Development and Validation of A Spectrophotometric Method for Quantification and Dissolution Studies of Glimepiride in Tablets

MADHUSUDHANAREDDY INDURI*, BHAGAVAN RAJU M², RAJENDRA PRASAD Y³ AND PAVANKUMAR REDDY K²

^{*1}Department of Pharmaceutical Chemistry, Malla Reddy College of Pharmacy, Maisammaguda, Dhulapally, Secunderabad 500014

²Department of Pharmaceutical Chemistry, C.M. College of Pharmacy, Maisammaguda, Dhulapally, Secunderabad 500014

³Department of Pharmaceutical Chemistry, A. U. College of Pharmaceutical Sciences, Andhra University, Visakhapatnam 530003, Andhra Pradesh, India

E-mail: imsreddychem@yahoo.com

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ABSTRACT: The objective of present study was to develop and validate an analytical method for quantitative determination and dissolution studies of glimepiride in tablets. The glimepiride shows absorption maxima at 225 nm and obeyed Beer's law in the range of 6.0 – 14.0 µg/mL. The limit of detection and limit of quantitation were 0.06, and 0.17 µg/mL respectively. Percentage recovery of glimepiride for the proposed method ranged from 99.32 to 100.98% indicating no interference of the tablet excipients. It was concluded that the proposed method is simple, easy to apply, economical and used as an alternative to the existing spectrophotometric and non-spectrophotometric methods for the routine analysis of glimepiride in pharmaceutical formulations and *in vitro* dissolution studies.

Key words: Glimepiride, Dissolution studies, Tablets, UV Spectrophotometry.

Introduction

Chemically, Glimepiride, shown in Figure 1, is 1-[(p-[2-(3-ethyl-4-methyl-2-oxo-3-pyrroline-1-carboxamide) ethyl] phenyl) sulfonyl]-3- (trans-4-methylcyclohexyl) urea, is 3rd generation sulfonylurea derivative used for the treatment of type II diabetes mellitus¹. A survey of pertinent literature revealed that few liquid chromatography^{2, 3} and derivative spectrophotometry^{2, 4} methods has been developed for the determination of glimepiride in pharmaceutical formulations. Liquid chromatography-electrospray ionization tandem mass spectrometry⁵ method has been developed for the quantification of glimepiride in human

plasma. Spectrophotometry ^{6, 7} and Liquid chromatography ^{8, 9} methods have also been developed for the estimation of glimepiride in combination with other drugs in pharmaceutical formulations. Most of these are either time consuming; involve expensive instrumentation or the use of excess organic solvents, dimethyl formamide is used as a solvent in the reported UV spectrophotometry method⁴, which is expensive and carcinogenic. Dissolution studies have emerged in the pharmaceutical field as a very important tool based on the fact that for a drug to be absorbed and available to the systemic circulation, it must previously be solubilized. Therefore the dissolution studies are used not only to assess batch-to-batch consistency of drug release from solid dosage forms, but they are also essential in several stages of formulation development, for screening and proper assessment of different formulations. Moreover, the *in vitro* dissolution studies obtained from dissolution rate profile has been used for the successful characterization of the *in vivo* behavior of drugs ¹⁰. The aim of the present work is to develop and validate a simple UV spectrophotometric method to be applied for the quantification and dissolution studies of glimepiride in tablets, which therefore serves as a tool for the quality control of pharmaceutical dosage forms.

Figure 1: Chemical Structure of Glimepiride.

Materials and Methods

Instrumentation

A Labindia 3000⁺ UV-Visible Spectrophotometer with spectral bandwidth of 2.0 nm and wavelength accuracy of ± 0.5 nm with automatic wavelength correction and a pair of 10 mm quartz cells were used for the absorbance measurements connected with UVWIN version 5.2.0 software. The dissolution studies were performed on Electro lab, TDT-08L USP dissolution apparatus.

Materials

The glimepiride (assigned purity 99.68%) was kindly supplied as a gift sample by Matrix Laboratories Ltd., Hyderabad, India. All chemicals and solvents used in the spectrophotometric analysis were of analytical reagent grade obtained from Rankem Ltd, India.

Methods

Preparation of standard solution

Standard stock solution (100 $\mu\text{g/mL}$) was prepared by transferring 10 mg of glimepiride into a 100 mL volumetric flask, 30 mL of 0.1 M sodium hydroxide was added, and the mixture was sonicated to dissolve and make up the volume with methanol. Aliquots of these standard solution was transferred using A-grade bulb pipette into 100 mL volumetric flasks and made up to volume with methanol to get final concentration of 6.0 – 14.0 $\mu\text{g/mL}$.

Figure 2. UV-spectra of glimepiride against methanol as blank.

Table 1. Calibration data of the proposed method.

Parameters	Results
$\lambda_{\max}$ (nm)	225
Beer's law range ($\mu\text{g/mL}$)	6-14
Molar extinction coefficient ($1/\text{mol/cm}$)	0.06159
Sandell's sensitivity ($\mu\text{g/cm}^2$)	0.016364
Limit of detection ($\mu\text{g/mL}$)	0.06
Limit of quantitation ($\mu\text{g/mL}$)	0.17
Regression equation	
Intercept (a)	0.1621
Slope (b)	0.0438
Correlation coefficient (r^2)	0.9993

Table 2: Recovery of glimepiride standard solution added to sample solution analyzed by proposed method.

