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Studies on the Microspheres of Baclofen

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ABSTRACT

The sustained release of Baclofen is desired because of its short biological half-life. Microspheres of Baclofen were prepared using the non-aqueous emulsification solvent evaporation method. The impacts of different factors such as type of Eudragit polymer as matrix polymer, Eudragit: HPMC K4M ratio on the characteristics of the microspheres were investigated. The morphology of microspheres was studied using optical and scanning electron microscopy and it was shown that microspheres had a spherical shape and smooth surface. The percentage yield of microspheres of all formulation was in the range of 94.01% to 99.12%. The drug content determination showed that even if the polymer composition was changed the solvent evaporation process was highly efficient to give microspheres having maximum drug loading. In termination, the prolonged sustained release time and enhanced stability resulting from the Baclofen microspheres might make contribution to its use.

Keywords: sustained release microsphere, non-aqueous emulsification solvent evaporation method, Baclofen, entrapment efficiency.

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INTRODUCTION

Baclofen is a derivative of gamma-aminobutyric acid (GABA). It is primarily used to treat spasticity of spinal or cerebral origin. To treat severely disabling spasticity, a small amount of Baclofen must be injected continually into the intrathecal space, as lifetime treatment.[1]

Until now, the only solution available to solve this challenging drug delivery problem is to use electronic pumps surgically implanted in the patient's body and connected to indwelling catheters. However, the need for surgery, the risk of infection or catheter dysfunctions, dislodgement of the catheter and several side effects still limit the treatment for prolonged periods.[2]

Baclofen has absorption window in upper G.I. tract; on arrival to colon its absorption is diminished or nonexistent.[3] It is freely soluble in simulated gastric fluid[4] and having a half-life of 2-4 hrs[5] which require frequent administration produce high incidence of adverse effects. Orally disintegrated tablets, conventional tablets are marketed oral formulations that neither site specific nor sustained release which causes fluctuation in plasma drug levels. [6] Therefore it is suitable drug to design in sustained release formulation. One of the methods to solve problems is to design the drug in sustained release microsphere formulation. Hence Baclofen is used in microspheres preparation to deliver drug in sustained manner to improve the performance of therapeutic system.

Biodegradable microspheres of Baclofen can release the drug over a period of time. To develop a sustained release microspheres formulation of a water soluble drug – Baclofen, different polymers such as HPMC K4M, Eudragit S100, Eudragit L100-55 were used. Eudragit S100 and Eudragit L100-55 are water insoluble, low permeable and have pH independent swelling property. But HPMC K4M is water soluble having pH independent swelling nature.[7] So, they were used as the retardant material.

MATERIALS AND METHODS

Baclofen was supplied by the Neon Lab Pvt. Ltd, Palghar. Eudragit S 100, Eudragit L 100-55 and hydroxyl propyl methyl cellulose K4M were procured from Lupin Pharmaceuticals, Aurangabad, India. Acetone, Light liquid paraffin and n-hexane were supplied from Research Lab Fine Chem Industries, Mumbai, India and span-80 from Loba Chemicals, Mumbai, India.

Solubility study[8]

Baclofen in an amount of excess of its solubility was added to 15 ml of dissolution medium in a 25 ml beaker maintained at 37 ± 0.5^0C in a constant temperature water bath for 4h. At

appropriate times aliquots of 1ml were taken from the dissolution medium, filtered and then diluted to 100 ml. Drug content of the samples were assayed spectrophotometrically (Shimadzu UV 2100 S, Japan) at 221 nm. Calibration curves were used for the determination of the amounts dissolved.

Compatibility Study of drug:

Baclofen and all the polymers were subjected to drug-excipients compatibility studies. The drug and polymer were mixed physically and FTIR measurements of drug, individual polymer and drug-polymer mixtures were obtained on Shimatzu FTIR. Samples were prepared by mixing with KBr (2mg sample in 200mg KBr) and placing in the sample holder. The spectra were scanned over the wave number range of 4000-400 cm^{-1} at the ambient temperature.

Method of Preparation of microspheres[9]

Baclofen microspheres were prepared by Emulsion solvent evaporation method. Acetone was used as the polymer solvent; light mineral oil as the microcapsulating vehicle and n-hexane as the decanter of paraffin oil. The internal phase consists of Eudragit S 100 or Eudragit L 100-55 or both, Hydroxy Propyl Methyl Cellulose K4M (HPMC K4M) dissolved in 15 ml of acetone. Weighted amount of the drug (100mg) was added to this solution and dispersed under ultrasonication for 20 minutes to obtain homogeneous solution. The dispersion was added to 100ml of light liquid paraffin containing 1% v/v span 80, while stirring. The emulsion was stirred for 3 hours at room temperature at 750 rpm to facilitate the evaporation of solvent and formation of microspheres. A mechanical stirrer (Remi Motors) was used for stirring. After evaporation of acetone, the microspheres formed were filtered and washed 4-5 times with 50 ml n-Hexane. Microspheres were dried at room temperature for 24 hours and stored in tightly closed glass tubes. The Experimental Runs are given in table 1.

Table1: Experimental Runs for microsphere formulation

Batch Code	Drug (mg)	HPMC K4M (mg)	Eudragit S100 (mg)	Eudragit L100-55 (mg)
F1	100	100	100	-
F2	100	100	-	100
F3	100	100	50	50
F4	100	100	200	-
F5	100	100	-	200
F6	100	100	100	100
F7	100	100	300	-
F8	100	100	-	300
F9	100	100	150	150

CHARACTERIZATION OF MICROSPHERES

Surface Morphology (SEM)

SEM studies were carried out by using JEOL JSM T-330A scanning microscope (Japan). Dry microspheres were placed on an electron microscope brass stub and coated with in an ion sputter. Picture of microspheres were taken by random scanning of the stub.

Frequency Distribution Analysis[10]

Determination of average particle size of microspheres was carried out by optical microscopy in which stage micrometer was employed. A minute quantity of microspheres was spread on a clean glass slide and average size of 200 microspheres was determined in each batch. The frequency distribution can be broken down into different size ranges, which can be presented in the form of a histogram.

