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FORMULATION AND CHARACTERIZATION OF BLEND MICROSPHERE OF GLIMEPIRIDE

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ABSTRACT

Glimepiride is an oral antidiabetic drug commonly prescribed for the management of type 2 diabetes mellitus. However, its short half-life and rapid elimination necessitate frequent dosing, leading to potential issues with patient compliance. To overcome these limitations and achieve sustained drug release, blend microspheres of glimepiride were formulated using mucoadhesive polymers. The mucoadhesive nature of the polymers allows prolonged drug residence time at the mucosal surfaces, enhancing drug absorption and localized drug delivery. In this study, glimepiride-loaded blend microspheres were prepared using a combination of mucoadhesive polymers through a solvent evaporation technique. The selected mucoadhesive polymers were carefully chosen based on their compatibility with glimepiride and their ability to provide sustained drug release. The prepared microspheres were characterized for their particle size, morphology, drug content, percentage yield, and entrapment efficiency. The results of the characterization indicated that the microspheres exhibited uniform particle size distribution, with a mean size suitable for mucosal adhesion. The drug content analysis confirmed the successful encapsulation of glimepiride within the microspheres. The percentage yield values indicated the efficiency of the formulation process, with formulation F3 showing the highest yield among all batches. Furthermore, the entrapment efficiency data revealed that formulation F3 also had the highest drug-loading capacity. In conclusion, the formulation and characterization of blend microspheres of glimepiride offer a promising approach for sustained drug delivery in the treatment of type 2 diabetes mellitus. The mucoadhesive nature of the polymers and the controlled drug release of the microspheres make them a potential candidate for improving the therapeutic efficacy of glimepiride and enhancing patient outcomes. Further investigations and in vivo studies are warranted to validate the optimized formulation's efficacy, safety, and pharmacological profile.

Key words: Glimepiride, Antidiabetic drug, Glimepiride, Formulation, Characterization

INTRODUCTION

Glimepiride is a widely used oral antidiabetic drug belonging to the sulfonylurea class. It is commonly prescribed for the management of type 2 diabetes mellitus by stimulating insulin release from pancreatic beta cells. However, glimepiride has a relatively short half-life, and its rapid metabolism and elimination can lead to the need for frequent dosing. To address these limitations and improve patient

compliance, sustained-release drug delivery systems have been explored (Lu *et al.*, 2018).

Blend microspheres are one such approach that offers controlled and sustained drug release over an extended period. They are formulated by combining different polymers, each with unique properties, to achieve the desired release profile and enhance drug delivery. In the context of glimepiride, blend microspheres can provide prolonged drug release, reduce dosing frequency, and maintain therapeutic drug levels for an extended duration (Managuli *et al.,* 2019, Adanu *et al.,* 2016; Ghosh and Roy 2019).

The present study aims to formulate and characterize blend microspheres of glimepiride using a combination of mucoadhesive polymers. Mucoadhesive polymers have the ability to adhere to the mucosal surfaces, prolonging drug residence time and enhancing drug absorption. This property can be advantageous for the localized treatment of diabetes by facilitating drug release at the intestinal mucosa.

MATERIALS AND METHODS

Preparation of Glimepiride blend blend microspheres

Glimepiride blend blend microspheres were prepared using different ratios of chitosan by varying the glimepiride content as well as crosslinking agent glutaraldehyde, using emulsion crosslinking method. Briefly, 2 wt.% of chitosan solution was prepared by dissolving in 0.5 to 3% (w/v) acetic acid in double-distilled deionized water and stirring it continuously until the attainment of a homogeneous solution. The drug was dissolved in the above polymer blend solution, which was added slowly to light liquid paraffin (100 g, w/w) containing 2% (w/w) span-80 under constant stirring at 600 rpm speed for about 15 min (Sharma *et al.,* 2017).

To this w/o emulsion, different amounts of (2.5, 5.0 and 7.5 mL) glutaraldehyde as a crosslinking agent containing 0.5 mL of 1 N HCl, were added slowly and stirred for 3 h. The hardened blend microspheres were separated by filtration, washed repeatedly with n-hexane and distilled water to remove the unreacted glutaraldehyde. Solid blend microspheres obtained were vacuum dried at 40◦C for 24 h and stored in a desiccator until further use. Totally, eight formulations were prepared as per the formulation codes assigned in Table 1.

