EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 4
Issue: 8
434-438
Year: 2017

STUDIES ON DEVELOPMENT AND CHARACTERIZATION OF GLIMEPIRIDE MICROSPHERES

Sai Charitha CH* **and Rama Rao Nadendla**

Department of Pharmaceutics, Chalapathi Institute of Pharmaceutical Sciences, Lam, Guntur.

***Corresponding Author: Sai Charitha CH**

Department of Pharmaceutics, Chalapathi Institute of Pharmaceutical Sciences, Lam, Guntur.

Article Received on 23/05/2017 **Article Revised on 13/06/2017** **Article Accepted on 04/07/2017**

ABSTRACT

The present study is to develop glimepiride microspheres, an orally administered anti-diabetic drug with an idea of improving its oral bioavailability and giving a prolonged drug release. Glimepiride microspheres were successfully formulated by emulsification solvent evaporation technique using polymers such as ethyl cellulose and combination of HPMC and ethyl cellulose. The percentage yield obtained in all the formulations was good. The particle size of microspheres was increased with increase in the concentration of polymer. Scanning electron microscopy showed that microspheres of drug with combination of HPMC and ethyl cellulose showed smooth surface and a good spherical shape. The *in-vitro* drug release studies showed that drug release was more in case of formulations F7 containing both hydrophilic and hydrophobic polymers in the ratio 1:1 as compared to other formulations.

KEYWORDS: Glimepiride, HPMC, Ethyl cellulose, Oral bioavailability.

INTRODUCTION

Glimepiride is the third generation sulphonyl urea, which lowers the blood glucose level in the healthy subjects as well as in patients with type II diabetes. Its biological half life is 2-3hrs. Due to its low biological half life, it requires frequent administration of drug in order to maintain plasma concentration. This causes inconvenience to the patient and also leads fluctuations in plasma concentration. Therefore, development of controlled release dosage forms is necessary to decrease dosage requirements, and thus to increase patient compliance. Microparticulate drug delivery system is one of the processes to provide the sustained & controlled delivery of drug for extended period of time and maintain an effective drug concentration in the serum for longer time. The microspheres are characteristically free flowing powders consisting of proteins or synthetic polymers, which are biodegradable in nature. Solid biodegradable microspheres incorporating a drug dispersed or dissolved throughout particle matrix have the potential for controlled release of drugs where their spherical particles ranging from 1 to 1000 micrometers. Where here the microspheres are prepared from the solvent evaporation method, microspheres are prepared by two particles core material and coating material, where the core material is made up of drug and particulate is of polymers. Microencapsulation for oral use has been employed to sustain the drug release, and to reduce or eliminate gastrointestinal tract irritation. In addition, multiparticulate delivery systems spread out more uniformly in the gastrointestinal tract. This results in more reproducible drug absorption and reduces local irritation when compared to single-unit dosage forms such as no disintegrating, polymeric matrix tablets. Unwanted intestinal retention of the polymeric material, which may occur with matrix tablets on chronic dosing, can also be avoided. Microencapsulation is used to modify and retard drug release, due to its small particle size they are widely distributed throughout the gastrointestinal tract which improves drug absorption and reduces side effects due to localized build-up of irritating drugs against the gastrointestinal mucosa.

MATERIALS AND METHODS

Glimepiride was a gift sample from Dr. Reddy's Laboratories, Hyderabad, Ethyl Cellulose and HPMC (Richer chemicals pvt.LTD., Hyderabad, India), Eudrajit RL100 (Richer chemicals pvt.LTD., Hyderabad, India), Dichloromethane (Merck specialities private limited, Mumbai), Poly vinyl alcohol (S D fine-chem limited, Mumbai), Ethanol (Merck specialities private limited).