Percent Yield[11]

The percentage of production yield (wt/wt) was calculated from the weight of dried microspheres (W_1) recovered from batches and the sum of the initial dry weight of starting materials (W_2) as the following equation:

$$\% \text{ Production Yield} = \frac{W_1}{W_2} \times 100$$

Micromeretic Characterisation[12]

The microparticles were characterized by their Micromeritics properties, such as bulk density, tapped density, Carr's compressibility index, Hausner ratio and flow property. The bulk density, tapped density were measured in a 10ml graduated measuring cylinder. The cylinder containing the sample was dropped at 2 second intervals onto a hard wood surface 100 times from a height of 1 inch. The initial bulk volume and final tapped volume were noted from witch, their respective densities were calculated.

Entrappement Efficiency[13]

10 mg of microspheres were crushed and dissolved completely in 50 ml phosphate buffer pH 7.4 to produce clear solution. The volume was adjusted to 100ml with phosphate buffer pH 7.4. Then the solution was filtered with 0.45 micron membrane filter. By making suitable dilutions the drug content was determined spectrophotometrically at 220 nm by using UV spectrophotometer. Encapsulation efficiency was calculated by using following formula:

$$\text{Encapsulation efficiency} = \frac{\text{Actual drug loading}}{\text{Theoretical drug loading}} \times 100$$

X-Ray Power Diffractometry (XRD)

X-ray power Diffractometry (XRD) was carried out to investigate the effect of microencapsulation process on crystallinity of drug. Powder X-RD patterns were recorded on Bruker AXS Analytical Instruments Pvt. Ltd. Germany; D2-PHASER based diffractometer using a voltage of 30kV, and a current of 10 mA. The scanning rate employed was 5^0 min^{-1}, over the 5 to 40 diffraction angle (2θ) range. The X-RD patterns of drug powder were recorded.

Swelling Index Study[14, 15]

A known weight (50mg) of microspheres were placed in basket assembly of dissolution apparatus(USP XXIV) rotated at 50 rpm in 500 ml of pH 7.4 phosphate buffer solution maintained at 37±0.5^{0}C and allowed to swell for the required period of time. The microspheres were periodically removed, blotted with filter paper and their changes in weights were measured during the swelling until equilibrium was attained. Finally, the weight of the swollen microspheres was recorded after a period of 6 h, and the swelling ratio (SR) was then calculated from the formula.

$$\text{Swelling index} = (\text{mass of swollen microspheres} - \text{mass of dried microspheres}) \times 100$$

***In Vitro* Drug Release Study[16]**

The release rate of Baclofen from Microspheres was determined using USP Dissolution Testing Apparatus II at pH 1.2 and 7.4 under sink conditions. The Microspheres equivalents to 100 mg Baclofen were placed directly in a dissolution basket kept at 37±0.5 ◦C. At preset time intervals aliquots were withdrawn and replaced by an equal volume of dissolution medium to maintain constant volume. After suitable dilution, the samples were analyzed spectrophotometrically at 220nm. The kinetics data obtained from release rates were also evaluated.[17, 18]

Stability Studies [16, 19]

The optimum batch of microspheres containing Baclofen was stored in closed amber-colored glass vials at refrigerator temperature (2-8^{0}C), room temperature (25±2^{0}C) and 40^{0}C at RH of 75% for a period of 60 days and observed for any change in morphology and drug loading efficiency. Samples were analyzed at the end of each month.

RESULTS AND DISCUSSION

Solubility Study:

As shown in table 2, the equilibrium solubilities of baclofen in water, 0.1N HCl and pH 7.4 phosphate buffer solutions were found to be 4.852 mg/ml, 19.304±0.16 mg/ml and 19.805±0.42 mg/ml, respectively, indicating the sink condition limits for the dissolution studies. Results show that it is freely soluble in water, 0.1N HCl& Phosphate Buffer pH 7.4.

Table 2: Solubility Study data for Baclofen

Solvent	The Equilibrium Solubilities of Baclofen (mg/ml)	
	Test	Standard
Water	4.852±0.71	4.3
0.1N HCl	20.304±0.16	>20
pH 7.4 Phosphate Buffer	20.805±0.42	>20

Compatibility Study of drug:

From the spectra of Baclofen and combination of Baclofen with polymer, it was observed that all characteristic peaks of Baclofen were present in the combination spectrum, thus indicating compatibility of the drug and polymer. IR spectr as are shown in figure 1 to 5.

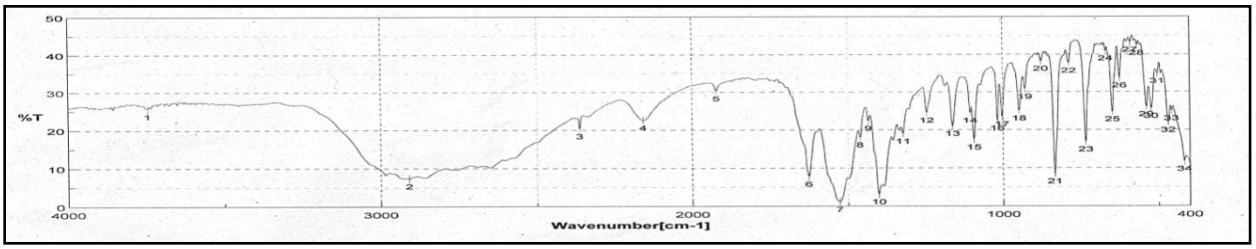


Figure 1: IR spectra of Baclofen.

