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Formulation & evaluation of baclofen loaded sustained release microspheres using HPMC-k4m

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Abstract
This study aimed to develop and evaluate floating microspheres of Baclofen to enhance its gastric retention and prolong its release within the upper gastrointestinal tract. The microspheres were formulated using the solvent evaporation method. A 32 full factorial design was employed to investigate the combined effects of two independent variables: the concentration of PLGA (X1) and PEO (X2), on the dependent variables such as particle size (Y1), drug entrapment efficiency (Y2), buoyancy (Y3), *in-vitro* drug release at 1 hour (Y4), and *in-vitro* drug release at 6 hours (Y5). The results from multiple regression analysis indicated that increasing the concentrations of PLGA and PEO led to a decrease in drug release, while particle size, entrapment efficiency, and buoyancy increased. The optimized formulation demonstrated a particle size of 115.96 µm, a drug entrapment efficiency of 90.06%, and buoyancy of 90.76%. The *in-vitro* release profile of Baclofen from the floating microspheres exhibited sustained drug release for up to 24 hours. The microspheres were found to be free-flowing, porous, and nearly spherical. The release kinetics followed the Higuchi model, with drug release governed by Fickian diffusion.

Keywords: Baclofen, floating microspheres, PLGA, PEO, solvent evaporation, *in-vitro* drug release, sustained release, drug entrapment efficiency, buoyancy, Higuchi model, Fickian diffusion

Introduction
Drugs that are rapidly absorbed from the gastrointestinal tract (GIT) and have short half-lives are eliminated quickly from the bloodstream, necessitating frequent dosing to maintain therapeutic levels. To address this challenge, the development of oral sustained-release formulations aims to release the drug gradually into the GIT, ensuring a steady drug concentration in the bloodstream over an extended period [1, 2]. Gastro-retentive drug delivery systems (GRDDS) are specifically designed to remain in the stomach for an extended duration, releasing their active ingredients slowly. This sustained release ensures a prolonged drug concentration in the upper GIT, improving therapeutic outcomes.
GRDDS can be categorized into several types [3, 4].

- Bio adhesive Drug Delivery Systems
- Expandable Drug Delivery Systems
- Floating Drug Delivery Systems (FDDS)
- High-Density Systems

Among these, FDDS are the most commonly employed systems. Floating drug delivery systems are low-density systems designed to float on the gastric contents, allowing them to remain in the stomach for extended periods. This floating behaviour ensures sustained drug release, reducing fluctuations in drug levels and improving bioavailability. A key advantage of floating systems is that only a small amount of gastric content is needed to achieve buoyancy. The dosage form stays afloat by generating a minimal floating force, making it an effective approach, particularly for drugs that are absorbed primarily in the upper small intestine. This slow and controlled release minimizes systemic exposure while maintaining local therapeutic concentrations in the stomach.
Drugs that exhibit poor bioavailability due to site-specific absorption in the upper GIT are prime candidates for formulation as floating drug delivery systems.

These systems enhance drug absorption by increasing the time the drug stays in the stomach. Floating microspheres, a type of non-effervescent gastro-retentive system, offer a promising solution. These microspheres are characterized by their free-flowing nature, and their hollow core enhances buoyancy, allowing them to remain afloat. Typically, they are composed of proteins or synthetic polymers and have a size less than 200 micrometres [5, 6].

Baclofen, a gamma-amino butyric acid (GABA) agonist, is a skeletal muscle relaxant used to alleviate muscle spasms caused by various conditions. It is particularly effective for treating muscle spasticity associated with spinal cord injuries and multiple sclerosis. Baclofen is rapidly absorbed from the GIT, with bioavailability ranging from 70% to 85%. Peak plasma concentrations are typically observed 2 to 3 hours after oral administration. However, its absorption is dose-dependent and decreases with higher doses. Baclofen has a relatively short half-life of 2.5 to 4 hours, and its absorption window is limited to the upper GIT. This makes Baclofen difficult to formulate into sustained-release dosage forms, as its absorption diminishes in the colon [7-10]

In this study, efforts were made to develop floating Baclofen microspheres to improve its absorption in the stomach. The objective was to formulate spherical floating microspheres, evaluate their sustained-release effects, examine the impact of different polymers on buoyancy and drug release, and optimize the formulation using statistical methods.

Materials and Methods

Materials Used: Baclofen (Gift Sample form VV Med Labs), PEO and PLGA (Viro Lab Chemicals, Vijayawada), HPMC K4M, and Magnesium stearate (Viruchi Chem Ltd), DMSO (SD Fine Chem), Light Liquid Paraffin and Heavy Liquid Paraffin (Viro Lab Chemicals).

Method

Drug-Excipient Compatibility Study using Differential Scanning Calorimetry (DSC): The compatibility between the drug and excipients is crucial for ensuring the proper release of the drug from the formulation. To assess the physicochemical compatibility of the optimized formulations, Differential Scanning Calorimetry (DSC) was used [11, 12].

The DSC spectra were recorded for the following samples:

i) Baclofen,
ii) A mixture of PEO and PLGA polymers, and
iii) A combination of Baclofen and the polymer mixture (PEO and PLGA).

The analysis was conducted using a DSC (DCS-60, Shimadzu Corporation, Japan). The obtained DSC spectra for Baclofen and the polymer mixtures are discussed in the results and discussion section [13, 14].

