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Microcrystalliation of Glipizide: Effect of type of Stabilizer on Particle Size, Solubility and Dissolution

Steffy B Manjila, Jomon N Baby, EN Bijin, Icey Constantine, K Pramod, and J Valsalakumari*

College of Pharmaceutical Sciences, Govt. Medical College, Thiruvananthapuram – 695011, Kerala, India.

ABSTRACT

Glipizide is an oral hypoglycemic agent which is a second generation sulphonylurea belonging to BCS class 2. This study is intended to prepare Glipizide microcrystals using different polymers and to study the effect of these polymer microcrystals on particle size, solubility and dissolution. The results of the present study showed that mean particle size and dissolution is highest for microcrystals prepared with Tween 80 whereas solubility was highest for microcrystals prepared with PVA. Further research work is necessary to clarify the conflicting results obtained with our study.

Keywords: Glipizide, Microcrystals, Particle size, Solubility, Dissolution

Correspondence Author

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INTRODUCTION

In the case of orally administered drugs, the two factors affecting absorption rate of dissolution and rate of permeation through the membrane. For hydrophobic, poorly aqueous soluble drugs, absorption is dissolution rate limited and for hydrophilic drugs, it is permeation rate limited. Our drug of consideration, Glipizide, comes under Class 2, with low solubility and high permeability and the absorption being dissolution rate limited [1]. For such drugs, enhancement of dissolution by suitable techniques helps in reaching required blood levels for therapeutic efficacy. Thus, to improve dissolution and bioavailability of such drugs, several method like particle size reduction, conversion to amorphous state, combining with cyclodextrin etc. are employed. Size reduction can be by micronisation by milling, supercritical fluid etc. milling will produce considerable size reduction but particle size distribution will not be uniform and there can be instability due to disruption of crystal lattice. Supercritical fluid method is a good method. But owing to its increased cost and low yield, it is not much preferred.

Considering all the above mentioned limitations, a relatively new method of solvent change or solvent precipitation was developed in recent years producing microcrystals with enhanced solubility [2]. As there is surface adsorption of excipients, surface inhibits particle growth and thus size reduction is achieved. Also, if required, morphology can be changed by preferential adsorption of stabilizing agent. The technique has the following advantages that it is a direct process, easy to perform, rapid and doesn't require any sophisticated equipments. Glipizide is an oral hypoglycemic agent which is a second generation sulphonylurea belonging to BCS class 2. This study is intended to prepare Glipizide microcrystals using different polymers and to study the effect of these polymer microcrystals on particle size, solubility and dissolution.

MATERIALS AND METHODS

Glipizide was obtained as gift sample from Supra Chemicals, Mumbai, India. Polyvinyl alcohol (PVA) (cold), Tween 80 and Polyethylene glycol (PEG) 200 were purchased from Central Drug House, New Delhi.

Preparation of Microcrystals

The method followed is emulsion solvent diffusion method. Glipizide (250mg) is dissolved homogeneously in 10 mL of acetone. This organic phase is added drop wise (using a syringe) to100 mL of 0.25% w/v of each of stabilizer (PVA, Tween 80and PEG 200) while stirring in a magnetic stirrer at 250 rpm. Continued stirring for 30 minutes. Obtained microcrystals were filtered in a Whatmann No.1 filter paper and dried at room temperature.

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Particle Size Determination

Particle size determination was done using optical microscopy. Eyepiece micrometer was calibrated using the stage micrometer and particle size was determined.

Solubility Studies

The solubility of pure glipizide and the prepared microcrystals were determined in distilled water by placing excess quantities in test tubes containing 10 ml distilled water. The samples are stirred for 72 h at room temperature and the aliquots were filtered, diluted suitably and assayed spectrophotometrically at 276 nm using a UV-Vis spectrophotometer.

Dissolution Studies

Release of glipizide from microcrystals was investigated in simulated intestinal fluid as a dissolution medium using paddle method specified in USP [3]. Dissolution studies were carried out 25 mg of pure drug and microcrystals formed with three different surfactants. The dissolution test was carried out at 50 rpm and a temperature of 37±0.5 °C was maintained. At predetermined time intervals of 5, 10, 15, 20, 30 and 45 min 5 mL of sample were withdrawn and replaced with fresh media. The concentration of drug dissolved at different time intervals were determined by measuring absorbance at 276 nm in a UV –Vis spectrophotometer.

RESULTS AND DISCUSSION

Particle Size Determination

Particle size determination was done and the results are shown in Fig. 1. The microcrystals formed with Tween 80 was found to have highest mean particle diameter of 43.44 µm.