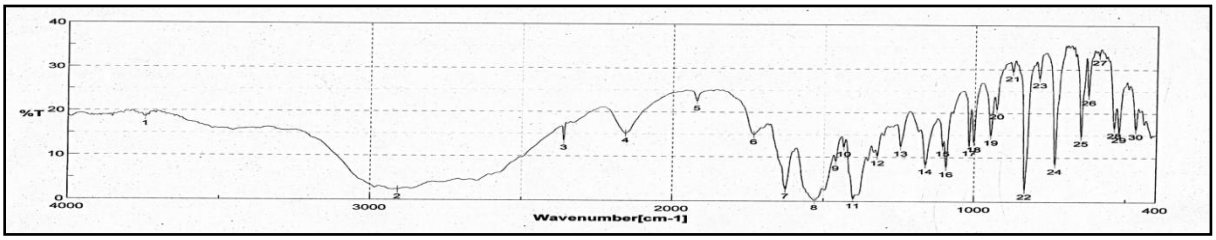


Figure 2: IR spectra of Baclofen and Eudragit S100, L100-55 and HPMC K4M

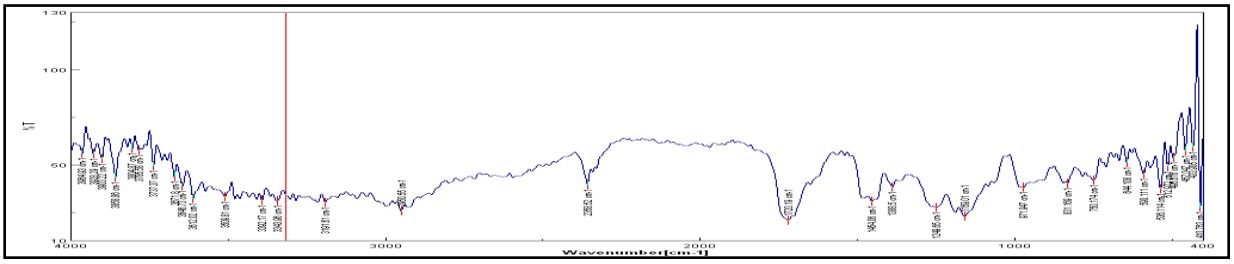


Figure 3: IR spectra of Eudragit S 100.

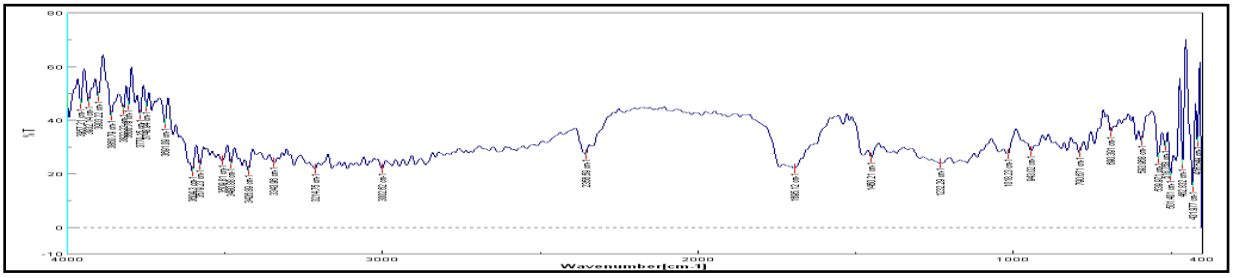


Figure 4: IR spectra of Eudragit L 100-55.

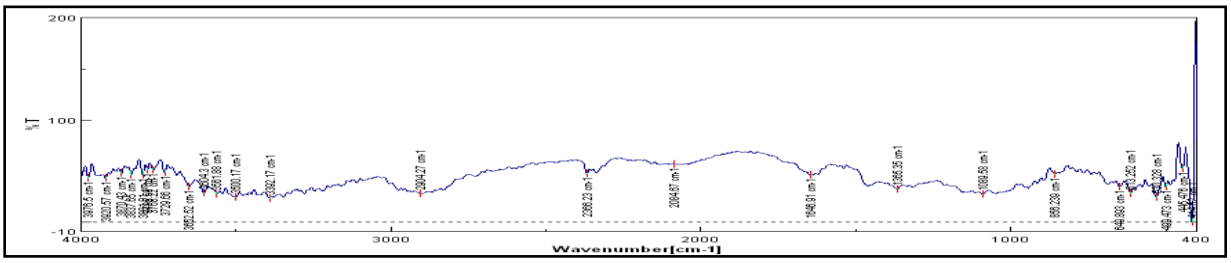
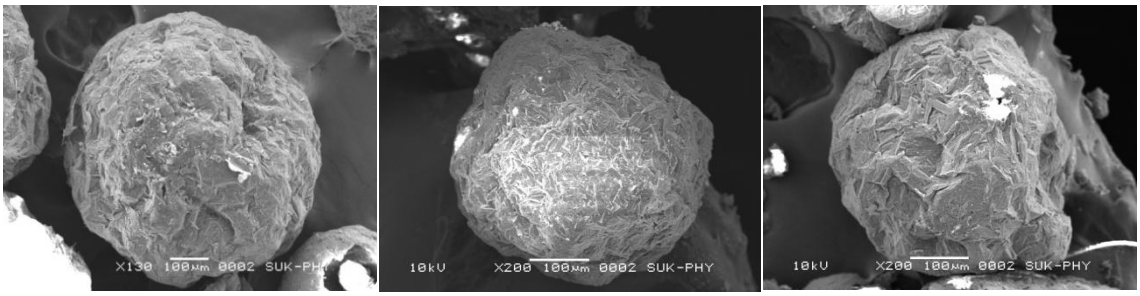


Figure 5: IR spectra of Hydroxy Propyl Methyl Cellulose K4M (HPMC K4M)

Surface Morphology (SEM)

SEM micrographs of the microsphere formulations coded F7, F8 and F9 were reported in Figure 6 a, b and c, respectively. The microspheres were quite spherical in shape indicated that spherical solid microspheres could be prepared by this method. In comparison the surface of smaller particles had a smoother and closer surface structure than that of lager particles.