Preparation of Baclofen Floating Microspheres: Floating microspheres containing Baclofen were prepared using the solvent evaporation method. Initially, the polymers (PEO, PLGA, and Hydroxypropyl Methylcellulose) were dissolved in an organic solvent (DMSO). Baclofen was then dispersed into the polymer solution. The drug-polymer mixture was added drop wise using a hypodermic needle into a continuous phase consisting of light and heavy liquid paraffin. The organic solvent was allowed to evaporate due to continuous stirring with a propeller mixer. After 2 hours, the floating microspheres were washed several times with hexane, filtered, and left to dry at room temperaturB1 is shown in table 01. [15-18].

Table 1: Composition of Formulation Batches

Ingredients	Baclofen	PLGA	PEO	HPMC K4M	Mg stearate	Solvent (DMSO) (ml)
Batches	Quantity taken (mg)					
B1	100	100	100	50	5	10
B2	100	200	100	50	5	10
B3	100	300	100	50	5	10
B4	100	100	200	50	5	10
B5	100	200	200	50	5	10
B6	100	300	200	50	5	10
B7	100	100	300	50	5	10
B8	100	200	300	50	5	10
B9	100	300	300	50	5	10

Evaluation of Baclofen Floating Microspheres

Particle Size Analysis: The particle size of the Baclofen-loaded Eudragit microspheres was determined using optical microscopy. A compound microscope was used to examine the microspheres, and at least 300 particles were measured using a calibrated ocular micrometre. The average particle size was calculated by dividing the total size of the microspheres by the number of particles [19].

Percentage Yield: The microspheres were collected, weighed, and the percentage yield was calculated by dividing the actual weight of the microspheres by the theoretical weight of the drug and polymers used in the preparation. The percentage yield was calculated using the following formula [20, 21].

% Yield = Practical yield / Theoretical yield × 100

{Yield} = \frac{\text{Practical Yield}}{\text{Theoretical Yield}} \times 100% Yield=Theoretical Yield Practical Yield×100

Percentage Drug Entrapment Efficiency [22, 23]: To evaluate drug entrapment efficiency, 25 mg of microspheres were crushed and dispersed in 100 ml of 0.1 N HCl and sonicated for 10–15 minutes. The mixture was then stirred on a magnetic stirrer for 24 hours. After filtering the dispersion, the drug content was analysed spectrophotometrically at 226.5 nm. The percentage drug entrapment efficiency (DEE) was calculated using the following formula:

% DEE = Actual drug content / Theoretical drug content × 100

{DEE} = \frac{\text{Actual Drug Content}}{\text{Theoretical Drug Content}} \times 100% DEE=Theoretical Drug Content Actual Drug Content ×100

Percentage Buoyancy Study [24, 25]: For the buoyancy study, 100 mg of floating microspheres were placed on the surface of a type II USP dissolution apparatus filled with 900 ml of 0.1 N HCl. The solution was stirred at 100 rpm for 8 hours. After this period, the buoyant particles were separated by filtration and dried, then weighed. The sinking

particles were also collected, dried, and weighed. The percentage buoyancy was determined by comparing the weight of the floating particles to the total weight of both floating and sinking particles. The buoyancy was calculated using the following equation:

% Buoyancy = Initial weight of microspheres / Weight of floating microspheres × 100

{Buoyancy} =\frac{\text{Initial Weight of Microspheres}}{\text{Weight of Floating Microspheres}}times
100% Buoyancy=Weight of Floating MicrospheresInitial W eight of Microspheres×100

***In-vitro* Drug Release [26, 27]:** Cumulative drug release was studied for all formulations by placing 20 mg of drug-equivalent microspheres in a USP type II dissolution apparatus with 900 ml of 0.1 N Hydrochloric acid (Hcl) at pH 1.2, maintained at 37 ± 0.2°C and a stirring rate of 100 rpm. The drug release was monitored spectrophotometrically at 226.5 nm using the first derivative (D1) method, adopting the peak height technique.

Residual Solvent Analysis [28]: The residual solvent analysis was performed using Gas Chromatography to ensure that no harmful solvents remained in the final formulation.

Surface Morphology Study [29]: The surface morphology of the microspheres was analysed using Scanning Electron Microscopy (SEM). Dry microspheres were placed on a SEM brass stub and gold-coated using an ion sputter. The microspheres were then imaged by scanning the stub in random patterns.

Statistical Analysis [30]: A statistical model incorporating interactive and polynomial terms was used to analyse the responses. Mathematical modelling, evaluation of the model fit, and response surface modelling were conducted using Design-Expert software. The equation used for the analysis is

Yi=b0+b1X1+b2X2+b12X1X2+b11X12+b22X22Y

i = b_0 + b_1X_1 + b_2X_2 + b_{12}X_1X_2 + b_{11}X_1^2 + b_{22}X_2^2Yi=b0+b1X1+b2X2+b12X1 X2+b11X12+b22X22
Where YiY_iYi is the dependent variable, b0b_0b0 is the intercept (arithmetic mean response of all runs), b1,b2,b12,b11,b22b_1, b_2, b_{12}, b_{11}, b_{22}b1, b2, b12,b11,b22 are the regression coefficients, and X1X_1X1 and X2X_2X2 are the independent variables. The dependent variables include particle size (Y1), percentage yield (Y2), percentage drug entrapment efficiency (Y3), percentage buoyancy (Y4), *in-vitro* drug release at 1 hour (Y5), and *in-vitro* drug release at 6 hours (Y6), while the independent variables are the concentrations of PLGA (X1) and PEO (X2).

