of Microspheres

- **Purpose:** To evaluate stability profile of drug product (Microspheres of Carvedilol and Nifedipine) for storage under refrigeration, room and accelerated temperature.
- **Method:** The Microspheres were subjected to room temperature (25°C), refrigeration temperature (4°C) and accelerated temperature conditions (40 °C, 50 °C, 60 °C). Samples were withdrawn at predetermined time intervals of 15, 30, 45 and 60 days and analyzed for physical

appearance and drug content in UV spectrophotometer.

Results and Discussion

Average particle size of various formulations is shown in Table No. 1. The average particle size of various formulations was found in the range of 339.14 to 399.69.As the result shows different microspheres using different polymers shows varying in particle size. Eudragit L 100 showed the least particle size.

Tapped density of microspheres was determined by using test density apparatus. The values of tapped density of formulations range between 0.172. to 0.183 gm/cm^3.

The true densities of microspheres were determined by liquid displacement method. The true densities range between 0.684 to 0.869 gm/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 1.

The flow property of prepared micro sphere was determined by various tests such as angle of repose, Carr's index and Hausner ratio. The results obtained are tabulated in Table 1 of different formulations cellulose acetate, Ethyl cellulose, sodium alginate, chitosan and Eudragit respectively.

When compared with calculated values of the Angle of Repose to that standard values it was observed that Eudragit L100 and Sodium Alginate microspheres exhibit excellent flow properties where as microspheres of Cellulose acetate and Ethyl Cellulose showed good flow properties and microspheres prepared by Chitosan showed fair to passable flow properties.

In the case of Car's Index comparing of the observed result with standard values it was observed that the microspheres of Eudragit L100, Sodium Alginate and Ethyl Cellulose showed excellent flow property while microspheres of Chitosan and cellulose Acetate showed good flow properties.

As per Hausener's Ratio microspheres of Eudragit L100, Sodium Alginate and Cellulose Acetate showed excellent flow property while microspheres of Chitosan and Ethyl cellulose showed good properties.

So according to all test performed for flow properties it was found that microspheres of Eudragit L 100 showed excellent flow property and Cellulose acetate, sodium alginate and ethyl cellulose showed good flow property as compared to chitosan microspheres.

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

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Table 1 : Mean Particle Size and Flow Properties of microspheres

S. No.	Formulation[a]	Mean Particle Size[a]	Tapped density[a]	True density[a]	Angle of Repose[a]	Carr's Index[a]	Hausener's[a] Ratio
1	Cellulose Acetate	359.62±3.547	0.173±0.052	0.774±0.012	25.63°±0.012	17.21±1.363	1.20±0.002
2	Ethyl Cellulose	367.82±3.635	0.175±0.014	0.745±0.005	26.77°±0.063	16.63±1.154	1.21±0.023
3	Chitosan	399.69±2.125	0.183±0.006	0.869±0.148	27.63°±0.178	18.21±1.745	1.25±0.013
4	Sodium Alginate	358.75±1.245	0.178±0.245	0.787±0.075	24.45°±0.569	17.32±1.235	1.20±0.027
5	Eudragit L 100	339.14±2.178	0.172±0.365	0.684±0.112	20.47°±0.115	14.92±1.854	1.18±0.022

a=mean±S.D.; n=3

the required magnification at the acceleration voltage of 10 kV. Scanning electron micrographs were indicating a spherical shape of

