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DEVELOPMENT AND CHARACTERIZATION OF THE BACLOFEN-LOADED MICROSPHERES

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ABSTRACT

The microsphere can act as a promising choice for conventional parenteral dosage forms. Microspheres are more stable, biocompatible, and easy to administer. This research article is aimed at the formulation and evaluation of the Baclofen microspheres. In this study, the solvent evaporation method was used to manufacture sustained release baclofen Microspheres. Baclofen Microspheres could be a potential drug delivery technique for oral baclofen administration with a 12-hour drug release, according to the findings. With a high percentage of drug entrapment and a high recovery yield, the formulation was determined to be successful. In FT-IR tests, no notable drug interactions were detected. Baclofen microspheres are a promising pharmaceutical dosage form because they allow long-acting medication administration while avoiding dose-related side effects. Out of all the formulations evaluated, microspheres containing F-5 had the maximum drug release at the 12th hour, with 89.83 0.21 percent. The F5 formulation's diffusion has non-fiction zero order kinetics and fits into the Korsmeyer-Peppas model. The baclofen microspheres (F5) formulation was finished successfully. There is less dose dumping because the medicine is released over a longer period, up to 12 hours.

KEYWORDS: In-situ, Sustained release, Microspheres.

INTRODUCTION

Over the last few decades, drug delivery strategies have progressed from tablets to polymers comprising new systems and bioengineered systems. Drug distribution systems focus on maximizing the active ingredient's benefits while reducing its side effects and other drawbacks.[1] Although the oral route is preferred by patients, it has drawbacks, such as medications with a high first-pass metabolism, resulting in reduced bioavailability, and protein-peptide therapies degrading in the stomach's hostile environment.[2] Apart from these drawbacks, the majority of oral drug delivery systems do not release the medicine for weeks or months. Parenteral continuous medication delivery systems are another option for overcoming these challenges.[3] Parenteral sustained drug delivery systems have gained popularity in recent decades due to several advantages over other systems, including reduced drug delivery frequency due to controlled drug release for several days to months, minimizing side effects by achieving an intravenous infusion type profile, and reducing peak valley plasma fluctuations, and achieving good patient compliance due to drug release for extended periods ranging from weeks to months.[4-6]

Baclofen, a centrally acting skeletal muscle relaxant, is used to treat spasticity caused by multiple sclerosis and spinal cord injury over the long term. Baclofen is absorbed and removed quickly and completely. In plasma, the medication has a half-life of 2.5 to 4 hours. Baclofen has a narrow absorption window in the upper gastrointestinal system, resulting in limited bioavailability.[7,8] Thus, an attempt was undertaken to build a baclofen microsphere system employing rosin polymer to optimise the drug's release profile for a longer period of time.

MATERIAL AND METHODS

Materials

Baclofen and Rosin Gift sample was obtained from Madras. Dichloromethane, Sodium chloride, Methanol, and Polyvinyl alcohol Nice Chemicals Private Limited, Chennai. UV-Visible double beam spectrophotometer (Shimadzu UV 1700, Japan.), Electronic Balance (Sartorius Single Pan), Programmable Dissolution test apparatus (Electro Lab), pH meter (Elico L 1120), Environmental stability testing chamber (Heco Environment Chamber).

Methods

Baclofen-loaded microspheres were formulated using the solvent evaporation method. Mathematical models were used to assess the effect of formulation variables on the

release rate, mean dissolution time, and release mechanism.

Formulation of Microspheres loaded with Baclofen

Baclofen microspheres were prepared using solvent evaporation with rosin as a polymer. Microspheres were made using the solvent evaporation method with 500 mg of baclofen and various proportions of polymer dissolved in 5ml of dichloromethane. This flowable mass was added to a 50ml aqueous saline phase (0.9 percent NaCl) containing 0.04 percent PVA (20 mg) and 10% methanol (5ml). For 2-3 hours, the system was agitated with a propeller at 300 rpm in the room.[9]

Table 1: Different formulations of baclofen-loaded microspheres.

Ingredients	Formulation Ratios					
	F1	F2	F3	F4	F5	F6
Baclofen	50mg	50mg	50mg	50mg	50mg	50mg
Rosin	150mg	200 mg	250 mg	300 mg	350 mg	400 mg
Dichloromethane	5ml	5ml	5ml	5ml	5ml	5ml
Sodium chloride	450mg	450mg	450mg	450mg	450mg	450mg
Poly vinyl alcohol	20mg	20mg	20mg	20mg	20mg	20mg
Methanol	5ml	5ml	5ml	5ml	5ml	5ml
Water	50ml	50ml	50ml	50ml	50ml	50ml