Stability Study [31]: A stability study was performed on the formulated microspheres by storing them at 40°C and 75% relative humidity for one month, following ICH guidelines.

Results and Discussion

Drug-Excipient Compatibility Study using Differential Scanning Calorimetry (DSC) [32, 33, 34]: The DSC analysis of Baclofen and the physical mixture of Baclofen with polymers showed that the characteristic peaks of Baclofen were largely unaffected by the presence of the polymers. No significant shifts in the spectra were observed, indicating that there were no apparent incompatibilities between Baclofen and the selected polymers. The DSC thermograms of Baclofen and the polymer mixtures, shown in Figures 1, 2, further confirm the compatibility of the drug with the excipients used in the formulation.

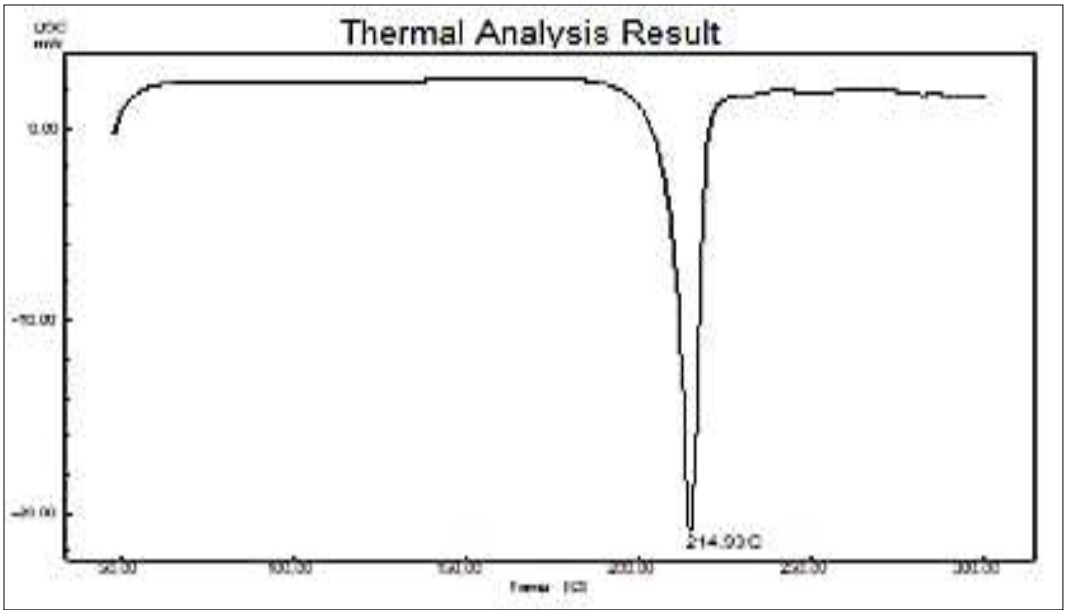

Fig 1: DSC of Pure Drug Baclofen

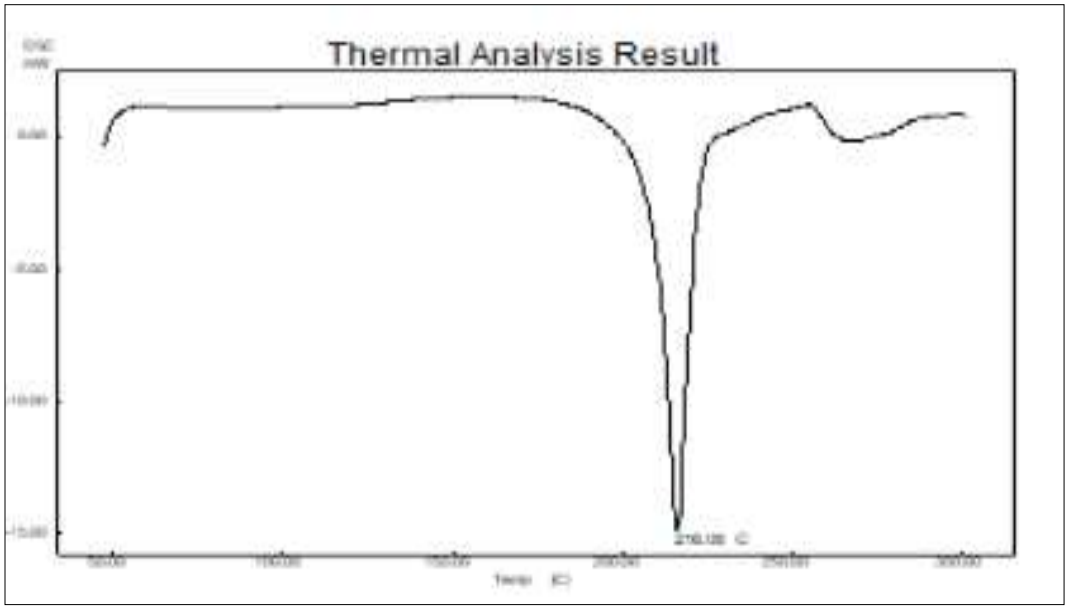

Fig 2: DSC of Pure Drug Baclofen and Polymers

Results of Batches of Baclofen Floating Microspheres: The Baclofen floating microspheres were fabricated using the solvent evaporation technique with selected polymers. The results obtained for the Baclofen floating microspheres are summarized a visual representation of the Baclofen floating microspheres is shown in Figure 3 and resulted in table 02."