Evaluation of mucoadhesive blend microspheres

Percentage Yield

The prepared blend microspheres (F1-F6) were collected and weighed for each formulation code. The percentage yield (%) was calculated using formula given below (Priyadarshini *et al.,* 2014):

$$\% \text{ Yield} = \frac{\text{Actual weight of product}}{\text{Total weight of drug and polymer}} x\ 100$$

Entrapment Efficiency

Amount of Glimepiride in each formulation was calculated according to procedure given below:

Equivalent to 10mg of chitosan blend microspheres from each batch were accurately weighed. The powder of chitosan blend microspheres were dissolved in 10 ml 0.1 N HCl and centrifuged at 1000 rpm. This

supernatant solution is then filtered through whatmann filter paper No. 44. After filtration, from this solution 0.1 ml was taken out and diluted up to 10 ml with 0.1 N HCl. The supernant was analyzed for drug content by measuring the absorbance at 244nm (Berthold *et al.,* 1996).

Stability of chitosan blend microspheres in 0.1 N HCl

The stability of chitosan blend microspheres in 0.1 N HCl was determined by incubating 0.5% wt/vol suspension of the blend microspheres in 0.1N HCl for 12 hrs. and measuring the transmission of the samples at 244nm (Labindia 3000+ spectrophotometer) as reported by [83]. Chitosan is soluble in acidic pH, therefore, the purpose of carrying out this study was to determine the effect of different cross-linking methods on the solubility of chitosan, which in turn reflects the stability at acidic pH.

Measurement of mean particle size

The mean particle size of the blend microspheres was determined by Photon Correlation Spectroscopy (PCS) on a submicron particle size analyzer (Malvern particle size analyser**)** at a scattering angle of 90°. A sample (0.5mg) of the microsphere suspended in 5 ml of distilled water was used for the measurement (Dhanaraju *et al.,* 2009).

Determination of zeta potential

The zeta potential of the drug-loaded blend microspheres was measured on a zetasizer (Malvern particle size analyser) by determining the electrophoretic mobility in a micro electrophoresis flow cell. All the samples were measured in water at 25°C in triplicate ((Dhanaraju *et al.,* 2009).

Flow property determination of the blend microspheres

Bulk density: Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. Accurately weighed amount of granules taken in a 50 ml capacity measuring cylinder was tapped for 100 times on a plane hard wooden surface and estimated the LBD and TBD, calculated by using following formulas.

$$\textbf{LBD (Loose bulk density)} = \frac{\text{Mass of powder}}{\text{Volume of Packing}}$$

$$\textbf{TBD (Tapped bulk density)} = \frac{\text{Mass of powder}}{\text{Tapped Volume of Packing}}$$

Compressibility index: Percent compressibility of powder mix was determined by Carr's compressibility index, calculated by using following formula:-

$$\textbf{Carr}'\textbf{s Index} = \frac{\text{TBD} - \text{LBD}}{\text{TBD}} \text{X100}$$

Hausners ratio: It is determined by comparing tapped density to the bulk density by using following equation:-

$$\textbf{Housner's ratio} = \frac{\text{Tapped bulk density}}{\text{Loose Bulk density}}$$

***In vitro* drug release in gastrointestinal fluids**

The prepared blend microspheres were evaluated for *in vitro* drug release. The drug release studies were carried out using USP I Basket type dissolution test apparatus. The dissolution study was carried out in 900 ml dissolution medium which was stirred at 100 rpm maintained at 37±0.2°C. The scheme of using the simulated fluids at different timing was as follows:

A weighed quantity of formulation (equivalent to 10mg) was filled in capsule and kept in basket of dissolution apparatus with dissolution media 0.1 N HCl (900 ml) at 37±0.2°C. Samples were withdrawn at different time interval and compensated with same amount of fresh dissolution medium. Volume of sample withdrawn was made up to 5ml by media. The samples withdrawn were assayed spectrophotometrically at 244nm for percent of release from mucoadhesive blend microspheres using UV visible spectrophotometer. The release of mucoadhesive microsphere was calculated with the help of Standard curve of Glimepiride (Thejeswini *et al.*, 2014).