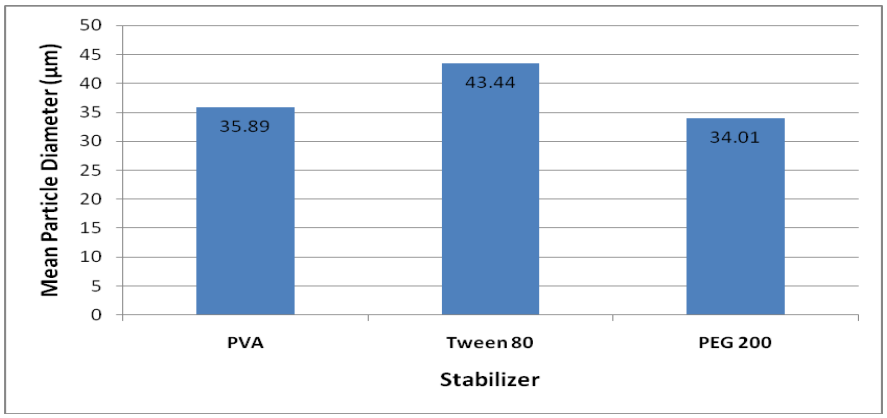

Figure 1: Mean particle diameter of microcrystals formed

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Solubility Studies

The results of solubility studies are shown in Fig. 2. It was noted that highest solubility was noted when PEG 200 was used as stabilizer. PVA was found to slightly decrease the solubility of glipizide. Tween 80 slightly increased the solubility of glipizide when used as stabilizer in the preparation of microcrystals.

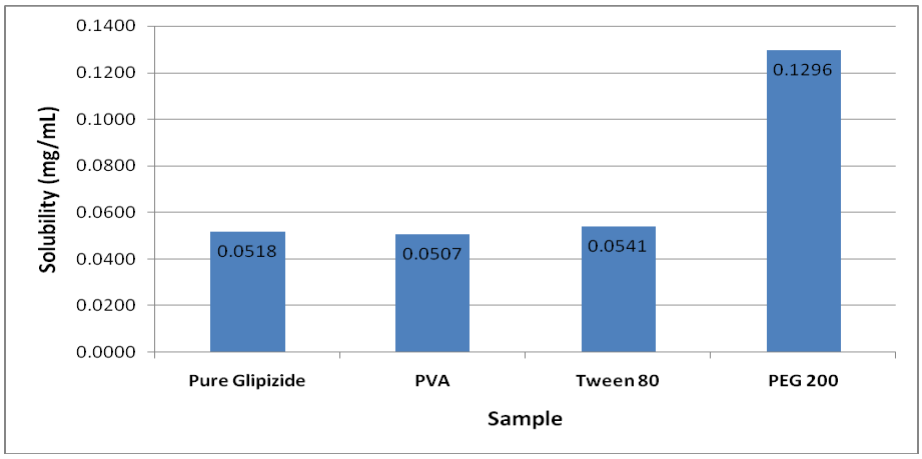

Figure 2: Solubility of pure glipizide and glipizide microcrystals prepared with different stabilizers

Dissolution Studies

The results of dissolution studies are shown in Fig 3. It was noted that dissolution was highest in microcrystals prepared with Tween 80 and lowest for microcrystals prepared with PEG 200.

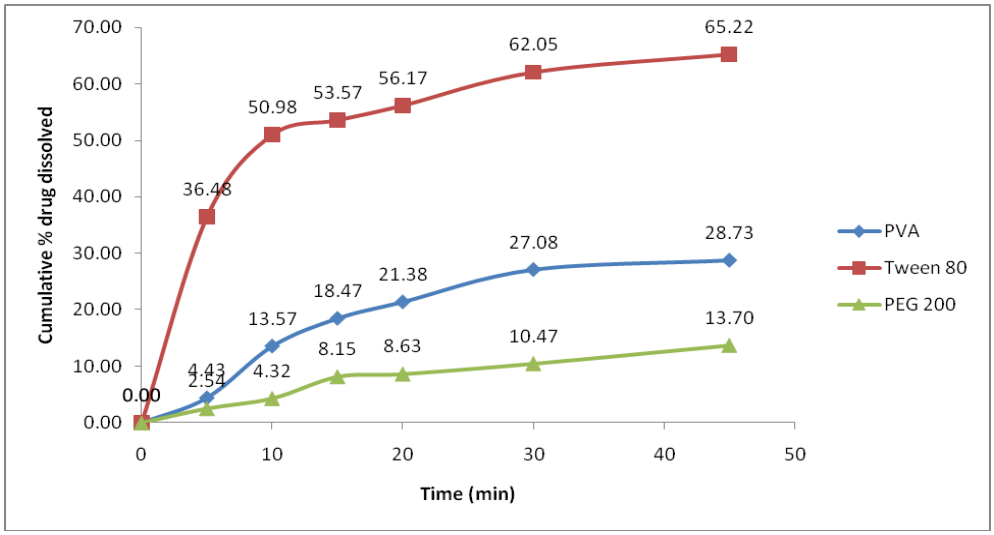

Figure 3: Dissolution profile of glipizide microcrystals prepared with different stabilizers

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CONCLUSIONS

The results of the present study showed that mean particle size and dissolution is highest for microcrystals prepared with Tween 80 whereas solubility was highest for microcrystals prepared with PVA. Further research work is necessary to clarify the conflicting results obtained with our study.

REFERENCES

[1] Patel GC, Asodaria KV, Patel HP, Shah DR. Curr Drug Deliv. 2012;9(4):395-404.
[2] Reddy PS, Sujani S, Reddy KR. Asian J. Pharm. Tech. 2011:1(3), 64-69.
[3] United States Pharmacopeia and National Formulary, Asian edition 2005, United States Pharmacopeial Convention. Rockville, MD, 2005, p.903-904.