Fig 3: Floating Microspheres of Baclofen as Balloons

Table 2: Particle Size, % Yield, % Drug Entrapment Efficiency, % Buoyancy

Batch	Particle size (µm)	Percentage yield (%)	DEE (%)	Percentage Buoyancy (%)
B1	68.20±2.32	52.12±1.96	71.25±1.2	80.60±1.2
B2	81.30±2.23	57.23±2.24	75.12±2.3	83.66±1.7
B3	95.41±1.52	65.06±2.45	83.32±3.2	85.12±1.2
B4	85.12±1.61	59.02±2.47	80.21±1.5	85.21±1.8
B5	98.15±1.29	67.51±2.21	78.12±2.5	82.16±1.5
B6	105.13±2.18	74.22±2.52	85.28±3.5	88.01±2.1
B7	100.01±1.56	67.89±2.50	87.41±2.3	87.50±1.6
B8	112.03±1.94	77.91±2.55	89.42±2.8	90.12±1.9
B9	119.05±2.45	85.11±3.16	92.06±3.8	92.21±2.5

Particle Size Analysis [35, 36]: Floating microspheres containing Baclofen were successfully prepared using the solvent evaporation method. The particle size distribution of the prepared microspheres is presented. The smallest average particle size was observed in the B1 formulation (68.2 µm), while the largest was in the B9 formulation (119.05 µm). The results suggest that increasing the drug-to-polymer ratio (core-to-coat ratio) led to an increase in particle size. This can be attributed to the higher viscosity of the solution when both the drug and polymer concentrations increase, as the same amount of solvent was used for solubilizing the drug and polymer. Additionally, PEO had a more significant impact on particle size compared to PLGA.

% Yield

As seen in data the % yield of the microspheres increased with a higher drug-to-polymer ratio. This indicates that a greater amount of polymer leads to a higher yield in the formulation.

Percentage Drug Entrapment Efficiency [37]

The drug entrapment efficiency was found to be highest in the B9 formulation (92.06%). The increase in entrapment efficiency with a higher drug-to-polymer ratio suggests that a larger proportion of the polymer coating provides more capacity to retain the drug. Additionally, the drug's low solubility in the non-aqueous media (light liquid paraffin and heavy liquid paraffin) used for microsphere preparation contributed to reducing drug loss during the formulation process.

Percentage Buoyancy [38]: As shown that the B1 formulation had the lowest buoyancy (80.6%), while the B9 formulation exhibited the highest buoyancy (92.21%). Formulations with a higher ratio of PEO and PLGA polymers demonstrated better floating ability. The smaller particle size in formulations with a lower polymer ratio may lead to a higher density, causing the microspheres to settle more quickly. PEO, with its lower bulk density and permeability compared to PLGA, contributed to better floating properties.

Table 3: *In vitro* Drug Release Studies

Time (hour)	Batch code								
	B1	**B2**	**B3**	**B4**	**B5**	**B6**	**B7**	**B8**	**B9**
1	42.32±1.81	44.41±1.15	39.56±1.77	32.15±1.72	31.21±1.04	33.56±1.99	27.31±1.82	26.37±1.85	25.35±1.16
2	52.35±1.05	55.76±1.64	45.23±1.09	40.28±1.71	41.28±1.96	42.53±1.05	34.23±1.90	31.9±1.13	31.12±1.08
3	65.67±1.48	68.40±1.93	54.36±1.76	55.16±1.89	56.12±1.19	49.25±1.63	47.42±1.38	45.35±1.65	38.25±1.90
4	83.33±1.17	79.29±1.77	63.26±1.45	64.23±1.19	64.56±1.16	57.63±1.95	54.82±1.04	52.33±1.92	43.21±1.19
6	91.57±1.84	89.49±1.01	74.36±1.78	72.15±1.69	71.1±1.85	69.12 ±1.83	63.15±1.14	58.91±1.95	50.35±1.05
7	99.42±1.55	96.20±1.01	79.56±1.59	79.20±1.95	77.27±1.06	75.69±1.83	69.56±1.44	66.53±1.56	64.56±1.13
8		100.01±1.09	87.26±1.14	85.5±1.29	82.26±1.99	81.23±1.05	73.21±1.02	70.1±1.98	73.45±1.10
9			93.5±1.89	92.21±1.94	88.15±1.69	84.56±1.45	85.56±1.45	77.21±1.02	75.21±1.12
10			96.33±1.17	99.13±1.24	93.6±1.62	90.11±1.78	93.42±1.64	81.62±1.16	79.85±1.92
12			102.9±1.26		99.08±1.09	95.1±1.32	99.56±1.94	85.62±1.70	82.56±1.14
14						99.32±1.28	100.03±1.39	92.93±1.97	85.33±1.84
16								98.63±1.26	88.27±1.56
18									92.56±1.02
20									97.02±1.59
24									98.12±1.02

*Values are expressed as mean ± SD (n=3)

