Vol 6 | Issue 1 | 2016 | 9-11.

International Journal
of
Pharmacy Review & Research
www.ijprr.com

e-ISSN: 2248 – 9207
Print ISSN: 2248 – 9193

SOLUBILITY ENHANCEMENT OF POORLY SOLUBLE DRUG GLIMEPIRIDE BY SOLID DISPERSION TECHNIQUE

Valarmathi S*, Senthil Kumar M, Sujinidevi V, Nachammai V, Dhanalakshmi J

Annai Veilankanni Pharmacy College, Saidapet, Chennai - 600015, Tamil Nadu, India.

ABSTRACT

Solid dispersion is the most widely used and accepted technique for improving the solubility of poorly soluble drugs. It is basically a drug-carrier two component system. Glimepiride is an anti-diabetic drug which is poor soluble and the attempt was made to enhance the solubility by using solid dispersion technique and the carriers used were hydroxypropyl methylcellulose (HPMC) and sodium starch glycolate (SSG).The glimepiride were formulated as solid dispersion with the carriers and evaluated. The drug release using SSG was found to be high than that of the plain drug and the formulation with HPMC.

Key words: Solid dispersion, Dissolution rate, Bioavailability, Solubilization, Glimepiride, Carrier.

INTRODUCTION

The term solid dispersion refers to a group of solid products consisting of at least two different components, generally a hydrophilic matrix and a hydrophobic drug. The matrix can be either crystalline or amorphous and the drug can be dispersed molecularly in amorphous particles (clusters) or in crystalline particles. Oral bioavailability of a drug depends on it solubility and/or dissolution rate, therefore efforts to increase dissolution of drugs with limited water solubility is often needed. Improvement in the dissolution rate of the poorly soluble drugs after oral administration is one of the most crucial challenges in modern pharmaceutics. Many methods are available to improve the characteristics including salt formation, micronization and addition of solvent or surface-active agents. In this study HPMC and SSG were selected as carriers and solid dispersion was prepared by the method of solvent evaporation [1].

Glimepiride is a medium-to long-acting sulfonylurea anti-diabetic drug indicated to treat type 2 diabetes mellitus. The hypoglycaemic action appears to be dependent on stimulating the release of insulin from functioning pancreatic beta cells and increasing sensitivity of peripheral tissue to insulin. Poor aqueous solubility and slow dissolution rate of glimepiride lead to irreproducible clinical response or therapeutic failure in some cases due to sub therapeutic plasma drug levels. It shows low, pH dependent solubility. In acidic and neutral aqueous media, glimepiride exhibits very poor solubility at 37°C (<0.004 mg/ml). In media pH >7, solubility of drug is slightly increased to 0.02 mg/ml. Thus the solid dispersion technique proved to be the most successful in improving dissolution by delivering it in an active and absorbable form to the desired absorption site using physiologically safe excipients [2]. Glimepiride was selected as a model drug for dissolution improvement studies. Solid dispersion with HPMC (F1) and SSG (F2) as carrier were formulated by solvent evaporation method. The formulations were evaluated for physical characteristics, UV spectroscopy, IR spectroscopy, in vitro dissolution profiles and drug content [3-5].

MATERIALS AND METHODS

Materials

Glimepiride was obtained from Madras Pharmaceuticals, Chennai. Sodium starch glycolate (SSG) and hydroxypropyl methylcellulose (HPMC) were obtained from Madras Pharmaceuticals, Chennai and Sodium lauryl sulphate from Alzer, Tanjore. Other reagents and solvents used were of pharmaceutical or

***Corresponding Author S. Valarmathi** E mail: sahanashree2012@gmail.com

analytical grade.

METHODS

Preparation of Glimepiride Solid Dispersion

Method of Preparation: Solvent Evaporation Method

To the methanolic solution, specified amount of Sodium starch glycolate (SSG) was added and the mixture was heated to 50°C on a mantle with continuous stirring until the solvent gets evaporated. Then the mixture was collected and packed in an amber coloured glass container and was hermetically sealed and stored at ambient conditions [6-7].

Characterization and Evaluation of Solid Dispersion

1. Physical characterization

Preformulation studies were performed for assessing flow property by funnel method, particle size determination by sieve analysis.

2. Drug Content Analysis

100 mg of glimepiride solid dispersion was dissolved in 50 ml of methanol. From this 0.5 ml is pipette out and make up the volume to 100 ml standard flask using 6.4 phosphate buffer.