METHOD

Solvent evaporation technique

Emulsification (o/w) solvent evaporation method was employed in the preparation of Glimepiride microspheres using ethyl cellulose and combination of ethyl cellulose and HPMC as the polymers. Polymer was dissolved in

10ml of dichloromethane. To this 1mg of drug was added and mixed thoroughly. The above organic phase was added drop wise to 100ml of 1% PVA solution under magnetic stirrer at 800 rpm by keeping at 40˚c till the DCM evaporated. Different formulations were prepared by taking different drug to polymer ratios.

Characterization of Glimepiride Microspheres

Determination of practical yield

The prepared microspheres were dried at room temperature and weighed. The yield of microspheres was calculated using the formula.

$$\text{Percentage yield} = \frac{\text{Amount of microspheres obtained}}{\text{Amount of Non-volatile material taken}} \times 100$$

Estimation of drug content

An accurately weighed portion of microspheres equivalent to 5 mg of Glimepiride were weighed and transferred in to a mortar. Powdered and dissolved in 100 ml of pH 7.4 phosphate buffer, suitably diluted, the absorbance of the resulting solution was measured at 225 nm.

Encapsulation Efficiency

Glimepiride microsphere (100mg) was dissolved in 100ml distilled water. Then the suspension was warmed for a few minutes, filtered then the 1ml of filtrate was made up to 10ml with distilled water. The solution was analyzed at 225nm using UV spectroscopy (Lab India).

$$\%\ \text{Encapsulation efficiency} = \frac{\text{Amount of drug encapsulated}}{\text{Theoretical amount of drug}} \times 100$$

Determination of mean particle size of microspheres

A minute quantity of dried microspheres was suspended in glycerin and the particle size of 100 microspheres was determined in each batch by optical microscopy (Olympus, India) and the mean particle size was calculated.

Scanning electron microscopy (SEM)

For the external morphology studies, the samples were mounted on a metal slab with double adhesive tape and coated with platinum under vacuum and the air dried particles were visualized using scanning electron microscopy (FEI-Quanta 200F) operating at 15kv.

Fourier transform infrared spectroscopy (FTIR)

FTIR spectra of the formulated microspheres and drug were recorded. Microspheres were taken in a KBr pellet. Approximately 5mg samples were mixed with 50mg of spectroscopic grade KBr, samples were scanned in the IR range from 500-3500cm-1, with a resolution of 4 cm-1.

Drug Release Studies

In vitro release profile for microspheres performed using USP type II dissolution apparatus. Sample equivalent to 5 mg of Glimepiride was added to 900ml phosphate buffer of pH 7.4 at 37±0.5ºC and stirred at 100 rpm. Aliquot of 5 mL was withdrawn at time intervals of 0.5, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 10 and 12 h. The withdrawn volume was replenished with the same volume of dissolution medium in order to keep the total volume constant. The absorbance of the samples was measured at λmax 225 nm using phosphate buffer of pH 7.4 as blank. Results of *in vitro* drug release studies obtained from absorbance data were tabulated and shown graphically as Cumulative % drug released Vs Time.

RESULTS AND DISCUSSION

The solutions of Glimepiride were prepared and the absorbance of resulting solutions was measured in UV spectrophotometer at 225 nm. The absorbance is noted and the standard graph between concentration Vs absorbance was given in figure 1. Glimepiride microspheres were successfully formulated by solvent evaporation method. A total number of seven batches were formulated by varying the polymer concentration. The detailed composition of microspheres was shown in Table 1. These microspheres were evaluated for their percentage yield, percent drug content, percent encapsulation efficiency and morphological characterization, FTIR studies, *in vitro* release studies. The results were depicted in Table No. 2 & 3. FTIR spectroscopy ensured that no chemical interactions between the drugs and polymer occurred. The FTIR spectrum for drug and optimized formulation is shown in Fig: 2 & 3. The particle size analysis reveals that, with the considerable increase in the concentration of polymers the mean particle size of microspheres also increased. The % yield varies from 79 to 96.76%. The % drug content in the microspheres was found to be 28.09 to 52.76%. The % drug content decreases with increase in polymer concentration. The % of encapsulation efficiency ranges from75.09 to 96.09. The encapsulation efficiency increases with the increase in polymer concentration. The SEM studies clearly showed that the obtained microspheres exhibit good spherical nature. Scanning electron microscopic photographs of microspheres are shown in Fig.4. The glimepiride microspheres were subjected to In-vitro release studies by employing 7.4 pH phosphate buffer and the drug release profiles were shown in Fig.5.