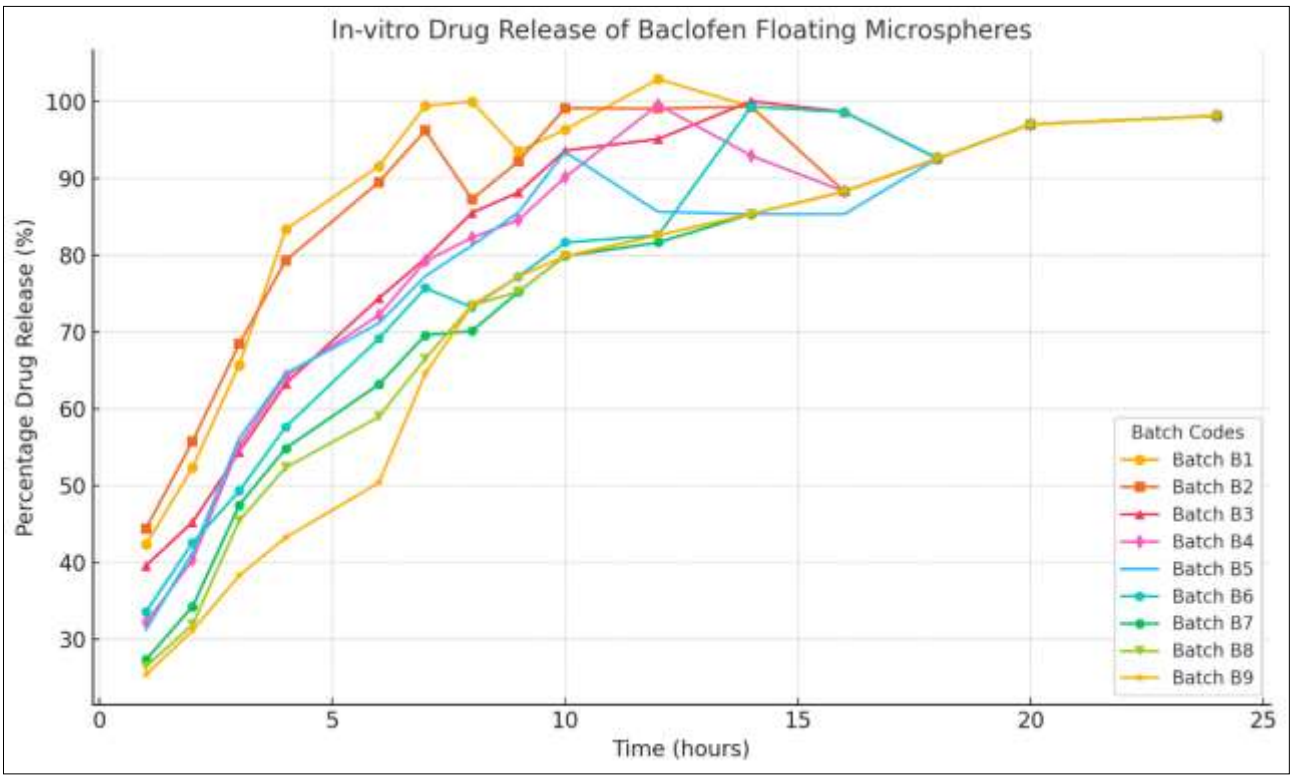

Fig 4: *In vitro* Drug Release profile of Baclofen Microspheres

Drug Release Behavior [39]: From the graph and the data it is evident that an increase in the drug-to-polymer ratio resulted in a decrease in the drug release rate. This can be attributed to the thicker matrix walls of the microspheres formed with a higher polymer concentration, which leads to fewer pores in the structure. Initially, the drug release followed a burst pattern, followed by a sustained release phase. This burst release is likely due to the presence of drug crystals on the surface of the microspheres. Additionally, it was observed that the drug release rate was higher for the (1:2) drug-to-polymer ratio compared to the (1:6) ratio and invitro drug release studies were observed in table no 03 and shown in figure no 04.

Surface Morphology Study [40]: From scanning electron microscopy study, it is concluded that microspheres were fairly smooth and spherical in shape having porous structure. The surface of microspheres consists of crystals of remaining drug which is responsible for initial bursting effect was shown in figure no 05.

