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Glipizide Microspheres: In-Vitro Characterization

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A B S T R A C T

The main aim of present investigation is to determine best grade of HPMC among HPMC K4M, HPMC K15M and HPMC K100M for preparing floating microspheres. The drug excipient compatibility was checked by DSC and FTIR studies. Physicochemical evaluation was performed for prepared floating microspheres was performed. Glipizide was found to be compatible with excipients used. The prepared microspheres showed good buoyancy, physicochemical characteristics and release characteristics. Among the prepared microspheres HPMC K4M was found to be better polymer for preparing Glipizide floating microspheres.

Keywords: Glipizide, microspheres, diabetes, polymer.

A R T I C L E I N F O

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1. Introduction

Diabetes patients and complication are increasing day by day. Glipizide is used to control hyperglycemia in type II diabetes. The gastro retentive drug delivery system of Glipizide can be prepared to improve the bioavailability and extend the release of Glipizide by retaining the system in the stomach for prolonged period of time[1]. The floating microspheres beneficially alter the absorption of a drug, thus enhancing its bioavailability. They prolong dosing intervals which would allow development of once a day formulations and thereby increase patient compliance beyond the level of existing dosage forms by achieving control over gastric residence time[2-4]. Floating microspheres are gastro retentive drug delivery systems based on a non-effervescent approach. As the system floats over gastric

contents, the drug is released slowly at the desired rate, resulting in increased gastric retention with reduced fluctuations in plasma drug concentration. The objective of the present work was to develop and characterize floating microspheres of Glipizide, which after oral administration could prolong the gastric residence time and increase the drug bioavailability.

2. Materials and Methods

Glipizide is used to control hyperglycemia in type-II diabetes was procured from Hetero Drugs Ltd, Hyderabad, Ethyl cellulose, Dichloromethane and Tween -80 were procured from SD Fine Chemicals, Mumbai. HPMC K 4 M, HPMC K 15 M and HPMC K 100 were purchased from Qualigens Fine Chemicals, Mumbai.

Drug-Excipient compatibility studies

The compatibilityof Glipizide with different polymers was tested using FTIR spectroscopy and differential scanning calorimeter (DSC) studies.

FTIR Spectroscopy

FTIR spectrums of Glipizidewith excipients used were obtained individually and in combinationson a FTIR spectrophotometer, (Perkin Elmer, spectrum-100, Japan using the KBr disk method (2 mg sample in 200.05 mg KBr). The spectrums were obtained by scanning at 400 to 4000 cm-1 with a resolution of 1 cm-1. This spectral analysis was employed to check the compatibility of drugs with the excipients used.

Differential scanning calorimetry (DSC)

Differential Scanning Calorimetry (DSC) of Glipizide and excipients used were studied to investigate any changes in melting points of the drug after combining it with the excipients. DSC curves were obtained by a differential scanning calorimeter (Schimadzu DSC-50, Tokyo, Japan) at a heating rate of 10°C/min from 30°-300°C in nitrogen atmosphere (20 ml/min) with a sample weight of 5.03mg.

Preparation of floating microspheres of Glipizide

Floating microspheres loaded with Glipizide were prepared using solvent diffusion-evaporation method using HPMC K4M (F1, F2 and F3), HPMC K 15M (F4, F5 and F6) and HPMC K100M (F7, F8 and F9). Ethyl Cellulose was added in all the formulations. Dichloromethane was used as a solvent to dissolve all the ingredients. This clear solution was poured slowly drop wise into the aqueous solution of 0.06% Tween 80. The emulsion was continuously stirred for 3 h at a speed of 500 rpm at 27±2°C. The floating microspheres were collected by decantation, while the non-floating microspheres were discarded [5-7]. The microspheres were dried overnight at 40±2°C and stored in desiccator. The formulae of various microspheres were shown in table 1.

Evaluation

Size and shape of microspheres

The size of microspheres was determined using microscope (Olympus NWF 10x, Educational Scientific Stores, India) fitted with an ocular micrometer and stage micrometer.

Production yield (%)

The production yield of various formulations of microspheres were calculated by using the following formula [8].

Percent yield (%) = Practical mass of microspheres/ theoretical mass of drug and excipientsX100

Angle of repose (Θ)

Angle of repose was determined by using funnel method. Powder was poured from a funnel that can be raised vertically until a maximum cone is formed then height and radius of heap were measured. The angle of repose, Θ, was calculated by the following equation[9].

$$\Theta = \tan^{-1} (h / r)$$

Where, Θ is the angle of repose, h is the height in cm and r is the radius.

Bulk Density (D_b)

Bulk density was determined by pouring pre sieved drug excipient granules into a graduated cylinder and measuring the volume and weight. It is expressed in g/ml and is given by the following equation[9].

$$D_b = M / V_0$$

Where, M is the mass of powder and V_0 is the Bulk volume of the powder

Tapped Density (D_t)

It was determined by placing a graduated cylinder, containing a known mass of granules on mechanical tapping apparatus. The tapped volume was measured by tapping the powder to constant volume. It is expressed in g/ml and is given by the following equation[9].

$$D_t = M / V_t$$

Where, M is the mass of powder and V_t is the tapped volume of the powder.