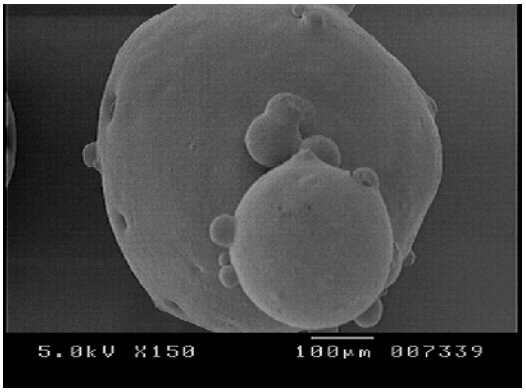

Fig. 1 Scanning Electron Micrographs of Nifedipine with Ethyl Cellulose

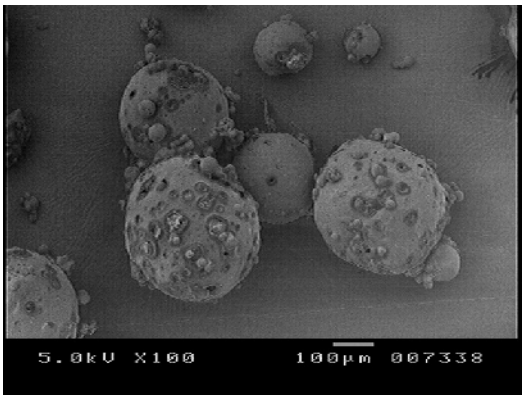

Fig. 2: Scanning Electron Micrographs of Nifedipine with Eudragit L 100

microspheres prepared with Eudragit L 100 and cellulose acetate, while microsphere prepared with chitosan were rough surface and irregular in shapes. Micrographs were represented in Fig. 1 & 2 of different formulations of cellulose acetate, Ethyl cellulose, sodium alginate, Eudragit and chitosan and respectively

Encapsulation Efficiency

The Encapsulation Efficiency of all the formulations was established by UV Spectrophotometeric method. The Encapsulation Efficiency of microspheres is shown in table 2. Encapsulation Efficiency of microspheres was found in the range of 39.36% to 44.83%.

Table 2 :Drug content of microspheres

Sr. NO.	Formulation	Encapsulation Efficiency (%)
1	Cellulose Acetate	42.44
2	Ethyl Cellulose	44.23
3	Chitosan	39.36
4	Sodium Alginate	43.23
5	Eudragit L 100	44.83

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In vitro drug release

In vitro release studies of all the formulation were performed in phosphate buffer pH 7.4 at 236 nm using USP XXII basket apparatus. It was found that the release behavior of the drug varies significantly with the types of polymer used. The study was performed for 12 hrs. and cumulative drug released was calculated at specific time intervals, the result of in vitro drug release of Nifedipine is shown in table No. 3 to 7. 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, first order kinetics Higuchi

Table 3:In vitro drug release data of Cellulose acetate microspheres

Time	√T	Cumulative % released	Log cumulative % released	Cumulative % retained	Log cumulative % retained	Log time	Log(Mt/ M
1	0	1.44	0.158	98.56	1.993701	0	1.322
2	1	3.12	0.494	96.88	1.986234	0.301	1.655
3	1.414	9.29	0.968	90.71	1.957655	0.477	2.132
4	1.732	15.092	1.178	84.908	1.928949	0.602	2.343
5	2	22.426	1.350	77.574	1.889716	0.699	2.515
6	2.336	29.092	1.463	70.908	1.850695	0.778	2.628
7	2.449	36.684	1.564	63.316	1.801513	0.845	2.729
8	2.645	42.202	1.625	57.798	1.761913	0.903	2.789
9	2.828	50.648	1.704	49.352	1.693305	0.954	2.869
10	3	57.49	1.759	42.51	1.628491	1	2.924
11	3.162	65.284	1.814	34.716	1.54053	1.041	2.979
12	3.316	68.462	1.835	31.538	1.498834	1.079	3

Table 4: In vitro drug release data of Ethyl Cellulose microspheres

Time	√T	Cumulative % released	Log cumulative % released	Cumulative % retained	Log cumulative % retained	Log time	Log(Mt/ M
1	0	1.346	0.129	98.654	1.994115	0	1.284
2	1	3.062	0.486	96.938	1.986494	0.301	1.641
3	1.414	6.924	0.840	93.076	1.968838	0.477	1.995
4	1.732	10.324	1.013	89.676	1.952676	0.602	2.169
5	2	18.64	1.270	81.36	1.910411	0.699	2.425
6	2.336	24.204	1.383	75.796	1.879646	0.778	2.539
7	2.449	32.246	1.508	67.754	1.830935	0.845	2.663
8	2.645	38.406	1.584	61.594	1.789538	0.903	2.739
9	2.828	44.65	1.649	55.35	1.743118	0.954	2.805
10	3	50.684	1.704	49.316	1.692988	1	2.860
11	3.162	60.242	1.779	39.758	1.599425	1.041	2.935
12	3.316	69.904	1.844	30.096	1.478509	1.079	3