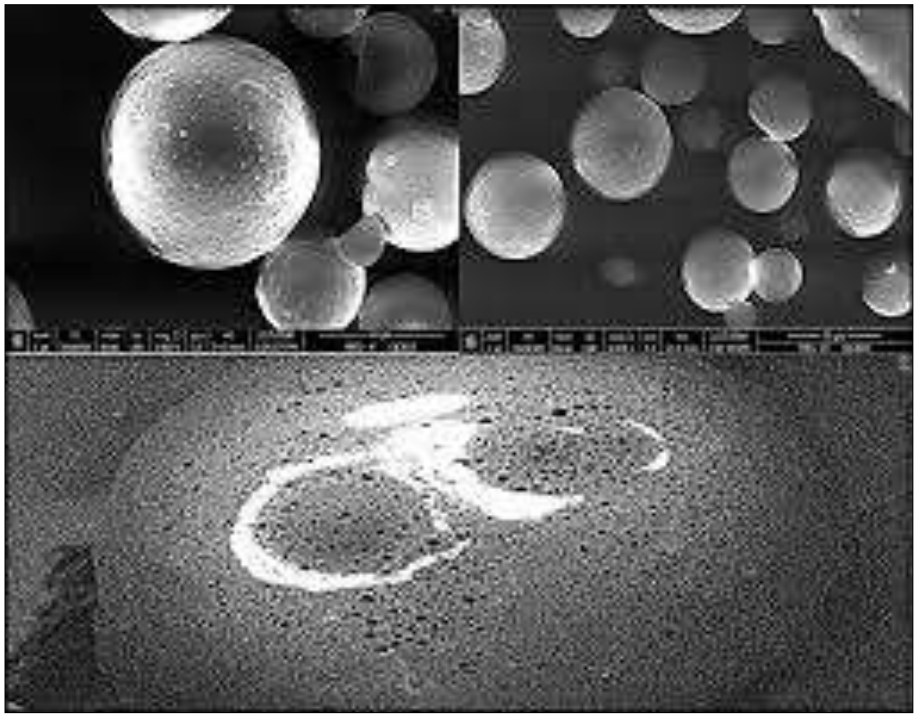

Fig 5: Scanning Electron Microscopy Images a) Spherical floating microspheres of baclofen b) Zoomed view of spherical floating microsphere of baclofen c) Porous surface of floating microsphere of baclofen

The average particle size varied between 68.2 µm and 119.05 µm, as shown with a correlation coefficient of 0.9955. The p-values were below 0.05, indicating that both X1 (PLGA) and X2 (PEO) significantly influenced the particle size. Both factors had a positive effect, meaning that an increase in the drug-to-polymer ratio resulted in a larger particle size. Of the two, X2 had a more pronounced effect compared to X1.

The percentage drug entrapment efficiency ranged from 71.25% to 92.06%, as detailed in Table and showed a correlation of 0.9705. With p-values below 0.05, both X1 and X2 were significant factors. Both had a positive impact, indicating that a higher drug-to-polymer ratio led to increased drug entrapment efficiency. Here again, X2 had a more substantial effect than X1.

Percentage buoyancy was observed to range from 80.6% to 92.21%, as shown with a correlation coefficient of 0.8817. The p-values were also below 0.05, confirming that X1 and X2 both significantly influenced buoyancy. An increase in the drug-to-polymer ratio led to higher buoyancy. Similar to the other properties, X2 had a more significant effect than X1. In the *in-vitro* drug release at 1 hour, values ranged from 42.32% to 25.35% for the B1 to B9 batches, as shown with a correlation of 0.9086. The p-values were below 0.05, indicating that X1 and X2 significantly impacted drug release. Both factors had a negative effect, meaning that as the drug-to-polymer ratio increased, the drug release decreased. Among the two, X2 had a stronger negative effect compared to X1. The p-value for X1 was greater than 0.05, making it insignificant in terms of its influence on the cumulative drug release (CDR) at 1 hour.

For the *in-vitro* drug release at 6 hours, the percentage ranged from 91.57% to 50.35%, as indicated for the B1 to B9 batches, with a correlation coefficient of 0.9271. Both X1 and X2 significantly affected the drug release, with negative effects observed. An increase in the drug-to-polymer ratio led to a reduction in the drug release. Here, X2 exhibited a more significant negative effect compared to X1, and the p-values for both factors were below 0.05, confirming their significant influence on the dissolution rate.

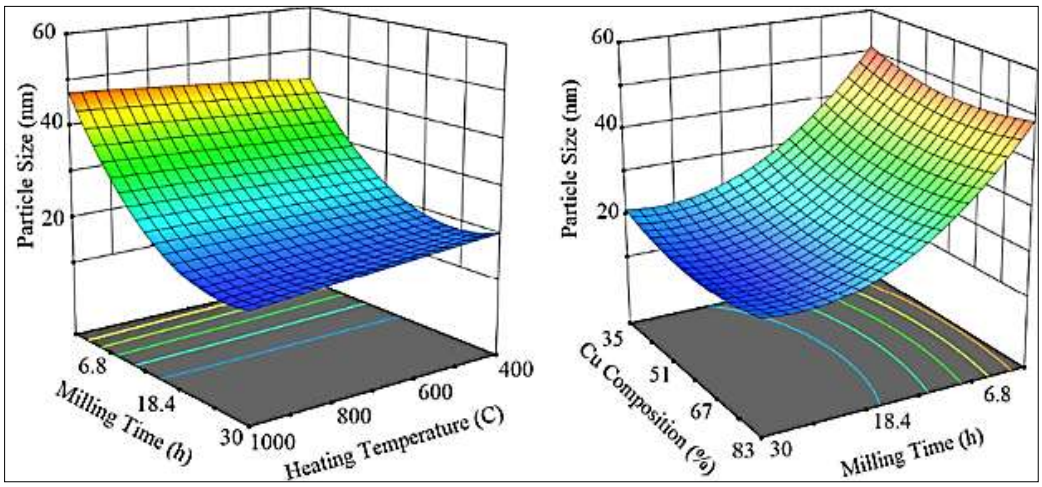

Fig 6: 3D Response surface graph for particle size

Table 4: Regression analysis for effect of X1(PLGA) & X2 (PEO)