It is seen from Figure 6 that surfaces of all microspheres are rough and there are several cracks on the surfaces. It is observed that in spite of using the constant polymer/solvent ratio, the depth of cracks on the surface of microspheres become greater while the polymer amount of formulation was decreased. This can be attributed to the increasing volume of dispersed phase against to the constant volume of dispersing medium, i.e. liquid paraffin resulting from the extended diffusion of organic solvent to the dispersing medium. It is thought that the surface characteristics of microspheres can depend both on the polymer characteristics and on the amount of polymer in the formulations. As the polymer ratio increased, more spherical microspheres with smoother surface were obtained



(a) (b) (c)

Figure 6: SEM micrographs of the microsphere formulations coded F7, F8 and F9 respectively.

Frequency Distribution Analysis

Particle size determination and Frequency distribution study:

The mean particle size ranged from 296.00 um- 503.00 um as shown in table 3 and figure 7. The mean particle size was influenced by the content and type of Eudragit polymer used and its ratio

with HPMC K4M polymer in the formulation. It is thought that when polymer mixtures were used, due to the changes in the solvent evaporation rate, formation rates and particle sizes of microspheres can also change correspondingly. The droplet stabilizer effect of span 80 differs when polymer mixtures are used. The mean particle size increased with increasing polymer concentration. Increasing polymer concentration produced a significant increase in the viscosity, thus leading to an increase of the emulsion droplet size and finally a higher microspheres size. Additionally, the high viscosity of the organic phase tends to restrict migration of the inner oil phase to the external oil phase. The Frequency distribution data of Baclofen microspheres are shown in figure 8.

Table 3: Mean Particle Size (um) of Baclofen Microspheres

Formulation	Mean Particle Size(µm)
F1	296.00
F2	322.00
F3	382.25
F4	347.20
F5	373.50
F6	423.00
F7	479.75
F8	417.00
F9	503.00

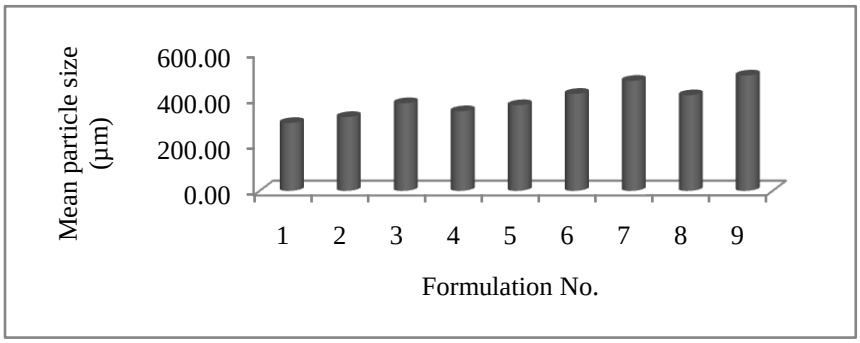


Figure 7: A plot of Mean Particle size vs Formulation number

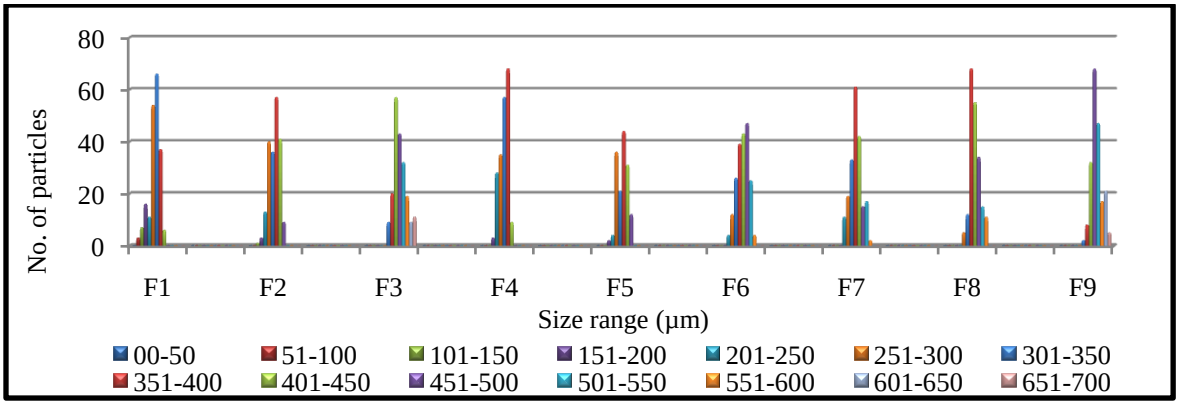


Figure 8: Frequency distribution data of Baclofen microspheres

Percent Yield:

The yields of preparation were very high (table 4) for all microspheres obtained and were not affected by the type of polymer, the polymer: drug ratio, the stirring speed of the system and the ratio of the mixture of polymers. The yields of preparation are shown in Figure 9.

Table1: Experimental Runs for microsphere formulation

Batch Code	Drug (mg)	HPMC K4M (mg)	Eudragit S100 (mg)	Eudragit L100-55 (mg)
F1	100	100	100	-
F2	100	100	-	100
F3	100	100	50	50
F4	100	100	200	-
F5	100	100	-	200
F6	100	100	100	100
F7	100	100	300	-
F8	100	100	-	300
F9	100	100	150	150