Amount (%) of drug added to analyte	Theoretical content ($\mu\text{g/mL}$)	Conc. found $\mu\text{g/mL} \pm \text{SD}^*$	Recovery (%)	RSD (%)	SEM
50	6	6.06 ± 0.0575	100.98	0.9484	0.0332
100	8	8.03 ± 0.0475	99.7	0.5958	0.0274
150	10	9.99 ± 0.0698	99.32	0.7023	0.0403

* Average of three determinations.

Determination of absorption maxima

Standard solution (10 µg/mL) approximately 3.0 mL was taken and scanned from 200 to 400 nm with fixed slit width of 2.0 nm. The methanol was used as blank.

Calibration curve

The calibration curve was constructed by analyzing five different concentrations of standard solution (6.0 - 14.0 µg/mL), prepared on the same day. All determinations were conducted in triplicate.

Preparation of sample solutions

For analysis of marketed formulations, twenty tablets were accurately weighed and powdered. The powder equivalent to 2.0 mg of glimepiride weighed accurately and transferred to 10 mL volumetric flask containing 1.0 mL of 0.1 M NaOH. The mixture was sonicated to dissolve, make up the volume with methanol and filtered through a 0.45 µm membrane filter. Aliquots of these standard solution was transferred using A-grade bulb pipettes into 100 mL volumetric flasks and the solutions made up to volume with methanol to give final concentration of 10 µg/mL. The above solution was then analyzed for the content of glimepiride using the proposed method.

Figure 3. Dissolution profile of different brands of glimepiride tablets.

Table 3. Assay results of glimepiride in tablet dosage forms.

Tablet Dosage Form	Label Claim mg/tab	% Label Claim± SD*	RSD (%)
DIBIGLIM	2	99.57±0.5917	0.5943
GLIMER	2	100.36±1.8546	1.8479
GLIMESTAR	2	100.14±0.3419	0.3414
GLIMIPREX	2	100.19±1.2758	1.2734
GLIMY	2	99.86±0.3627	0.3632

*Average of six determinations.

Dissolution Studies of glimepiride tablets

The dissolution studies of glimepiride tablets were performed on a paddle-stirrer type of apparatus. The dissolution studies were performed according to dissolution procedure recommended for single-entity products in 900 mL of pH 7.8 phosphate buffer (75 rpm). The temperature of the cell was maintained at 37 ± 0.5 °C by using a thermostatic bath. At each sample time interval, an exact volume of the sample was withdrawn from each flask and immediately replaced with an identical volume of fresh medium to maintain a dissolution sink conditions. At predetermined time intervals (0, 5, 10, 15, 20, 25, and 30 min) for the dissolution studies, and the proposed method was used to determine the concentration of glimepiride in dissolution medium. In order to obtain the dissolution profile, the cumulative percentage of drug released was plotted against time (min).

Method Validation

The method was validated according to International Conference on Harmonization (ICH) 2QB guidelines¹¹ for validation of analytical procedure in order to determine the linearity, limit of detection, limit of quantitation, accuracy and precision.

Results and Discussion

Glimepiride was analyzed by developed UV spectrophotometric method in tablets. The UV spectrum (Fig. 2) shows absorption maxima at 225 nm. The calibration curve showed linearity over a concentration range from 6.0 - 14.0 µg/mL, which follows the Beer and Lambert's law. The correlation coefficient of the curve obtained with linear regression method was 0.9993. The linear regression data for the calibration plot is indicating of a good linear relationship between absorbance and concentration over a wide range. The correlation coefficient was indicative of high significance. The low value of intercept of the ordinate showed the calibration plot did not deviate from linearity. The LOD and LOQ values were found to be 0.06 µg/mL and 0.17 µg/mL, respectively. The recovery was assessed from three replicate determinations of three different solutions containing 6.0, 8.0, 10.0 µg/mL. The absolute means obtained were 100.98, 99.7, and 99.32 % respectively as shown in Table 2. It is evident that the method is accurate within the desired range. The precision of the method was checked by carrying out six independent assays of glimepiride test samples against a working standard. Intermediate precision was checked by analyzing the samples by two different analysts using same instrument. The lower percentage RSD (<2.0%) values shows that the method is more precise. The developed method was applied to the quantification of glimepiride in tablets available in local market. The results were tabulated in Table 3. It can be seen that, the results obtained by proposed method was very much similar to that of established methods. Dissolution studies of different brands of glimepiride tablets by proposed method reveal that more than 75% of labeled amount is dissolved within 15 min, which is correlating with IP method. As per IP, the assay and dissolution studies of glimepiride tablets were done by using liquid chromatography, where as the advantage of this method can be used for both assay and dissolution studies of glimepiride in tablets.

Conclusion

The proposed method is rapid, accurate, precise and sensitive for the quantification of glimepiride from its pharmaceutical dosage forms. The method rely on the use of simple working procedure comparable to that achieved by sophisticated and expensive technique like HPLC, and hence this method can be routinely employed in quality control for analysis of glimepiride in tablets and dissolution studies.

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