Parameter	R Square	Adjusted R square	Observations	Source	Sum of squares	P-value
Average particle size (Y_1)	0.9955	0.9955	0.9955	Model	2003.21	<0.0001
				X1	731.51	<0.0001
				X2	1238.12	<0.0001
				X12	16.65	0.0089
				X 21	11.58	0.0202
				X 2	0.71	0.4825
Full model equation: $Y_1 = +97.87+11.04X_1+14.37X_2-2.04X_1X_2-2.05X^2-0.51X^2$						
Reduced model equation: Y1=+97.87+11.04X1+14.37X2-2.04X1X2-2.05X 212						
% drug entrapment efficiency (Y2)	0.9705	0.9705	0.9705	Model	416.88	<0.0001
				X1	79.13	0.0003
				X2	256.11	<0.0001
				X12	13.7	0.0281
				X 21	24.7	0.0077
				X 22	17.48	0.0171
Full model equation: Y2 = +78.59+3.63X1+6.53X2-1.85X1X2+2.99X 2+2.52X 212						
Reduced model equation: Y2= +78.59+3.63X1+6.53X2-1.85X1X2+2.99X 2+2.52X 212						
% buoyancy (Y3)	0.8817	0.8817	0.8817	Model	136.50	0.0038
				X1	24.12	0.0189
				X2	69.70	0.0013
				X12	9.025E-003	0.9548
				X 21	11.55	0.0738
				X 22	14.93	0.0483
Full model equation: Y3 = +82.25+2.00X1+3.41X2+0.048X1X2+2.04X 2+2.32X 212						
Reduced model equation: Y3=+82.25+2.00X1+3.41X2+2.32X 22						
%cumulative drug release at Q1 (*in-vitro* drug release at 1h) (Y4)	0.9086	0.9086	0.9086	Model	374.08	<0.0001
				X1	1.83	0.5020
				X2	372.25	<0.0001
Full model equation: $Y_4= +32.85-0.55X_1-7.88X_2$						
Reduced model equation: $Y_4= +32.85-7.88X_2$						
%cumulative drug release at Q6 (*in-vitro* drug release at 6h) (Y5)	0.9271	0.9271	0.9271	Model	1046.33	<0.0001
				X1	205.22	0.0005
				X2	841.11	<0.0001
Full model equation $Y_5= +70.21-5.85X_1-11.84X_2$						
Reduced model equation $Y_5= +70.21-5.85X_1-11.84X_2$						

The regression results were observed in table no 04 and 3D results were shown in figure no 06To prepare checkpoint batches based on the overlay plot, batches C1 and C2 were chosen by analysing the responses in the overlay plot. The selected amounts of PLGA and PEO were aligned with the predicted responses shown in the overlay plot or derived from the overlay data solutions. These two batches, C1 and C2, were then utilized to verify the accuracy and reliability of the predictive model their results were shown in table no 05and table no 06.

Table 5: Formulation of checkpoint batch

Ingredients	Batch C1	Batch C2
	Quantity taken (mg)	
Baclofen	100	100
PLGA	285.31	174.49
PEO	285.17	114.60
HPMC K4M	50	50
Mg-stearate	5	5
Acetone	10ml	10ml

HPMC K4m: Hydroxyl Propyl Methyl Cellulose

Table 6: Predicted response and actual response of checkpoint batch

Evaluation Parameters	Batch C1			Batch C2		
	Predicted value	Actual value	%Error	Predicted value	Actual value	% Error
Particle size(µm)	116.81	112.21	4.09	81.83	83.56	2.07
% Drug Entrapment	89.90	86.50	3.93	73.70	75.56	2.46
%Buoyancy	90.66	93.21	2.73	81.26	79.23	2.56
% CDR at Q1 (h)	25.67	26.96	4.78	39.72	41.26	3.73
% CDR at Q6(h)	55.13	53.12	3.78	81.81	84.5	3.18

CDR: Cumulative Drug Release

The actual responses for batches C1 and C2 were evaluated and compared to the predicted responses from the model. The observed deviations were found to be less than 5% for all parameters, confirming the validity of the model. Therefore, an optimized batch, is presented, can be reliably selected based on the overlay plot of this model observed in table no 07 abd dissolution profile was shown in table no 08 and table no 09.

Table 7: Optimized batch

Ingredients	Quantity(mg)
Baclofen	100
PLGA	297.56
PEO	278.78
HPMC K4M	50
Magnesium stearate	5
Acetone	10ml

HPMC K4M: Hydroxy Propyl Methyl Cellulose

Table 8: Dissolution profile of optimized batch

Time (hr)	% CDR
1	25.5
2	32.23
3	38.59
4	42.26
6	56.26
7	64.35
8	72.21
9	77.27
10	81.15
12	85.91
14	91.1
16	96.01
18	98.23
20	100.05
24	100.15

%CDR: Cumulative Drug Release

Evaluation of Optimized Batch

Table 9: Particle size, % drug entrapment and % buoyancy of optimized batch

Particle size	115.96 µm
% Drug entrapment	90.06%
% Buoyancy	90.76%

Kinetic Modelling and Mechanism of Drug Release for the Optimized Batch

The dissolution profile of the optimized batch was evaluated by fitting the release data to various kinetic models, including the Korsmeyer-Peppas equation, Zero-order, First-order, and Higuchi kinetics. This analysis was conducted to better understand the drug release mechanism and Behavior was shown in table no 10.