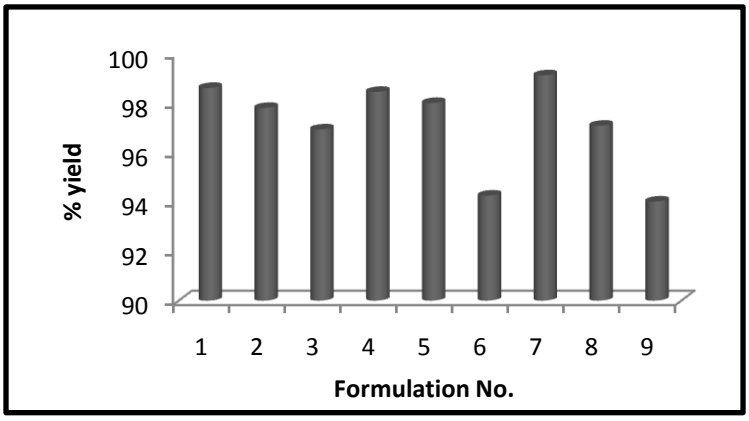


Figure 9: A plot of % Yield vs Formulation number

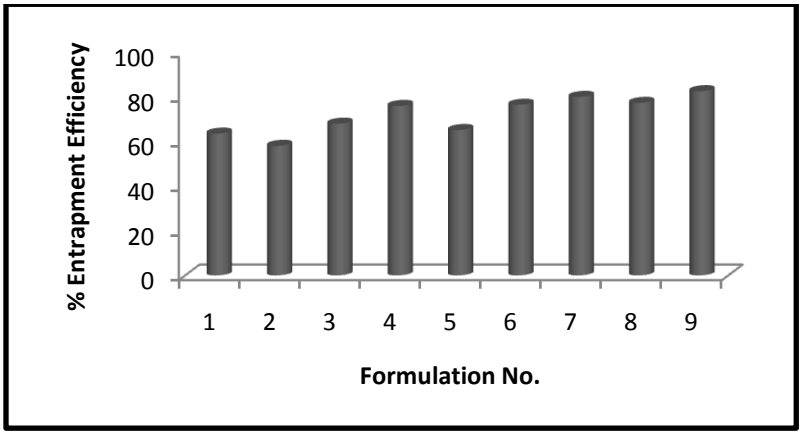


Figure 10: A plot of % Entrapment Efficiency vs Formulation number

Micromeritic Characterization

The prepared microspheres were evaluated for the micromeritic properties (table 5). The average

of three readings was taken. The mean particle size, flow properties and standard deviation were calculated. The low standard deviation of the measured mean particle size, % Compressibility, Hausner's Ratio and Angle of Repose of all the 9 formulations ensures the uniformity of the microspheres prepared by emulsion solvent evaporation method. The mean particle size was found to be in the range of 296.00 um- 503.00 um. The variation in mean particle size could be due to variation in drug to polymer ratio. The % Compressibility of all the microspheres was found to be in the range of 6.78±0.721 to 9.95±0.757. The Hausner's Ratio of all the microspheres was found to be in the range of 1.033±0.1 to 1.103±0.012. The Angle of Repose of all the microspheres was found to be in the range of 18.703±0.465 to 24.210±0.329.

Table 5: Micromeritic Properties of Baclofen Microspheres

Batch Code	Bulk Density (gm/mL)	Tapped Density (gm/mL)	Angle of repose	Carr's Index	Hausner's Ratio
F1	0.597±0.017	0.640±0.015	18.703±0.465	6.78±0.721	1.067±0.006
F2	0.635±0.005	0.685±0.006	18.880±0.526	7.29±0.99	1.070±0.01
F3	0.733±0.018	0.806±0.011	20.330±1.276	9.18±0.921	1.097±0.015
F4	0.665±0.025	0.737±0.033	20.950±0.541	9.95±0.757	1.103±0.012
F5	0.771±0.031	0.838±0.035	19.840±0.965	8.00±1.417	1.083±0.021
F6	0.718±0.067	0.742±0.045	22.120±0.756	9.45±1.149	1.033±0.1
F7	0.704±0.03	0.779±0.029	19.700±0.685	9.67±0.537	1.100±0.01
F8	0.678±0.059	0.743±0.058	19.510±0.592	8.74±1.41	1.090±0.017
F9	0.703±0.067	0.768±0.065	24.210±0.329	8.54±1.223	1.087±0.015

Where, ±SD=Standard deviation (n=3).

Table 6: % Entrapment Efficiency of Baclofen microspheres

Formulation	% Entrapment Efficiency
F1	63.55
F2	58.06
F3	68.01
F4	75.97
F5	65.15
F6	76.5
F7	80.01
F8	77.32
F9	82.57

Entrappement Efficiency

Entrapment efficiencies of all formulations are shown in table 6. The entrapment efficiency was influenced by the content and the type of eudragit polymer used and its ratio with HPMC K4M polymer in the formulation. Notably, in case of S100/L100-55 mixtures, entrapment efficiencies were higher than those of microspheres prepared by Eudragit S100 and Eudragit L100-55 microspheres (figure 10). An increase in the concentration of polymer in a fixed volume of

organic solvent resulted in an increase in entrapment efficiencies. Increasing the polymer solution concentration would enhance the viscosity of inner oil phase, and hence would lower the diffusion rate of drug towards the droplets surface. On the other hand, the higher viscosity of droplets synchronously resulted in droplets with larger size, which consequently lengthened the diffusion distance and also lowered the specific area.