Table: 1 Formulation table of glimepiride microspheres

Formulation Code	Drug (mg)	HPMC (%)	Ethyl Cellulose (%)	DCM (ml)
F1	1	-	0.5	10
F2	1	-	1	10
F3	1	-	1.5	10
F4	1	0.5	0.5	10
F5	1	1	0.5	10
F6	1	0.5	1	10
F7	1	1	1	10

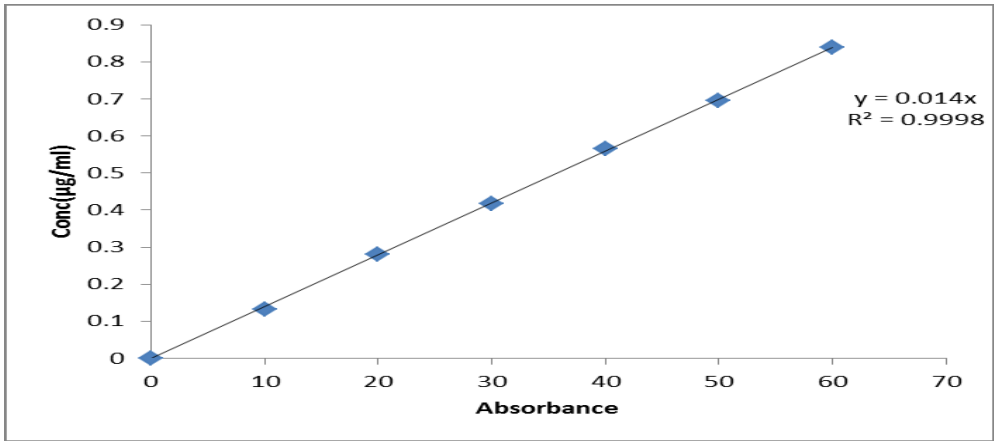

Fig: 1 Calibration curve of glimepiride

Table 2: Percentage yield, percent drug content and percent encapsulation efficiency of Glimepiride Microspheres.

Formulation Code	Particle Size (µm)	Percentage Yield	% Drug Content	% Encapsulation Efficiency
F1	130 ± 1.25	79.99	52.76	75.09
F2	145 ± 1.20	81.00	43.56	78.10
F3	165 ± 1.00	78.15	42.98	78.25
F4	200 ± 0.96	85.98	40.87	80.09
F5	210 ± 1.28	90.16	35.63	87.03
F6	225 ± 1.78	95.08	30.87	90.98
F7	250 ± 1.29	96.76	28.09	96.09