3. Dissolution Rate Studies

Dissolution rate studies of pure glimepiride and solid dispersion were performed in 8 stage Toshiba dissolution test apparatus with rotating paddle method at 50 rpm using 900 ml of 6.4 pH buffer containing 0.5% SLS. The temperature of the bath was maintained at 37 $\pm$ 0.5°C throughout the experiment.5 ml of sample were withdrawn at various time intervals and were further diluted with 6.4 pH phosphate buffer containing 0.5 % SLS medium. The absorbance of the sample was measured at 228 nm for determining the amount of drug released at various intervals, each time the same volume of buffer was added to the dissolution media for maintaining the sink condition.

4. Infrared Spectroscopy

Infrared spectroscopy was conducted using FT-IR (Fourier-Transform Infrared) Spectrophotometer and the spectrum was recorded in the region 500-4000 cm^{-1}. The procedure consists of dispersing a sample (drug and KBr preparation) into discs by applying a pressure of 5 tons for 5 min in a hydraulic pressure. The powder was placed in the path and spectrum was obtained.

Calibration Curve By UV Spectrophotometry

Preparation of Standard Curve of Glimepiride

10 mg of glimepiride dissolved in 100 ml standard flask using 6.4 phosphate buffer. From this 2.5 ml is pipette out and transferred to 100 ml standard flask and made up to the volume with 6.4 phosphate buffer solution. From the stock solution 1 ml is withdrawn and transferred to 10 ml standard flask and made up with phosphate buffer. Similarly 2 ml,3 ml, 4 ml, 5 ml is transferred to 10 ml standard flask and the volume made up with 6.4 phosphate buffer. Absorbance of the solution was measured at about 228 nm.

RESULTS AND DISCUSSION

The physical characterisation of the drug by performing the preformulation studies indicated that the drug is found to be passable from the angle of repose value (35.37°) and particle size of the given granules was determined by frequency distribution analysis using sieve technology. Average particle size of the powder was found to be 1.341 µm and the maximum % of weight retained was found to be 95.6 % on the sieve no. 85.

Table 1. Dissolution Rate Study for the pure drug and formulations F1 with HPMC as Carrier and F2 with SSG as carrier

S.No	Time (min)	% Drug Release		
		Pure Drug	F1 (HPMC)	F2(SSG)
1	30	29.3	65.6	91.4
2	60	31.6	76.8	94.9
3	90	32.1	75.4	98.0
4	120	33.8	84.4	98.9
5	150	33.9	86.1	99.3