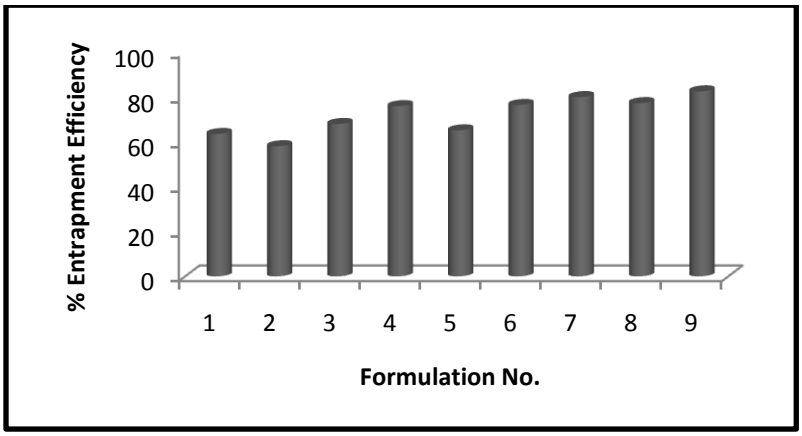


Figure 10: A plot of % Entrapment Efficiency vs Formulation number

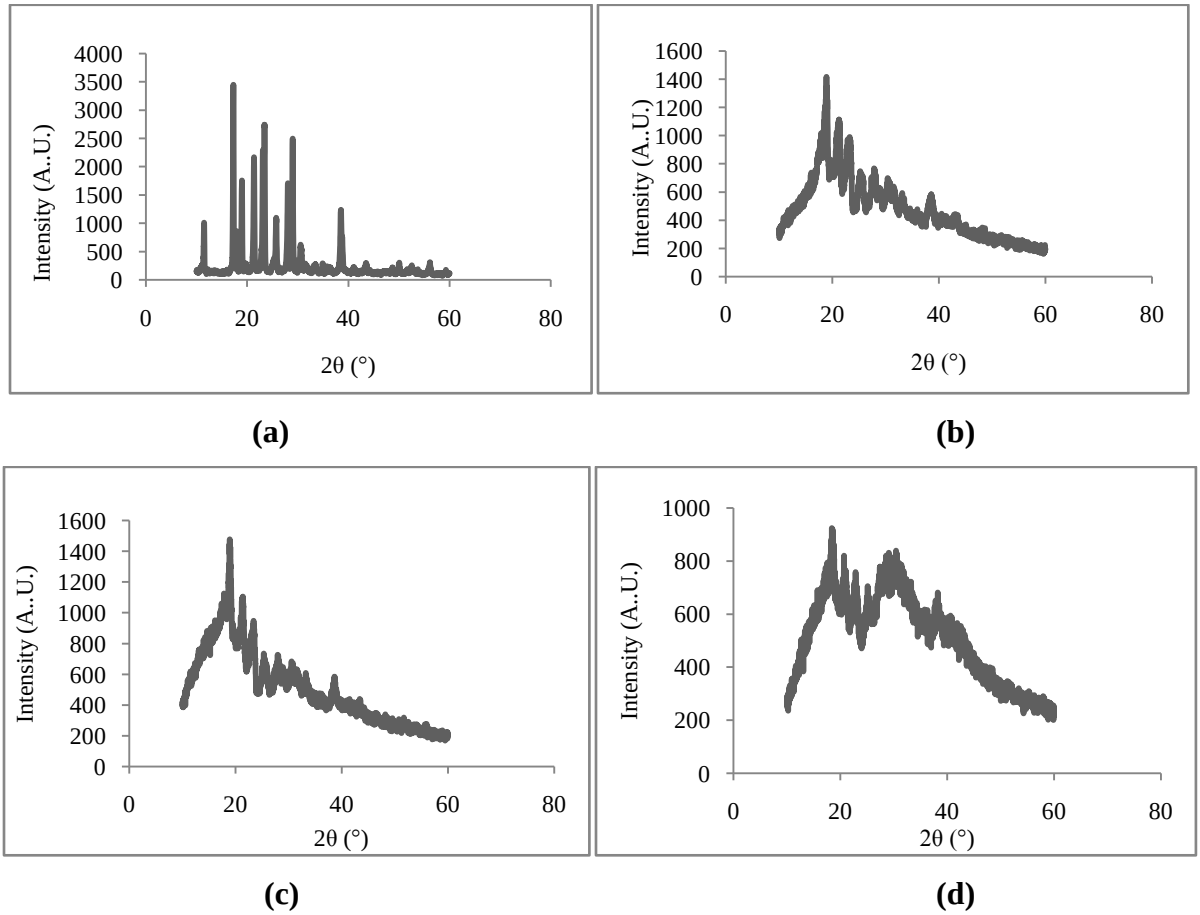


Figure 11: XRD of (a) Baclofen Pure drug, (b) Eudragit S100 microspheres, (c) Eudragit L100-55 microspheres, (d) Eudragit S100:L100-55 microspheres

X-Ray Power Diffractometry (XRD)

XRD directly detects the Crystallinity of a material. The diffraction pattern for Baclofen (Figure 11a), having high intensity peaks at 17.5, 19.0, 22.0, 23.4, 26.3 and 29.8 indicates that the drug is crystalline. The diffraction profiles of microspheres Figure 11 (b), (c), (d) showed a progressive disappearance of drug signals, proportional to the increasing polymer amount indicating loss of sharpness due probably decreased Crystallinity of the drug.

Swelling Index Study

The relative swelling study of Baclofen microspheres (figure 12, 13, and 14) shows that, as the concentration of HPMC K4M increases in the formulation, the relative swelling increases. The results clearly suggest that the swelling ratio depends upon concentration of polymer and type of polymer used in the formulation. Eudragit S100 and Eudragit L100-55 are water insoluble, low permeable and have pH independent swelling property. But HPMC K4M is having pH independent swelling nature.[20]