Carr's Index (I)

It is expressed in percentage and is expressed by the following equation[9].

$$I = D_t - D_b / D_t$$

Where, D_t is the tapped density of the powder and D_b is the bulk density of the powder.

Hausner ratio

It is expressed in percentage and is expressed by the following equation[9].

$$H= D_t / D_b$$

Where, D_t is the tapped density of the powder and D_b is the bulk density of the powder.

***In vitro* buoyancy**

Microspheres (100mg) were spread over the surface of a USP XXIV dissolution apparatus type II filled with 900 ml of 0.1 N HClcontaining 0.02% tween 80. The medium was agitated with a paddle rotating at 100 rpm for 10 h. The floating and the settled portions of microspheres were recovered separately. The microspheres were dried and weighed. Buoyancy percentage was calculated using following formula[10].

$$\text{Buoyancy \%} = [W f/ (W f+ W s)] \times 100$$

Where, W f and W s are the weight of the floating and settled microspheres respectively.

Incorporation efficiency (IE)

The prepared floating microspheres (100 mg) were crushed and dissolved in a minimal amount of dichloromethane. The extract was transferred to a 100 ml volumetric flask and the volume was made up using 0.1N HCl solution by evaporating dichloromethane. The solution was filtered through 0.45 m membrane, diluted suitably and analyzed for drug content spectrophotometrically at 223 nm using 0.1

N HClas blank. The incorporation efficacy was determined by following formula[11]. Percentage Drug entrapment = (Actual drug content/Theoretical drug content) X100.

***In vitro* drug release studies**

The drug release was studied using a USP 24 dissolution apparatus type II (Model Electro lab, TDT- 06T, Mumbai, India) at 100 rpm in 0.1N HCl as dissolution medium (900 ml) maintained at 37±0.5°C and 100 rpm speed[12]. Samples were taken at regular intervals and analyzed at 223 nm by using UV–visible spectrophotometer (Systronics Corporation, Mumbai, India). Cumulative percentage drug release was calculated using an equation obtained from a standard curve.

3. Results and Discussions

The characteristic peaks in the FTIR of Glipizide and the prepared microspheres indicates that there was no chemical incompatibility between the Glipizide and HPMC (Fig. 1 and 2).DSC curves obtained for pure Glipizide alone and in combination with HPMC were shown in Fig. 3. The prepared microspheres were found to have excellent flow properties. The prepared microspheres were in uniform size and it ranged from 221±1.24 to 325±2.25 µm. The prepared microspheres were found to have good flow properties (Table2). The percent yield for prepared microspheres was ranged from 55.32±0.26 to 89.62±0.25%. The microspheres prepared with HPMC K4M (F2) shown good buoyancy (94.29±0.31%) compared with other formulations. The incorporation efficiency was in the range of 69.26±0.05 to 91.23±0.23%. *In vitro* drug release studies reveals that the drug released from the F2 followed zero order release kinetics.