Fig. 1. Comparison of dissolution rate study for pure drug, F1 and F2

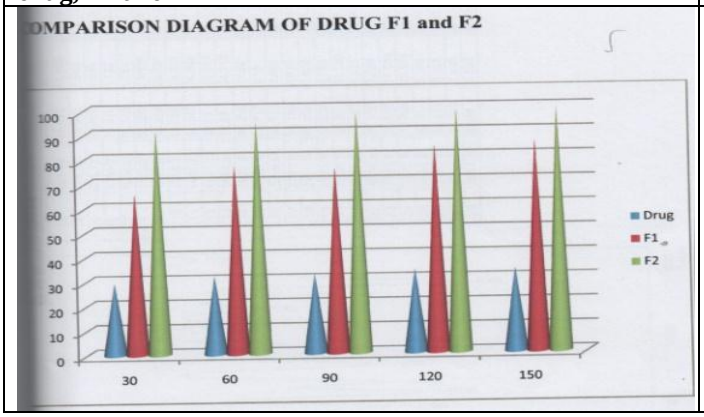


Fig. 2. IR spectra for pure drug

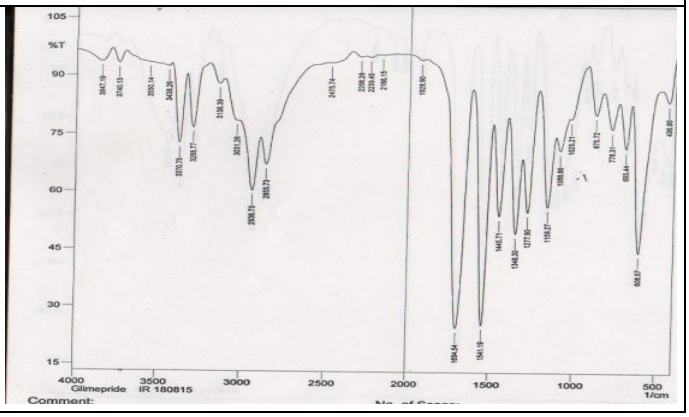


Fig. 3. IR spectra for the formulation with HPMC as carrier

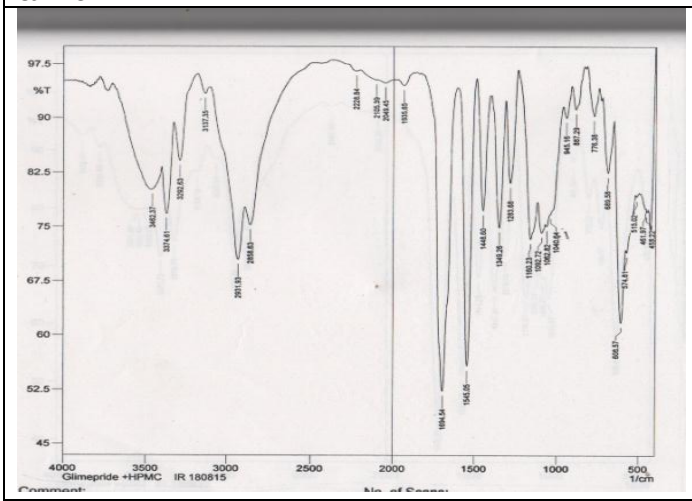
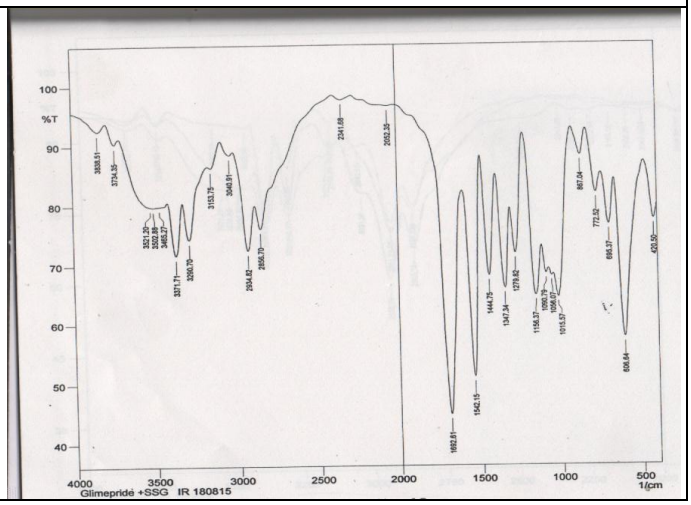


Fig. 4. IR spectra for the formulation with SSG as carrier



The drug content of the formulation containing hydroxypropylmethylcellulose (HPMC) and sodium starch glycolate (SSG) as carrier were found to be 44.79% and 44.38% respectively.

In vitro dissolution study for the glimepiride solid dispersion with HPMC polymer 2 as carrier has the percentage drug release maximum of 86.1 % at about 150 min whereas with that of SSG as carrier has 99.3 % at about 150 min (Table 1).

CONCLUSION

From the study it can be easily demonstrated that HPMC and SSG has the potential to improve solubility characteristics of poorly soluble pure drug glimepiride. It also illustrates the fact that HPMC and SSG used as carriers has characteristics to form molecular dispersion with the drug molecules, thereby increasing the dissolution rate of drug and decreasing the time of release of active ingredient from the formulated mixture. From the in vitro studies performed the best result was achieved in F2 formulation containing SSG as carrier when compared to formulation F1 containing HPMC as carrier and the plain drug.

ACKNOWLEDGEMENT

We render our thanks and glory to our parents and our Head of Department of Pharmaceutics who has been the source of encouragement, guidance and constructive criticism for the successful completion of this work. And we would like to thank Madras Pharmaceuticals, Chennai and Alzer, Tanjore for providing drug samples.

REFERENCES

1. Sethia S, Squillante E. Revival with greater possibilities and applications in oral drug delivery. *Crit rev ther drug carrier syst*, 20(2-3), 2000, 215-47.
2. Kumar S, Gupta SK. Pharmaceutical solid dispersion technology: a strategy to improve dissolution of poorly water-soluble drugs. *Recent pat drug delivery form*, 7(2), 2013, 111-21.
3. Dhirendra K, Lewis S, Udupa N, Atin K. Solid dispersions. *Pak J pharm sci*, 22(2), 2009, 234-46.
4. Vasconcelos T, Sarmento B, Costa P. Solid dispersions as strategy to improve oral bioavailability of poor water soluble drugs. *Drug Discov Today*, 12(23-24), 2007, 1068-75.
5. Naveen Dutt Dixit, Suneel Kumar Niranjan. Solid dispersion, 3(9), 238-257.
6. Ishwarya Sridhar, Abha Bhagyashri Joshi, Vandana Wankhede, Jesal Doshi. Solid dispersions: an approach to enhance solubility of poorly water soluble drugs. *JSIR*, 2(3), 2013, 685-694.
7. Mogal S.A, Gujar P.N, Yamger D.S, Kamod A.C. *Der Pharmacia Lettre*, 4, 2012, 1574-1586.