Table 10: Kinetic model for drug release of optimized batch

Batch	Zero-order	First-order	Higuchi	Korsmeyer-Peppa's model	
	R2	R2	R2	R2	N
Optimized batch	0.8783	0.7715	0.9793	0.9785	0.4857

The best fit model was selected on the basis of relatively high correlation coefficient values. Thus, it may be concluded that from the above data Higuchi model was followed by formulation. The drug release path was Fickian diffusion kinetic models were shown in figure no 07all the models were shown.

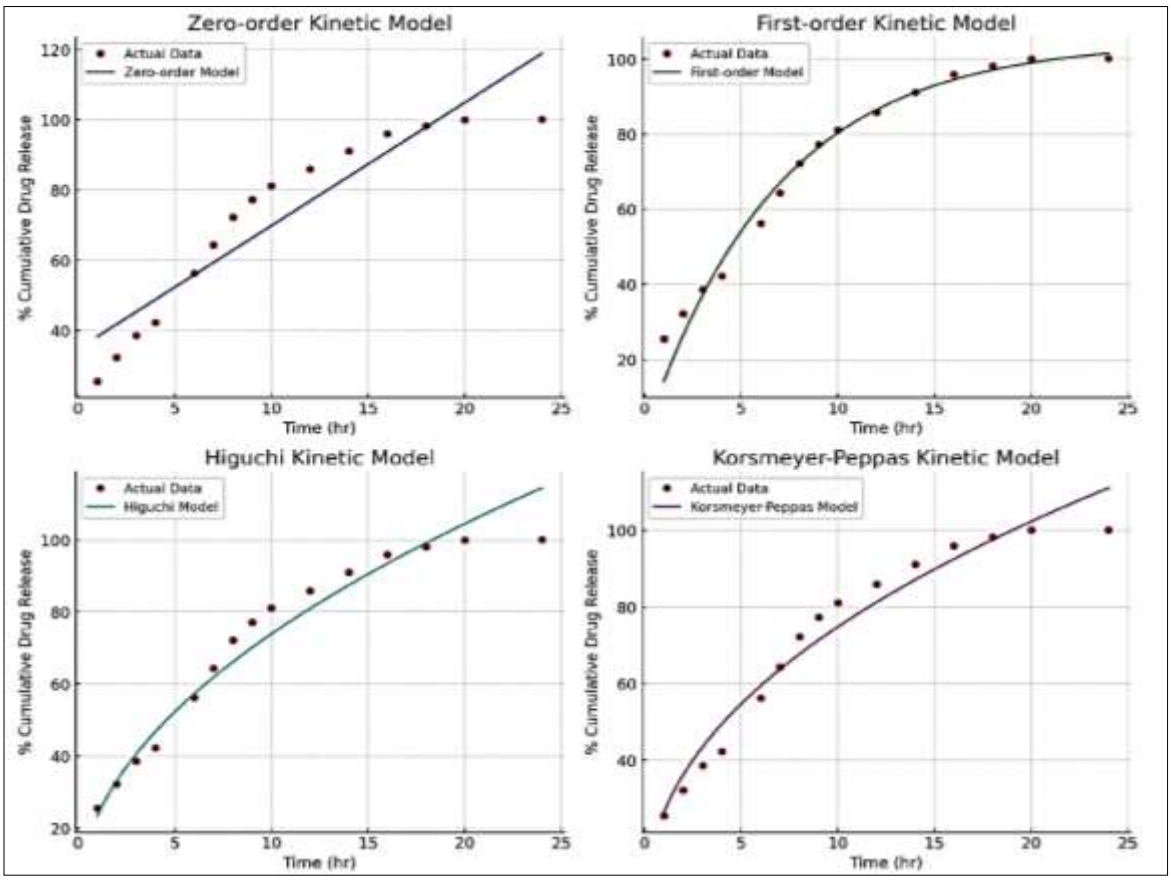

Fig 7: Zero Order, First Order, Higuchi, Korsmeyer-Peppas Models

Stability Study of Optimized Batch: A stability study was done to eth the effect of temperature and humidity (400 °C, 75% RH) on floating microspheres during the storage time. Floating microspheres were evaluated periodically (0 and1months) for particle size, % drug entrapment, % buoyancy, and *in vitro* drug release (% CDR) results for the evaluation of optimized batches were shown in Table no 11.

Table 11: Evaluation of optimized batch for stability

Parameter	Time	Initial	After Stability
Particle size	1 month	115.96 µm	114.56 µm
% Drug entrapment	1 month	90.06%	90.01%
% Buoyancy	1 month	90.76%	90.56%
%CDR at Q1	1 month	25.5%	26.01%
%CDR at Q6	1 month	56.26%	56.01%

Conclusion

In conclusion, this study emphasizes the significance of formulating and evaluating Baclofen-loaded floating microspheres. The microspheres were successfully prepared using the solvent evaporation method, demonstrating favorable characteristics such as appropriate particle size, high yield, excellent entrapment efficiency, buoyancy, and sustained *in-vitro* drug release. The Baclofen-loaded floating microspheres provided extended drug release for up to 24 hours, offering potential benefits such as reduced dosing frequency and minimized side effects associated with traditional Baclofen tablets. This sustained-release formulation is particularly advantageous for patients with spasticity. Additionally, no interactions between the drug and polymer were observed, and the formulations exhibited long-term stability.

Conflicts of Interest: Authors have no conflict of interest regarding this article.

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