Preparation of Rapidly Disintegrating Glipizide Tablets by Surface Solid Dispersion through Superdisintegrants

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ABSTRACT: The objective of this investigation was to enhance the dissolution of glipizide using solid dispersions containing different superdisintegrants and to prepare rapidly disintegrating glipizide tablets with rapid absorption through the oral cavity by direct compression of the prepared solid dispersion. Primojel, Ac-Di-Sol and Kollidon CL were used as superdisintegrants. These excipients were used in different ratios and by using solvent evaporation method, rapidly disintegrating glipizide tablets were prepared by direct compression of the prepared solid dispersion, as well as, by camphor sublimation method aiming for more enhancing of tablet disintegration. Glipizide loaded with Kollidon CL showed the best dissolution properties compared to the other tested excipients. The physical properties of all the prepared GZ tablet formulations were found to be acceptable according to USP/NF 2002. Kollidon CL containing formulations showed the most rapid disintegration time values reaching one second in tablets prepared by camphor sublimation method. The most effective formula in decreasing the blood glucose level was that containing glipizide loaded with Kollidon CL, with significant difference from the physically mixed ingredients or the pure GZ powder depending on Student’s T-test for area above the blood glucose level.

KEY WORDS: Glipizide- superdisintegrants- Primojel- Ac-Di-Sol- Kollidon CL.

Introduction

Oral administration of glipizide appears to lower the blood glucose acutely by stimulating the release of insulin from the pancreas, an effect dependent upon functioning beta cells in the pancreatic islets. Blood sugar control persists in some patients for up to 24 hours after a single dose of glipizide. Gastrointestinal absorption of glipizide in man is uniform, rapid, and essentially complete. Peak plasma concentrations occur 1-3 hours after a single oral dose. The half-life of elimination ranges from 2-4 hours in normal subjects, whether given intravenously or orally. Many formulations of glipizide was developed and evaluated for extending the release (Chung et.al, 2002, Hsieh et.al, 2006, and Jamzad et.al.,2006), or for enhancing solubility (Gan et.al.2002, and Aly et.al.2003).

With the increase in the average human life, drug administration for elderly patients has become more important. Due to a decline in swallowing ability with age, a great many elderly patients complain that it is difficult to take medication in the form of tablets (Mallet, 1996). Recently, useful dosage forms, such as rapidly disintegrating or dissolving tablets have been developed and applied clinically (Sugihara, 1995, Ishikawa et.al. 1999, and Sallam et.al., 1998). This dosage form can be used also for children instead of syrup, as well as, for local action within oral cavity as well as local anesthetics for toothache, cold sore, or teething product. Camphor sublimation method (Koizumi et.al., 1997) has proved to be effective for the production of tablets of higher porosity.

Thus, the objective of this investigation was the enhancement of dissolution and consequently rapid hypoglycemic effect of glipizide by preparing solid dispersion containing Primojel, Ac-Di-Sol or Kollidon CL as superdisintegrants, in different ratios, using a solvent evaporation method. Also, the objective is to prepare rapidly disintegrating glipizide tablets with rapid absorption through the oral cavity by direct compression of the prepared solid dispersion, as well as, by camphor sublimation method aiming for more enhancing of tablet disintegration. The influence of three tablet formulations, containing GZ-KollidonCL (1:9) loaded and physical mixture, as well as pure GZ powder on blood glucose level of mice was, also studied.

Experimental

Materials

Primojel and Kollidon CL were obtained from Avebe, Netherlands). Glipizide, Ac-Di-Sol, Direct compression sugar, Aspartam and Tutti Frutti: were obtained as gifts, from Dar Al-Dawa Pharmaceutical Manufacturing Co. Ltd., Amman, Jordan. Polyethylene glycol PEG₆₀₀₀ was obtained from Panreac Quimica, SA, Spain. All other chemicals employed were of analytical reagent grade.

Method

Preparation of surface solid dispersion by solvent evaporation method

The specified amount of GZ was dissolved in the least amount of methanol: dichloromethane (1:3) at room