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Table 5: In vitro drug release data of Sodium Alginate microspheres

Time	√T	Cumulative % released	Log cumulative % released	Cumulative % retained	Log cumulative % retained	Log time	Log(Mt/ M
1	0	1.024	0.010	98.976	1.99553	0	1.176
2	1	2.424	0.384	97.576	1.989343	0.301	1.551
3	1.414	4.24	0.627	95.76	1.981184	0.477	1.793
4	1.732	6.28	0.797	93.72	1.971832	0.602	1.963
5	2	16.68	1.222	83.32	1.920749	0.699	2.388
6	2.336	20.428	1.310	79.572	1.90076	0.778	2.476
7	2.449	24.442	1.388	75.558	1.87828	0.845	2.554
8	2.645	30.246	1.480	69.754	1.843569	0.903	2.646
9	2.828	40.442	1.606	59.558	1.77494	0.954	2.77
10	3	46.77	1.669	53.23	1.726156	1	2.835
11	3.162	60.212	1.779	39.788	1.599752	1.041	2.945
12	3.316	68.25	1.834	31.75	1.501744	1.079	3

Table 6: In vitro drug release data of Chitosan microspheres

Time	√T	Cumulative % released	Log cumulative % released	Cumulative % retained	Log cumulative % retained	Log time	Log(Mt/ M
1	0	1.004	0.001	98.996	1.995618	0	1.168
2	1	2.66	0.424	97.34	1.988291	0.301	1.592
3	1.414	5.96	0.775	94.04	1.973313	0.477	1.942
4	1.732	6.28	0.797	93.72	1.971832	0.602	1.965
5	2	13.16	1.119	86.84	1.93872	0.699	2.286
6	2.336	18.488	1.266	81.512	1.911222	0.778	2.434
7	2.449	22.468	1.351	77.532	1.889481	0.845	2.514
8	2.645	27.944	1.446	72.056	1.85767	0.903	2.613
9	2.828	32.266	1.508	67.734	1.830807	0.954	2.675
10	3	40.006	1.602	59.994	1.778108	1	2.769
11	3.162	49.966	1.698	50.034	1.699265	1.041	2.865
12	3.316	68.04	1.832	31.96	1.504607	1.079	3

model and Korsemeyers plot. 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).

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Table 7: In vitro drug release data of Eudragit L100 microspheres

Time	√T	Cumulative % released	Log cumulative % released	Cumulative % retained	Log cumulative % retained	Log time	Log(Mt/ M
1	0	1.224	0.087	98.776	1.994651	0	1.219
2	1	2.88	0.459	97.12	1.987309	0.301	1.590
3	1.414	6.024	0.779	93.976	1.973017	0.477	1.911
4	1.732	8.246	0.916	91.754	1.962625	0.602	2.047
5	2	17.324	1.238	82.676	1.917379	0.699	2.370
6	2.336	20.24	1.306	79.76	1.901785	0.778	2.437
7	2.449	26.326	1.420	73.674	1.867314	0.845	2.551
8	2.645	30.44	1.483	69.56	1.84236	0.903	2.614
9	2.828	37.326	1.572	62.674	1.797087	0.954	2.703
10	3	44.404	1.647	55.596	1.745044	1	2.778
11	3.162	56.88	1.754	43.12	1.634679	1.041	2.886
12	3.316	73.9	1.868	26.1	1.416641	1.079	3

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 were distinguishly different . At the end of 12 hrs. the percentage cumulative release of Nifedipine from cellulose acetate microspheres was found to be(68.46%) ,from Ethyl cellulose microspheres (69.90%), from sodium alginate (68.25%) and maximum amount of drug release(73.9%) was obtained from Eudragit L 100 microspheres while least amount of drug release(68.04%) was obtained from chitosan microspheres.