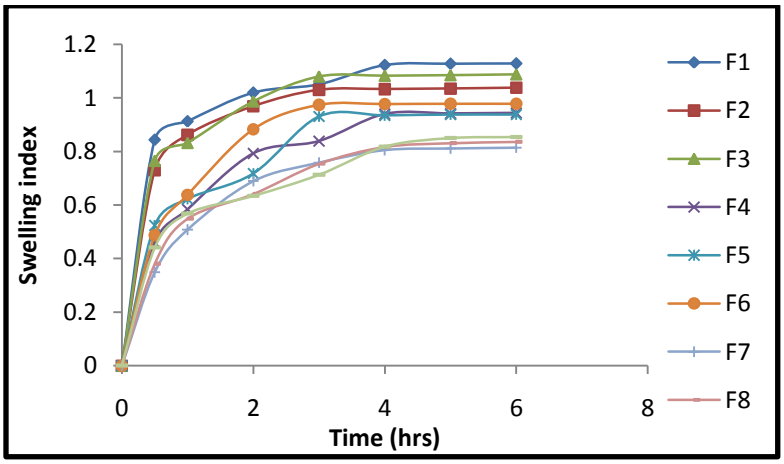


Figure 12: Swelling Index study of Baclofen microspheres in 0.1N HCl

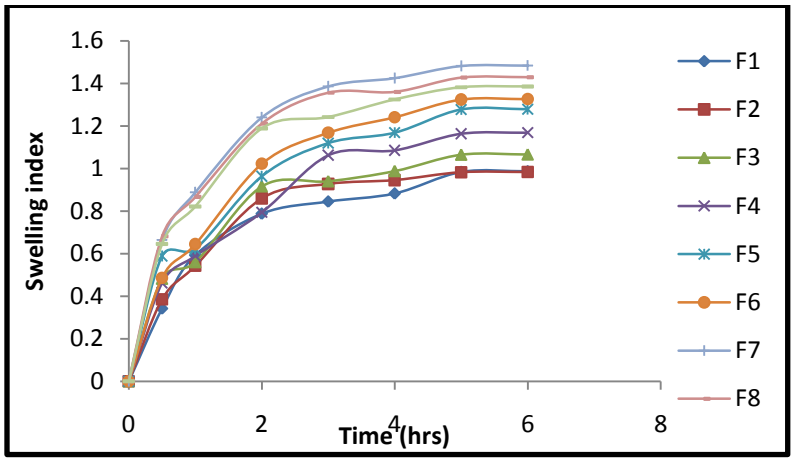


Figure 13: Swelling Index study of Baclofen microspheres in Phosphate buffer pH 7.4

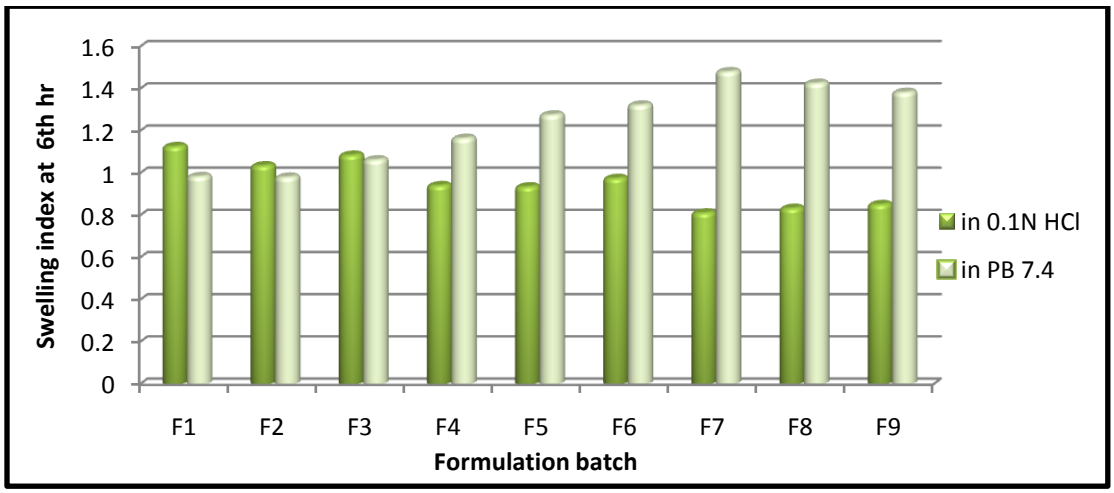


Figure 14: Comparison of Swelling Index studies of Baclofen microspheres in 0.1N HCl and PB 7.4

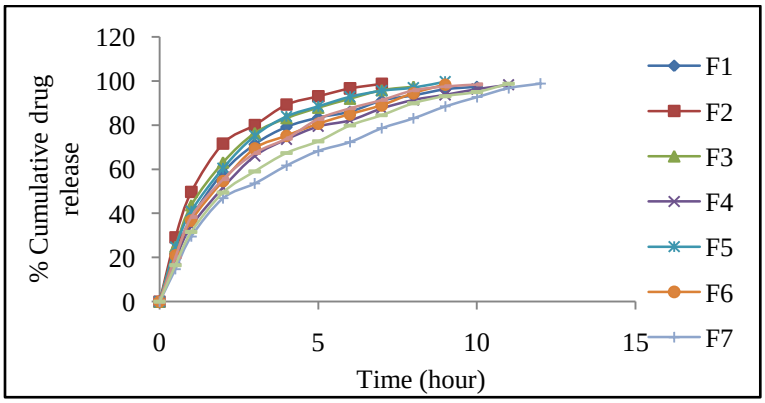


Figure 15: *In Vitro* Drug Release Profiles of Baclofen Microspheres

Thus Eudragit S100 and Eudragit L100-55 microspheres having 3:1 ratio of eudragit to HPMC K4M ratio show less swelling in 0.1 N HCl but more swelling ratio in and phosphate buffer pH 7.4. Whereas Eudragit S100 and Eudragit L100-55 microspheres having 1:1 ratio of eudragit to HPMC K4M ratio show more swelling in 0.1 N HCl but less swelling ratio in and phosphate buffer pH 7.4. The swelling depends upon the type of polymer, polymer concentration, ionic strength as well as type of medium.

***In Vitro* Drug Release Study**

Table 7 shows the drug release profiles from various formulations of microspheres. An initial burst effect was observed in all the batches of microsphere formulations. To provide an effective immediate action to treat spasticity and improve mobility in patients with multiple sclerosis and other spinal cord lesions it would be required to release drug rapidly in the initial stages to obtain the desired concentration following by slow release of the drug in order to replace drug lost, for example by gastric emptying.