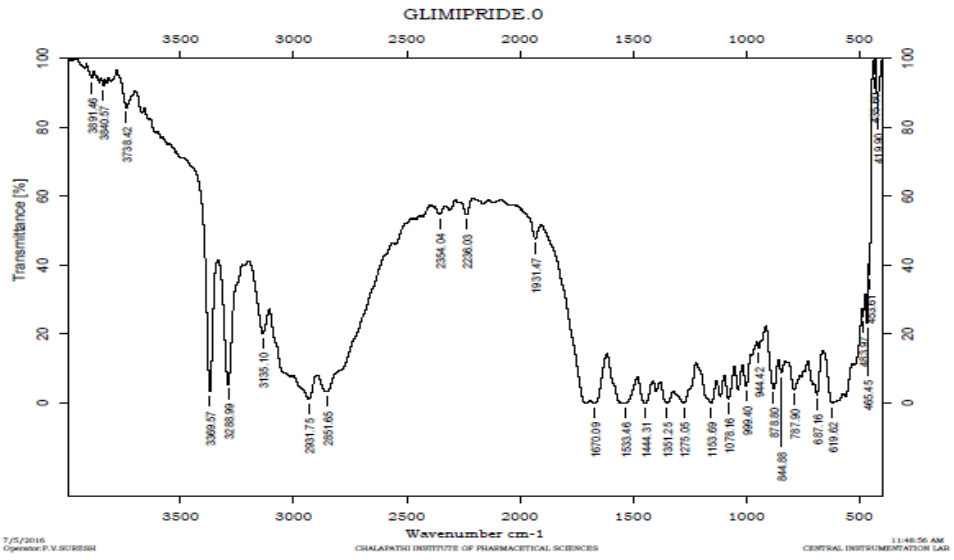

Fig: 2 FT-IR Spectra of Glimepiride

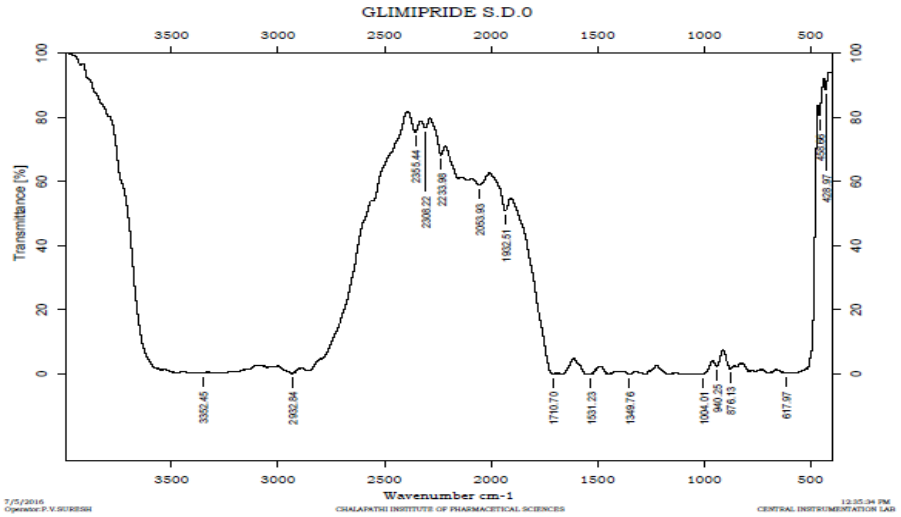

Fig: 3 FT-IR Spectra of optimized formulation F7

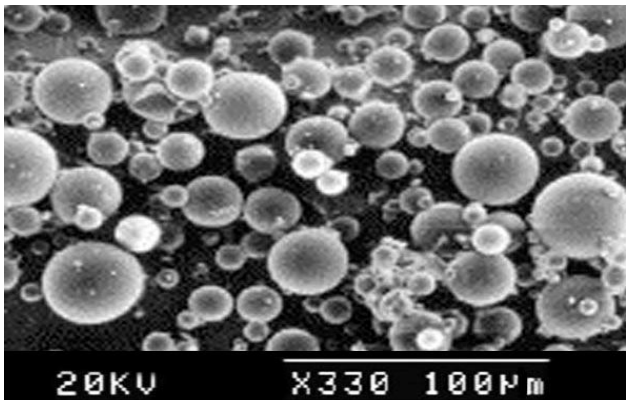

Fig: 4 SEM Photograph of Glimepiride Microsphere

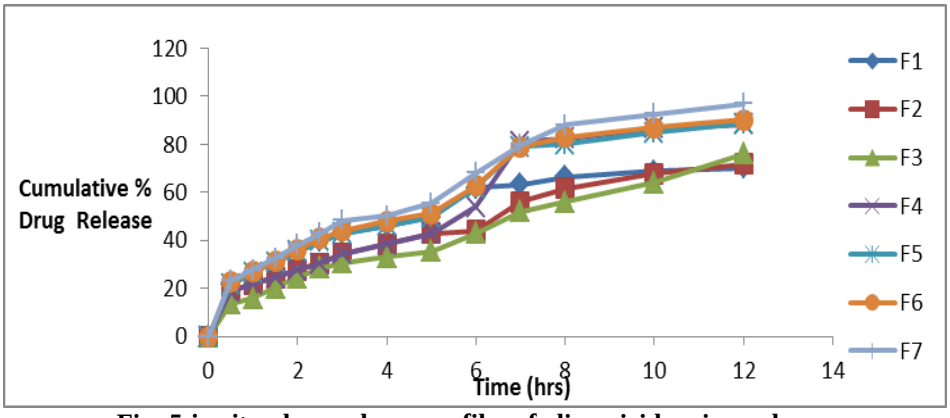

Fig: 5 *in vitro* drug release profiles of glimepiride microspheres

CONCLUSION

The present study is to formulate glimepiride microspheres, an orally administered antidiabetic drug with an idea of improving its oral bioavailability and giving a prolonged release of drug. FT-IR spectra of drug-polymer mixture showed no significant shifting of the peaks therefore it reveals that the drug is compatible with the polymer used. Microspheres with polymers such as ethyl cellulose and combination of HPMC and ethyl cellulose were successfully prepared by emulsification solvent evaporation method. The percentage yield obtained in all the formulations was good. The particle size of microspheres was increased with increase in the concentration of polymer. Scanning electron microscopy showed that microspheres of drug with combination of HPMC and ethyl cellulose showed smooth surface and a good spherical shape. The *in-vitro* drug release studies showed that drug release was more in case of formulations F7 containing both hydrophilic and

hydrophobic polymers in the ratio 1:1 as compared to other formulations.

REFERENCES

1. B Pavan Kumar and et. al. formulation and evaluation of glimepiride loaded cellulose acetate microparticles. *Int J Pharm Pharm Sci, 6(4): 511-515.*