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 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, The coefficient of regression and release rate constant values for Zero order, First order Higuchi and Korsemeyers models were computed and showed in Table No. 6.64 and presented graphically in Fig. 3 to 6

From the correlation coefficient values obtained it was concluded that 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

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Table 8: Release kinetic model for different microspheres

Formulation	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
Cellulose Acetate	0.991	7.2	0.963	0.063	0.965	33.68	0.992	1.231
Ethyl Cellulose	0.988	7.78	0.970	0.076	0.972	37.19	0.993	1.194
Chitosan	0.983	7.76	0.967	0.074	0.954	36.16	0.985	1.164
Sodium Alginate	0.995	7.99	0.988	0.091	0.972	37.19	0.991	1.174
Eudragit L 100	0.992	7.58	0.952	0.073	0.959	35.48	0.989	1.258

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.

Stability studies for all the formulations were performed, at 25+2^0 C (Room temperature), 2 to 8^0 C (Refrigeration temperature), at 37^{0}C & 70% RH (Humidity Chamber), at 40^{0}C, 50^{0}C 60^{0}C

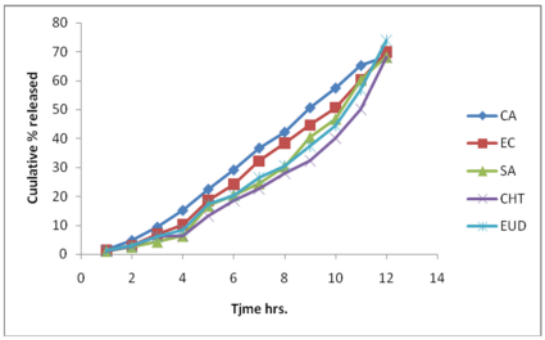

Fig. 3. Zero order kinetics plots of different formulations

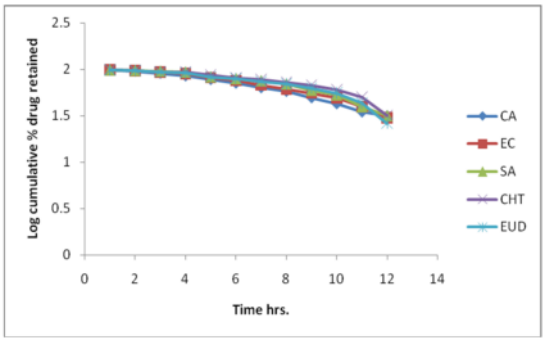

Fig. 4. First order kinetics plots of different Formulations

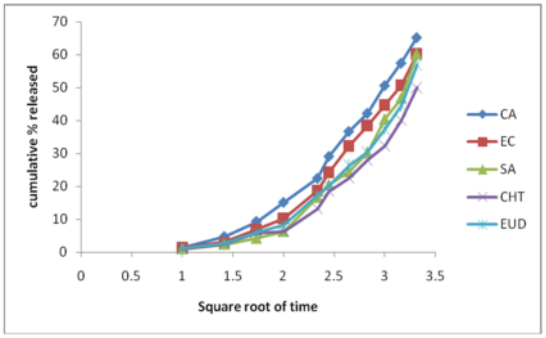

Fig. 5. Higuchi plots of different formulations

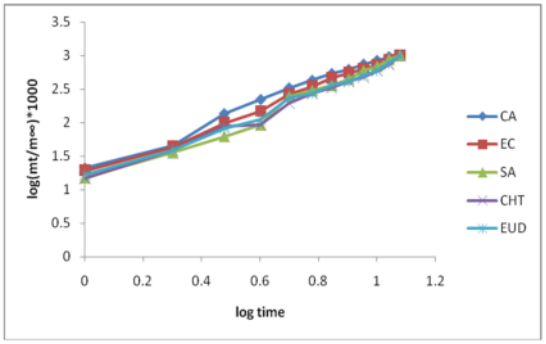

Fig. 6. Korsemeyer plots of different formulations

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Table 9: Temperature dependent stability studies of microspheres performed at different temperature