Evaluation of baclofen-loaded microspheres

Prepared baclofen-loaded microspheres are characterizedobyifferent parameters such as Particle size, surface morphology, entrapment efficiency, drug content, and an in-vitro drug release profile

Particle Size

The laser particle counting method was used foroptimized formulation.[10]

Scanning Electron Microscopy

Scanning Electron Microscopy was used to characterize the topography of microspheres. Using double-sided sticky tape, the microspheres were attached to brass stubs. SEM pictures were collected at room temperature with a scanning electron microscope (JSM-5610LV, Joel Ltd, Tokyo, Japan).[11,12]

% Yield of microspheres

The Microspheres that had been prepared were collected and weighed. The percent yield of Microspheres is calculated by dividing the actual weight of acquired Microspheres by the total amount of all non-volatile material used in their preparation multiplied by 100.[13,14] This was calculated by the use of the following formula.

[% yield= (Actual weight of the product / Total weight of excipients and drug) ×100]

Determination of drug content and entrapment Efficiency

Up to 24 hours were spent suspending 100 mg of precisely weighted microspheres in a phosphate buffer pH 7.2. The sample was shaken for many hours the following day using a mechanical shaker. It was then filtered, and a few ml of aliquot was obtained from the filtrate and used to make appropriate dilutions, which were then spectrophotometrically tested for drug content at 202.4 nm. Entrapment efficiency was calculated as a percentage.[15-17]

The drug entrapment efficiency was calculated using the formula:

[Percentage entrapment efficiency = Practical drug content / theoretical drug contents × 100]

Dissolution tests

The dissolution tests were performed at 50 pm and 370.5°C using a basket-type device. At 202.4 nm, the samples were examined (Shimadzu 1700).[18-21]

Stability Study

The leaking of the medication from the microspheres was studied in terms of percentage drug content during the stability investigations of formulations F1 to F2 at 45° C 2°C 75 percent 5 percent RH.[22]

RESULTS

Particle size

Particle size analysis was performed for all formulations F1 to F5 microspheres, with a mean particle size range of 40m to 50m. Baclofen microspheres with rosin were smooth, round, and did not agglomerate.

Table 2: Particle size and Zeta potential of formulations.

S. No	Formulation code	Size (nm)	Zeta Potential	PDA
1	F1	67.36	-08.1	0.57
2	F2	61.42	-08.6	0.61
3	F3	59.56	-08.9	0.59
4	F4	76.26	-10.5	0.51
5	F5	71.36	-09.8	0.53
6	F6	69.11	-10.4	0.49

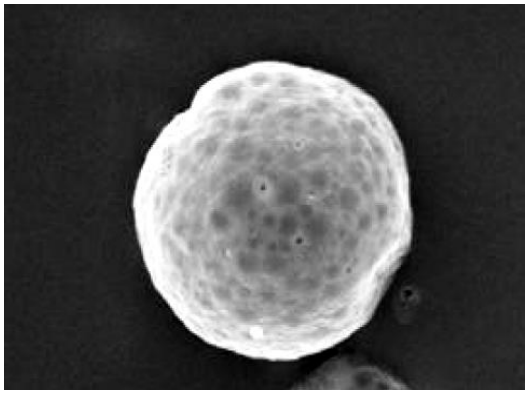

Figure 1: SEM Photomicrograph of Baclofen Microspheres F5.

Drug Content

The maximum drug content readings for the F5 are 92.63 percent. Table no-3 shows the percentage entrapment efficiency, with the F5 at 89.94 percent.

Table 2: % Drug content of baclofen-loadedmicrospheres.

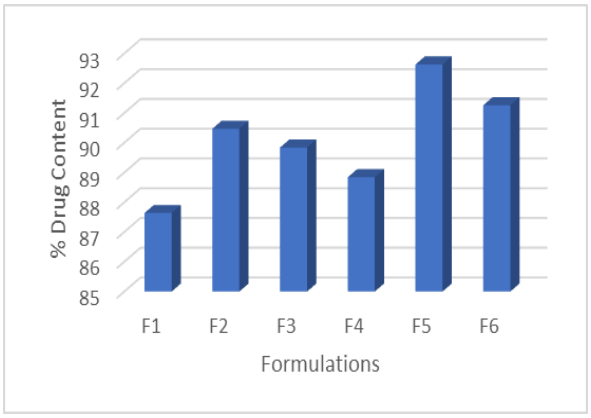

Figure 2 : % Drug content of formulations.

Entrapment efficiency of baclofen microspheres

The Entrapment efficiency of the formulation shown in tab the been 91.21%. The formulation F6 showedbetter encapsulation and drug loading efficacy than all formulations according to the results.

Table: % Entrapment efficiency of baclofen-loadedmicrospheres.