2. N Sriram and R Himabindhu. Formulation and evaluation of glimepiride microspheres. *IJPDT / 2013; 3(1): 7-12.*
3. Abhishek Pandey, Vivek singh Bhadoria. Formulation Development & Optimization of Glimepiride Microspheres Using Ionotropic Gelation Technique. Pharmacia, 2011; 1(2): 67-72.
4. Alagusundaram M, Madhu Sudana Chetty C, Umashankari K, Attuluri Venkata Badarinath, Lavanya C and Ramkanth S. Microspheres as a Novel Drug Delivery Sysytem - A Review. *International Journal of ChemTech Research*, 2009; 1(3): 526-534.
5. Salvadeo. Glimepiride-Glimepiride in the Treatment of Giuseppe Derosa and Sibilla Anna Teresa Type 2 Diabetes. *Clinical Medicine: Therapeutics*, 2009; 1: 835–845.
6. Harshad Parmar, Sunil Bakliwal, Nayan Gujarathi, Bhushan Rane, Sunil Pawar. Different Methods of Formulation And Evaluation Of Mucoadhesive Microsphere. *International Journal of Applied Biology and Pharmaceutical Technology*, 2010; 1(3): 1157-1167.
7. Kedar Prasad Meena, Dangi JS, Samal PK and Namdeo KP. Recent Advances in Microspheres Manufacturing Technology. *International Journal Pharmacy & Technology*, 2011; 3(1): 854-893.
8. *Kristi Monson, Arthur Schoenstadt. Pioglitazone Uses: An Overview*, 2007.
9. Satheesh Madhav NV, Shivani Kala. Review on Microparticulate Drug Delivery System. *Int.J. PharmTech Res*, 2011; 3(3): 1255-1259.
10. Prasanth VV, Akash Chakraborthy Moy, Sam T Mathew, Rinku Mathapan. Microspheres - An Overview. *International Journal of Research in Pharmaceutical and Biomedical Sciences*, 2011; 2(2): 1242-1254.