Code	Drug content (mg/)g											
	Temperature (40^0 C)				Temperature (50^0 C)				Temperature (60^0 C)			
	Time in days				Time in days				Time in days			
	0	30	60	90	0	30	60	90	0	30	60	90
F1	380	370	367	358	380	375	367	359	380	368	358	351
F2	383	381	375	356	383	374	369	361	383	374	370	366
F3	375	370	362	360	375	370	364	358	375	368	360	350
F4	382	364	364	358	382	376	368	361	382	372	368	358
F5	381	371	363	357	381	370	363	354	381	375	366	356
F6	378	362	365	354	378	363	356	350	378	371	365	355
F7	371	366	360	349	371	366	360	351	371	362	354	349
F8	372	363	359	346	372	363	358	350	372	366	360	352
F9	360	351	343	338	360	356	350	346	360	354	352	348

Table 10: Temperature dependent stability studies of microspheres performed at different temperature

Code	Drug content (mg/)g											
	Room Temperature (25+_2^0C)				Temperature (37^0 C &70% RH)				Refrigerator Temperature (2 - 8^0 C)			
	Time in days				Time in days				Time in days			
	0	30	60	90	0	30	60	90	0	30	60	90
F1	380	372	364	358	380	374	369	360	380	371	364	358
F2	383	376	371	362	383	371	368	361	383	377	371	364
F3	375	366	361	356	375	370	363	360	375	370	365	360
F4	382	374	370	365	382	377	370	364	382	375	370	366
F5	381	375	370	366	381	373	363	359	381	377	371	366
F6	378	371	365	359	378	371	365	356	378	371	359	356
F7	371	364	360	352	371	360	361	356	371	363	358	351
F8	372	368	361	354	372	368	360	352	372	363	356	350
F9	360	354	351	346	360	351	348	346	360	352	350	345

for RH (Humidity Chamber), at 40^0C, 50^0C 60^0C for a period of 90 days.. The data of stability studies are presented in table 9 &10 and are presented graphically in Fig. 7 to 12. The data depicts that the microspheres stored at room temperature, refrigeration temperature were found to be stable and the microspheres at 37^0C & 70% RH (Humidity Chamber) there were 5% degradation at end of three months.

The results of stability studies of microspheres at different temperatures and conditions is prepared as 25+2^0 C (Room temperature) > 2 to 8^0 C

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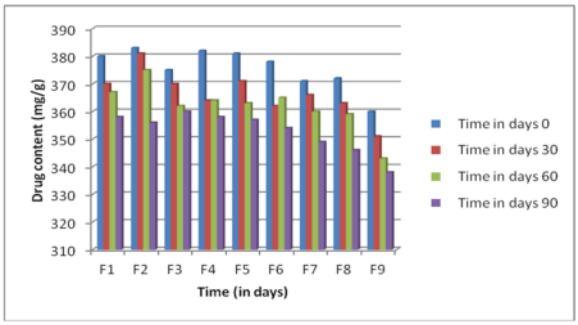