Table 7: *In Vitro* Drug Release Profile for Baclofen Microsphere Formulations

T	% Cumulative drug release								
(hr)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	21.69± 0.955	29.14± 0.531	24.84± 0.650	19.31± 0.849	24.77± 0.469	20.97± 0.780	14.75± 0.474	20.16± 0.629	16.58± 0.379
1	37.99± 0.780	49.73± 0.689	43.7 ± 1.016	34.25± 0.724	41.06± 0.743	36.74± 0.718	29.54± 0.320	38.45± 0.633	31.63± 0.533
2	58.56± 0.909	71.65± 0.697	63.12± 1.086	51.67± 0.788	60.47± 0.606	54.68± 0.825	46.83± 0.425	55.50± 0.270	49.45± 0.953
3	71.29± 0.967	80.07± 0.709	76.45± 0.558	66.02± 0.656	75.18± 0.594	69.40± 0.559	53.54± 0.902	67.37± 0.787	59.06± 0.319
4	79.16± 0.722	89.29± 0.260	83.21± 0.771	73.56± 0.416	83.96± 0.658	75.17± 0.601	61.63± 0.342	73.96± 0.907	67.40± 0.281
5	83.35± 0.927	93.11± 1.328	87.96± 1.049	79.40± 0.257	88.54± 0.492	80.62± 0.578	68.27± 0.772	82.84± 0.622	72.67± 0.967
6	86.05± 0.950	96.68± 0.815	92.04± 0.624	82.17± 0.438	92.88± 0.449	84.93± 1.006	72.31± 0.466	87.67± 0.666	79.87± 0.501
7	91.12± 0.829	98.74± 0.409	95.91± 1.153	87.56± 0.301	95.62± 0.618	89.02± 0.744	78.59± 0.506	91.44± 0.647	84.52± 0.480
8	93.47± 0.490	-	97.45± 0.904	91.42± 0.825	97.05± 0.789	94.46± 0.445	83.08± 0.756	95.83± 0.505	89.96± 1.017
9	96.21± 0.826	-	-	93.74± 0.693	99.75± 0.514	98.34± 0.294	88.46± 0.556	97.59± 0.734	93.18± 0.157
10	97.33± 0.835	-	-	96.32± 0.579	-	-	92.67± 0.647	98.47± 0.680	95.04± 0.695
11	-	-	-	98.26± 0.728	-	-	96.78± 0.660	-	98.83± 0.489
12	-	-	-	-	-	-	98.84± 0.665	-	-

Where, ±SD=Standard deviation (n=3).

Decrease in the rate and extent of drug release was observed with the increase in polymer concentration in microspheres and is attributed to increase in the density of the polymer matrix and also an increase in the diffusional path length which the drug molecules have to traverse. The release of drug from these gels was characterized by an initial phase of high release (burst effect). However, as gelation proceeds, the remaining drug was released at a slower rate followed by a second phase of moderate release. This bi-phasic pattern of release is a characteristic feature of matrix diffusion kinetics. The initial burst effect was considerably reduced with increase in polymer concentration. From figure it can be seen that the drug release rate is affected by the polymer type and polymer concentration.

A comparison of the drug release profiles of microspheres prepared with Eudragit S100, Eudragit L100-55 and Eudragit S100: Eudragit L100-55 mixture, Figure 15 indicates that Eudragit type

influenced the drug release from microspheres. Eudragit S100 was more effective in decreasing drug release than Eudragit L100-55. Eudragit S 100 is soluble at pH > 7: whereas Eudragit L100-55 is soluble at pH > 5.5, hence the relatively retarded drug release from the microspheres. It also indicates that the release rate decreases with increasing the amount of the polymer.

The release data obtained were evaluated kinetically by zero order, first order and Higuchi model. According to the determination coefficients (R^2) release, data was best characterized by Higuchi model suggesting a similarity to release from a matrix (Table 8). A linear graph was obtained by plotting the percentage of the drug released versus the square root of time. These profiles showed that drug release obeys Higuchi diffusion controlled model. The results obtained from the computer program were also supported by these profiles. When the microspheres are immersed into the buffer solution, they swell by absorbing buffer into their matrix and form a gel diffusion layer. This layer hinders the outward transport of the drug producing a diffusion controlled release effect.

Table 8: Release Kinetics data of Baclofen microspheres

Formulation	Zero Order	First Order	Higuchi Matrix	Peppas Plot	
				R^2 Value	n Value
F1	0.802	0.991	0.956	0.947	0.947
F2	0.798	0.984	0.959	0.947	0.947
F3	0.816	0.993	0.965	0.953	0.953
F4	0.833	0.974	0.970	0.960	0.960
F5	0.808	0.999	0.960	0.957	0.957
F6	0.856	0.926	0.979	0.967	0.967
F7	0.901	0.896	0.992	0.969	0.969
F8	0.840	0.980	0.973	0.958	0.958
F9	0.878	0.963	0.986	0.968	0.968

Table 9: Stability Studies of F7 formulation (HPMC K4M/ EudragitS100 1:3 ratio)

Temperature	Time in days	% Drug content	% Drug release
Room temp. (25 ± 2^0C)	0	80.01	99.47
	30	79.87	99.35
	60	79.03	99.20
40^0C/ 75% RH	0	80.01	99.47
	30	79.05	99.12
	60	78.27	98.73
Refrigerator temp. ($2\text{-}8^0$C)	0	80.01	99.47
	30	79.54	99.28
	60	78.63	98.90

Stability Studies

In view of the potential utility of formulation F7 (ERS100 microspheres) as a sustained release form; the stability studies were performed at Room temp (25 ± 2^0C), 40^0C/ 75% RH and

Refrigerator temp (2-8^{0}C) for 60 days. After storage, formulation was observed for physical appearance, particle shape, drug content studies and *in vitro* dissolution studies. The microspheres were found to be white and free flowing in nature. As shown in table 9, no significant change was observed in results of drug content studies and *in vitro* dissolution studies which confirm stable character of drug in microspheres.

CONCLUSIONS

Baclofen microspheres were prepared successfully using solvent evaporation method. Polymer: drug ratio and type of the polymer used were important to obtain spherical particles with smooth surfaces. The yields of preparation and encapsulation efficiencies were very high for all microspheres obtained. Baclofen release rates from microspheres were dependent on the type of polymer used. Baclofen release rates from Eudragit S100 microspheres were very slow whereas release rates from Eudragit L100-55 microspheres were faster. The drug release profile aimed for peroral administration could be obtained by adding Eudragit S100 to Eudragit L100-55 and changing the ratio of these polymers. Sustained release achieved with these microsphere formulations can reduce dosing frequency, decrease side effects and improve patient compliance.

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