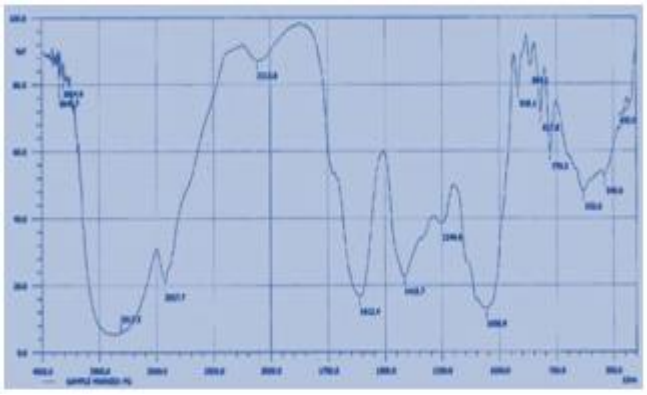

Figure 1: FTIR spectrum of pure Glipizide pure drug

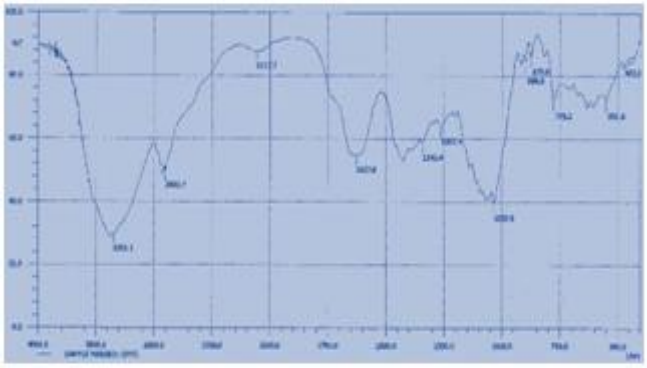

Figure 2: FTIR spectrum of Glipizide with excipient

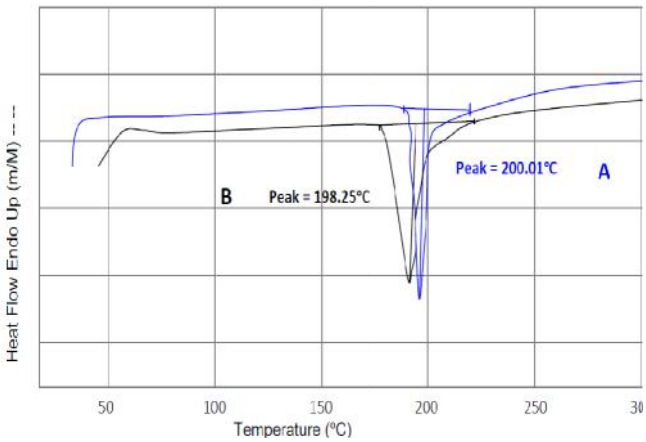

Figure 3: DSC spectrum of A) pure Glipizide B) Formulation blend

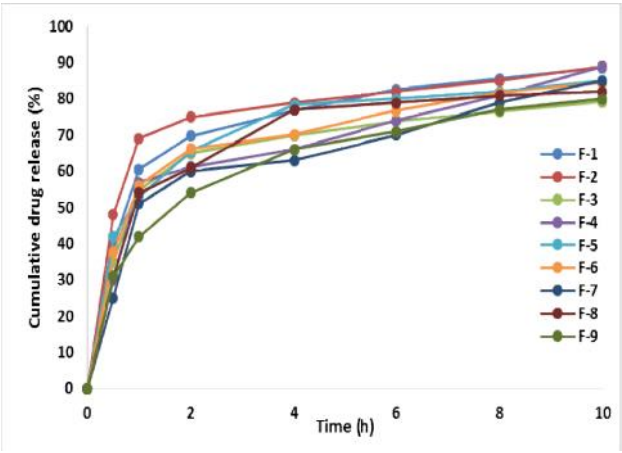

Figure 4: *In-vitro* drug release profile of formulated microspheres

Table 1: Formulations of various floating microspheres

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Glipizide	40	40	40	40	40	40	40	40	40
Ethyl Cellulose	1	1.5	2	1	1.5	2	1	1.5	2
HPMC K4M	0.5	0.5	0.5	-	-	-	-	-	-
HPMC K15M	-	-	-	0.5	0.5	0.5	-	-	-
HPMC K100 M	-	-	-	-	-	-	0.5	0.5	0.5
Dichloromethane	10	10	10	10	10	10	10	10	10
Tween 80	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06

Table 2: Flow properties of prepared microspheres

Formulations	Angle of Repose (¯)	Loose Bulk Density (g/cm^3)	Tapped Bulk Density (g/cm^3)	% Compressibility Index	Hasusner ratio
F1	28.14±0.23	0.56±0.01	0.66±0.01	15.15±0.05	1.17±0.09
F2	27.19±0.52	0.57±0.01	0.69±0.01	17.39±0.04	1.21±0.05
F3	24.12±0.91	0.57±0.01	0.67±0.01	14.92±0.03	1.17±0.05
F4	25.11±0.51	0.56±0.01	0.66±0.02	15.15±0.01	1.17±0.01
F5	27.16±0.12	0.62±0.02	0.75±0.01	17.33±0.02	1.20±0.09
F6	26.08±0.93	0.59±0.03	0.72±0.01	18.05±0.06	1.22±0.03
F7	28.07±0.62	0.56±0.01	0.67±0.02	16.41±0.07	1.19±0.09
F8	28.51±0.06	0.56±0.02	0.65±0.01	13.84±0.08	1.16±0.04
F9	26.41±0.02	0.56±0.02	0.63±0.01	11.11±0.02	1.12±0.01
All values mentioned as mean ± S.D; Number of trials (n) = 3					

Table 3: Particle size, percent yield, entrapment efficacy and Buoyancy of prepared floating microspheres

Formulations	Particle size (µm)	% yield	Entrapment efficacy (%)	Buoyancy (%)
F1	269±0.02	66.36±0.29	85.26±0.26	85.91±0.21
F2	274±0.25	89.62±0.25	91.23±0.23	94.29±0.31
F3	325±2.25	63.25±0.35	74.52±0.21	88.95±0.63
F4	315±1.36	65.35±0.25	69.29±0.20	76.95±0.21
F5	326±3.25	55.32±0.26	71.21±0.32	81.86±0.33
F6	324±0.25	66.91±0.24	73.94±0.21	74.51±0.31
F7	231±6.28	61.94±0.49	69.26±0.05	79.94±0.23
F8	221±1.24	58.24±0.79	75.25±0.25	81.52±0.23
F9	269±1.29	74.22±0.98	71.94±0.36	45.15±0.21
All values mentioned as mean ± S.D; Number of trials (n) = 3				

4. Conclusion

This study revealed that the microspheres prepared with HPMC K4M were found to have good buoyancy and release rate properties compared with microspheres prepared with HPMC K15M and HPMC K100M.

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