Fig. 7. Temperature dependent stability studies of microspheres at 40° C

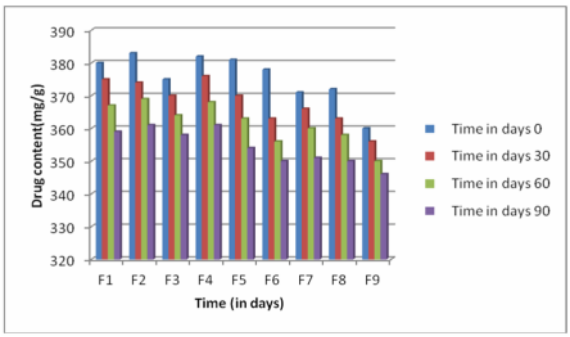

Fig. 8. Temperature dependent stability studies of microspheres at 50° C

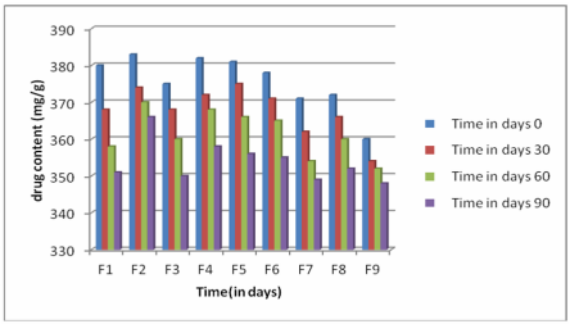

Fig. 9. Tempreture dependent stability studies of microspheres at 60° C

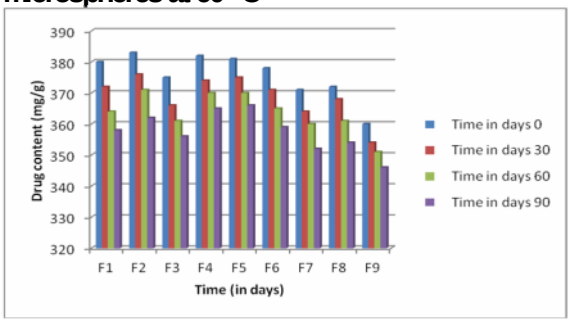

Fig. 10. Tempreture dependent stability studies of microspheres at Room Temperature (25+_2⁰ C)

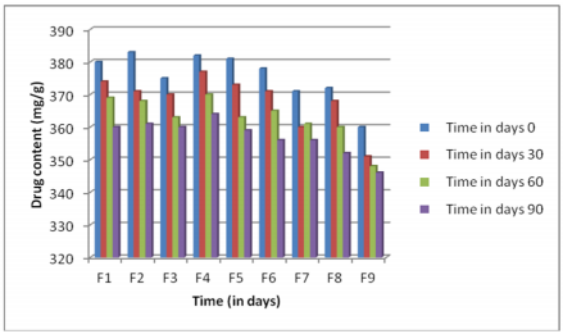

Fig. 11. Temperature dependent stability studies of microspheres at (37⁰ C &70% RH)

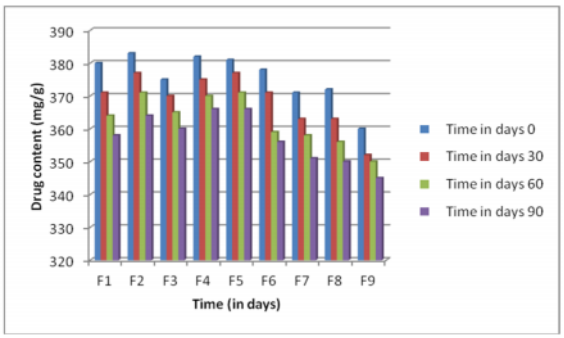

Fig. 12. Temperature dependent stability studies of microspheres at Refrigerator Temperature (2-8⁰ C)

(Refrigeration temperature) > 37⁰C & 7 0% RH(Humidity Chamber) > 37⁰C & 70% RH(Humidity Chamber) > 40⁰C temperature > 50⁰C temperature > 60⁰C temperature.**Summary and Conclusion**

In order to improve the therapeutic efficiency of Nifedipine sustained release formulatios have been developed to reduce side effects and improve patient compliance. The aim of this work was to prepare Nifedipine loaded microspheres using different polymers like cellulose acetate, ethyl cellulose, sodium alginate, chitosan and Eudragit L 100 by solvent evaporation method. The prepared dried microspheres were evaluated

for flow property, particle size and density of prepared microspheres encapsulation efficiency and in vitro drug release activity.

The flow property was determined by all the formulations and it was found that microspheres of EudragitL100 showed very good property as compare to other microspheres. Densities of all the formulations of microspheres were found to be less than the density of gastric fluid that supports the floating nature.In vitro drug release study was performed for all the formulations, microspheres prepared by different polymer exhibit different release and it found to Eudragit L 100>Cellulose acetate>Ethyl cellulose. On the basis of all this parameter the microsphere prepared by Eudragit L100 were selected for further optimization study.

Stability studies were performed on all prepared formulations. Stability studies for three months showed that nearly all formulations were stable at room temperature, refrigeration temperature, and at 37° & 70% RH, less than5% degradation was found. The prepared microspheres exhibited excellent drug content over the storage period of

90 days.

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