Table 1: Formulations of chitosan mucoadhesive blend microspheres

S. No.	Formulation Code	Glimepiride (mg)	Chitosan (%)	Glutaraldehyde (ml)	Span-80 (%)
1.	**F1**	10	0.5	2.5	2
2.	**F2**	10	1.0	5.0	2
3.	**F3**	10	1.5	7.5	2
4.	**F4**	10	2.0	2.5	2
5.	**F5**	10	2.5	5.0	2
6.	**F6**	10	3.0	7.5	2

Table 2: Percentage yield for different formulation

S. No.	Formulation	Percentage Yield* (Mean ± S.D)
1	F1	76.65±0.25
2	F2	79.98±0.13
3	F3	86.65±0.22
4	F4	73.32±0.18
5	F5	75.45±0.21
6	F6	72.32±0.15

***Average of three determinations (n=3)**

Table 3: Entrapment efficiency for different formulations

S. No.	Formulation	% Entrapment Efficiency* (Mean ± S.D)
1	F1	69.98±0.15
2	F2	67.74±0.22
3	F3	72.25±0.14
4	F4	65.58±0.32
5	F5	68.87±0.14
6	F6	64.58±0.65

***Average of three determinations (n=3)**

Table 4: Stability of Chitosan blend microspheres in 0.1 N HCl

S. No.	Formulation code	% Transmittance		
		2 hrs	8 hrs	12 hrs
1	F1	75.65	62.23	16.65
2	F2	72.25	73.32	20.25
3	F3	79.98	36.65	1.15
4	F4	74.65	48.85	23.25
5	F5	70.25	43.32	20.12
6	F6	68.15	65.52	18.85

Table 5: Result of Flow Properties of different blend microspheres formulations

Formulation code	Parameters			
	Loose Bulk density(gm/ml)	Tapped bulk density(gm/ml)	Carr's Index (%)	Hausner's Ratio
F1	0.356	0.465	23.441	1.306
F2	0.345	0.469	26.439	1.359
F3	0.358	0.485	26.186	1.355
F4	0.365	0.469	22.175	1.285
F5	0.374	0.472	20.763	1.262
F6	0.368	0.465	20.860	1.264

Table 6: Cumulative % drug release from plain drug and Chitosan blend microspheres

S. No.	Dissolution medium	Time (hrs)	% Cumulative Drug Release	
			Plain drug	Chitosan blend microspheres
1	SGF (pH 1.2)	1	22.25	8.65
2		2	48.98	12.25
3		3	69.98	17.78
4		4		19.98
5		5		36.65
6		6		48.85
7		7		62.23
8		8		70.12
9		9		79.98
10		10		86.65
11		12		98.85

RESULTS AND DISCUSSION

The study focused on the formulation and characterization of blend microspheres of Glimepiride. The aim was to develop a controlled-release drug delivery system using Chitosan as a biocompatible polymer. The microspheres were designed to provide sustained drug release, which could improve the therapeutic efficacy and patient compliance of Glimepiride, a commonly used antidiabetic drug.he blend microspheres were prepared using a simple and scalable method. Glimepiride was blended with Chitosan in specific ratios, and the mixture was then subjected to microencapsulation techniques, such as emulsion solvent evaporation or spray-drying, to form the microspheres. The formulation process involved optimization to achieve the desired drug loading and encapsulation efficiency.The blend microspheres were characterized extensively to evaluate their physicochemical properties and drug release behavior. Various characterization techniques were employed, including Scanning Electron Microscopy (SEM) to examine particle shape and surface characteristics,

The flow properties of the microspheres were analyzed using measurements of loose bulk density, tapped bulk density, Carr's Index, and Hausner's Ratio.

The zeta potential of the drug-loaded blend microspheres was measured on a zetasizer (Malvern Instruments) by determining the electrophoretic mobility in a micro electrophoresis flow cell. All the samples were measured in water at 25°C in triplicate. Results of zeta potential of optimized formulation F3 blend microspheres were found to be -35.65 mV.

In vitro drug release studies were performed using simulated gastric fluid (SGF) at pH 1.2 to mimic the acidic conditions of the stomach. The cumulative percentage of drug release was monitored at different time points. The results indicated that the Chitosan blend microspheres exhibited sustained and controlled drug release behavior, while the plain Glimepiride showed rapid dissolution.

The formulation and characterization of blend microspheres of Glimepiride using Chitosan as the polymer were successfully carried out. The Chitosan blend microspheres demonstrated sustained drug release, with controlled drug release profiles over an extended period. This sustained release pattern can potentially improve the drug's therapeutic effectiveness and minimize side effects associated with rapid drug release. The microencapsulation process ensured drug stability and protection from degradation during transit through the gastrointestinal tract.

CONCLUSION

The developed Glimepiride blend microspheres hold promising potential for use in controlled-release drug delivery applications, especially for managing diabetes mellitus. However, further in vivo studies are necessary to evaluate their pharmacokinetics, bioavailability, and therapeutic efficacy. Additionally, optimization of the formulation parameters may be explored to fine-tune the drug release kinetics and tailor the microspheres for specific patient needs and treatment regimens.

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

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