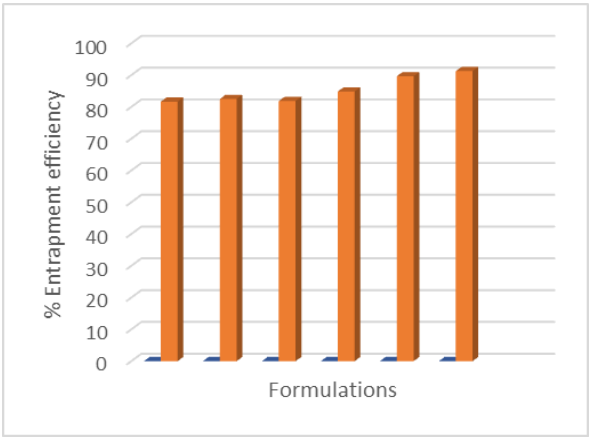

Figure 3: % Entrapment efficiency of baclofen microspheres.

5.4- Invitro drug release

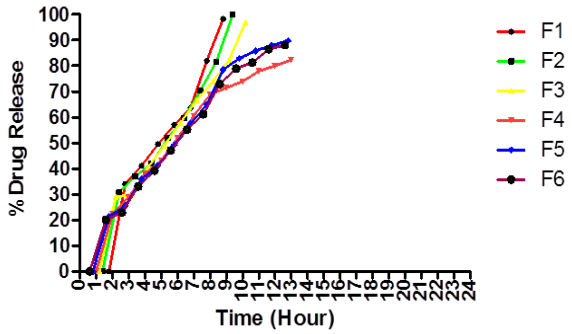

Figure 4: Cumulative In vitro drug release of Microsphere Formulations.

Stability Study

The results demonstrated that the F5 formulation remained stable over three months with no significant changes in drug content.

Table 3: Stability Study for F5 formulation

S. No	Formulations	Before storage	Stored at 40°Cand 75% ±5%RH		
			1st month	2nd month	3rd month
1	F5	92.63±0.74	91.63±0.74	90.63 ±0.74	89.63±0.74

DISCUSSION

Baclofen, because of its short half-life, As a model for a prolonged release formulation with higher oral bioavailability, a low single-dose medicine with 65% oral bioavailability was used. The drug baclofen was tracked down using a UV light source.

To improve absorption and bioavailability, microspheres were successfully manufactured for the administration of baclofen. Six formulations were created in response to this strategy. The polymer content was changed in each composition. Rosin is a naturally occurring polymer. The addition of Due to dichloromethane's high density, the dispersed phase settled in the aqueous phase, making dispersion and stabilisation of the droplets problematic. All formulas F1 through F5 have % yields.

Particle size analysis was performed on all formulations F1 to F6 microspheres with a mean particle size range of

40m to 50m. Baclofen microspheres with rosin were smooth, round, and did not agglomerate (F5).

The maximum drug content readings for the F5 are 92.63 percent. Because the viscosity of the solution increased as the polymer content was raised, A greater percentage of the substance was successfully trapped. Drug entrapment efficiency is greater in solvent-soluble medicines than it is in solvent-dispersed pharmaceuticals, according to the results of the present investigation. Microsphere entrapment efficiency improved as the concentration of polymer utilised in the microspheres increased, resulting in a rise in the quantity of polymer required in the manufacturing process.

A USP dissolving apparatus Type I was used to conduct dissolution investigations on all six formulations of baclofen microspheres. In vitro drug release findings are shown Figure 4 for all formulations. The cumulative percent drug release for F5 was determined to be 89.83 percent after 12 hours. The cumulative drug release decreased considerably as the polymer content rose. The density of the polymer matrix rises with higher concentrations, resulting in a longer diffusional route. As a consequence, the total release of drugs from the polymer matrix may be lowered. More surface area of the dissolving solution is exposed to the smaller microspheres that are produced at lower polymer concentrations.

CONCLUSION

The solvent evaporation approach was effectively used to make sustained release baclofen Microspheres in this work. It is possible to conclude that baclofen Microspheres could be a promising drug delivery technology for oral baclofen administration with a 12-hour drug release. The formulation was found to be effective, with a high percentage of drug entrapment and a high recovery yield. Baclofen microspheres are potential pharmaceutical dosage forms because they provide sustained release drug delivery systems while avoiding dose-related adverse effects throughout the body. Microspheres containing F-5 were shown to have the highest drug release of 89.83 ± 0.21% at the 12th hour, out of all the formulations tested.The diffusion of the F5 formulation follows non-fiction zero order kinetics and fits within the Korsmeyer-Peppas model.

The formulation of baclofen microspheres (F5) was completed successfully. The medicine is released over a longer period, up to 12 hours, with less dose dumping.

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