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Original Article

Characterization of Glibenclamide loaded cellulose acetate microparticles prepared by an emulsion solvent evaporation method

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ARTICLE INFO

Article history:
Received 23 July 2013
Accepted 15 August 2013
Available online 6 September 2013

Keywords:
Glibenclamide
Cellulose acetate
Microparticles
Solvent evaporation
Controlled/sustained release

ABSTRACT:

Aim: The objective of the present investigation was to formulate and evaluate micro-encapsulated Glibenclamide produced by the emulsion–solvent evaporation method.

Methods: Microparticles were prepared using cellulose acetate by emulsion solvent evaporation method and characterized for their micromeritic properties, encapsulation efficiency, particle size, drug loading, FTIR, DSC, SEM analysis. In vitro release studies were performed in phosphate buffer (pH 7.4). Stability studies were conducted as per ICH guidelines.

Results: The resulting microparticles obtained by solvent evaporation method were free flowing in nature. The mean particle size of microparticles ranges from 132.54 to 178.44 μm and encapsulation efficiency ranges from 89.96 to 98.48%. The infrared spectra and differential scanning calorimetry thermographs confirmed the stable character of Glibenclamide in the drug-loaded microparticles. Scanning electron microscopy revealed that the microparticles were spherical in nature. In vitro release studies revealed that the drug release was sustained up to 12 h. The release kinetics of Glibenclamide from optimized formulation followed zero-order and peppas mechanism. The mechanism of drug release from the microparticles was found to be non-Fickian type.

Conclusion: Cellulose Acetate microparticles containing Glibenclamide could be prepared successfully by using an emulsion solvent evaporation technique, which will not only sustain the release of drug but also manage complicacy of the diabetes in a better manner.

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0974-6943/$ – see front matter
http://dx.doi.org/10.1016/j.jopr.2013.08.015

1. Introduction[1–4]

Glibenclamide is an oral Antidiabetic agent which is widely used in the management of non-insulin dependent diabetes mellitus (type II). Glibenclamide is a second generation sulphonyl urea which is more potent than the first generation drugs in this class. Glibenclamide posses marked insulinaemic action and may work when other diabetic agents fails. It does not cross placenta and have been safely used in pregnancy i.e. gestational diabetes mellitus (GDM) without any adverse effect to the foetus. Its biological half life is 4–6 h. Due to its low biological half life (5 h), it requires frequent administration. In order to reduce the dosing frequency and to improve patient compliance, controlled/sustained release dosage forms are required. In the present investigation, an attempt has been made to formulate controlled/sustained release Glibenclamide microparticles by using Cellulose Acetate as rate retardant polymer.

2. Materials and methods

2.1. Materials

Glibenclamide was obtained as gift sample from Medley Pharmaceuticals Ltd., Daman Unit, Andheri East, Mumbai, India. Cellulose Acetate (Natco Pharma; Hyderabad, India), Acetone, liquid paraffin, tween 80, span 80 (Loba chemie Pvt. Ltd. Mumbai, India) and the chemical reagents used were of analytical grade.

2.2. Preparation of microparticles

The microparticles were prepared by emulsion solvent evaporation technique.[5] Glibenclamide microparticles were formulated by varying the drug and polymer ratios and by varying the surfactants. Weighed amount of drug and polymer were dissolved in 10 ml of acetone. The organic solution was then slowly added to 100 ml of liquid paraffin containing 1% surfactant with constant stirring for 1 h. The resulting microparticles were separated by filtration and washed with petroleum ether. The microparticles finally air dried over a period of 12 h and stored in a dessicator.

2.3. Characterization of microparticles

2.3.1. Drug–excipient compatibility studies by FTIR and DSC

2.3.1.1. Fourier transform infrared spectroscopy (FTIR) studies. The pure drug and optimized formulations were subjected for FTIR analysis. The samples were scanned over a range of 4000–400 cm^{-1} using Fourier transformer infrared spectrophotometer.[6] Spectra's were analyzed for drug polymer interactions.

2.3.1.2. Differential scanning calorimetry (DSC) studies. The pure drug and optimized formulation were subjected to differential scanning calorimeter equipped with an intra cooler (NETZSCH, Japan.). Indium/zinc standards were used to calibrate the DSC temperature and enthalpy scale.[7] The sample were sealed in aluminum pans and heated at a constant rate 20 °C/min over a temperature range of 20–300 °C. An inert atmosphere was maintained by purging nitrogen gas at a flow rate of 50 ml/min.

2.3.2. Percentage yield[8]

The prepared microparticles of all batches were accurately weighed. The measured weight of prepared microspheres was divided by total amount of all the excipients and drug used in preparation of the microspheres, which give the total percentage yield of microspheres. The percentage yield was then calculated by using the formula:

$$\text{Percent yield} = (\text{Amount of microspheres obtained} / \text{Theoretical amount}) \times 100$$

The theoretical amount is the sum of weight of all the non-volatile solid ingredients used in the process.

2.3.3. Flow properties[9]

2.3.3.1. Angle of repose. The flow characteristics of different microparticles were studied by measuring the angle of repose employing fixed funnel method. The angle of repose was calculated by using the following formula.

$$\text{Tan}\theta = h/r \text{ where } \theta = \tan^{-1}(h/r)$$

Where, h = height of pile, r = radius of the base of the pile, θ = angle of repose.

2.3.3.2. Bulk density & tapped density. Bulk density and tapped density were measured by using 10 ml of graduated cylinder. The pre weighed sample was placed in a cylinder; its initial volume was recorded (bulk volume) and subjected to tapings for 100 times. Then the final volume (tapped volume) was noted down. Bulk density and tapped density were calculated from the following formula.

$$\text{Bulk density} = \text{mass of microparticles}/\text{bulk volume}$$

$$\text{Tapped density} = \text{mass of microparticles}/\text{tapped volume}$$

2.3.3.3. Carr's index. Compressibility index (CI) or Carr's index value of microparticles was computed according to the following equation:

$$\text{Carrs index}(\%) = [(\text{tapped density} - \text{bulk density})/\text{tapped density}] \times 100$$

2.3.3.4. Hausner's ratio. Hausner ratio of microparticles was determined by comparing the tapped density to the bulk density using the equation: Hausner's ratio = tapped density/bulk density.

2.3.4. Size distribution and size analysis

For size distribution analysis, 250 mg of the microparticles of different sizes in a batch were separated by sieving, using a range of standard sieves. The amounts retained on different