

DEVELOPMENT AND VALIDATION OF A NOVEL UV-DERIVATIVE SPECTROSCOPIC METHOD FOR ESTIMATION OF GLICLAZIDE TABLETS

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ABSTRACT

In the present study, derivative spectrophotometric methods have been developed and validated for the determination of Gliclazide in bulk and in tablet dosage forms. The second, third and fourth order derivative spectroscopy was applied for the estimation of Gliclazide using zero-crossing method. These methods were adopted to eliminate the spectral interference. Based on spectrophotometric characteristics of Gliclazide a signal of second (219nm), third (204nm) and fourth (213nm) order derivative spectra were found to be relevant for quantification. The literature survey showed that no analytical method was reported so far for the estimation of Gliclazide in tablet dosage form using derivative

spectroscopy, though few simple UV-spectroscopic and HPLC methods exist. Hence the authors made an attempt to develop simple, accurate, sensitive, reliable and rapid derivative spectroscopic methods for the quantification of Gliclazide. The proposed methods obeyed Beer's law in the concentration range of 2-10µg/ml and were validated as per the ICH guidelines.

KEYWORDS: Gliclazide, Derivative spectroscopy, Validation.

INTRODUCTION

Gliclazide (GLZ), (Fig. 1) is chemically 1-(hexahydrocyclopenta[c]pyrrol-2(1H)-yl)-3- [(4-methylphenyl) sulphonyl] urea. It is a second-generation sulphonyl urea oral hypoglycemic agent used in the treatment of non-insulin dependent diabetes mellitus.^[1]

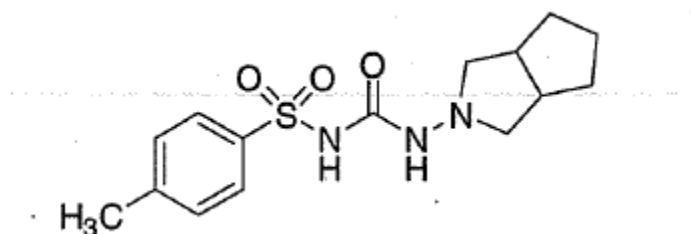


Fig. 1: Chemical structure of Gliclazide.

The literature survey revealed that there are only few spectroscopic and HPLC methods available for the estimation of Gliclazide in pharmaceutical formulations and to best of our knowledge, no reports were found for spectroscopic derivatisation of GLZ in bulk and in tablet dosage forms.^[2-10] The present article describes UV-derivative spectroscopic methods for the determination of Gliclazide in pharmaceutical dosage forms and the results were validated as per ICH Guidelines.^[11-15] The proposed methods can easily be applied to routine analysis of GLZ in tablet formulations. These methods are easy, rapid and economical for the estimation of GLZ in pharmaceutical dosage forms.

MATERIALS AND METHODS

Chemicals

Authentic drug sample of Gliclazide was given as a gift sample by BMR Chemicals, Hyderabad. Gliclazide tablets were procured from the local market. Analytical grade Methanol from Fisher scientific, Mumbai was used as solvent.

Instrument

Derivatization was performed on Agilent Cary 60 UV-Vis double beam Spectrophotometer with 1 cm matched quartz cells. Other equipment used in the study were Shimadzu (BL 220H) analytical balance and ultra sonic bath (Amkette Industries-ANM USC 100).

Method Development

Solvent selection: For optimization of the method, various solvents were tested and it was found that GLZ was soluble in Methanol and 0.1N NaOH. In the present investigation, methanol was used as solvent.

Preparation of Standard Solutions

A standard stock solution of GLZ having a concentration of 100 µg/ml was prepared by dissolving 10 mg of GLZ in 30 ml of methanol and allowed to ultrasonicate for 20 min.

Finally, the volume was made up to 100ml with methanol. From this stock solution, working standard solutions having a concentration of 2, 4, 6, 8 and 10 $\mu\text{g/ml}$ were prepared and scanned in the range of 200-400 nm against solvent blank and the absorption spectra were recorded. Then the zero order overlay spectrum obtained was derivatised to get second (Fig. 2), third (Fig. 3) and fourth (Fig. 4) order spectra.

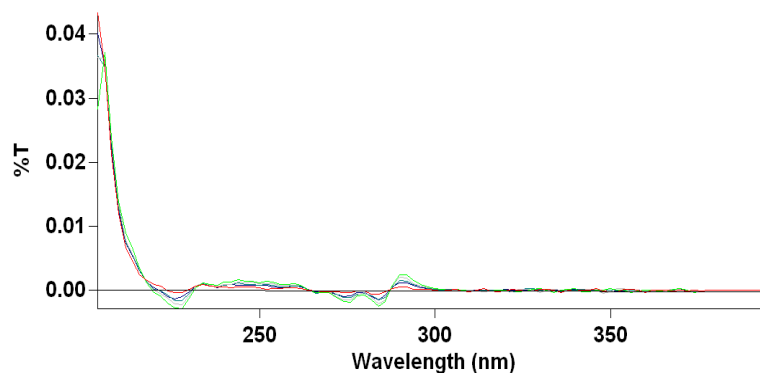


Fig. 2: Overlain of second order derivative spectrum of GLZ.

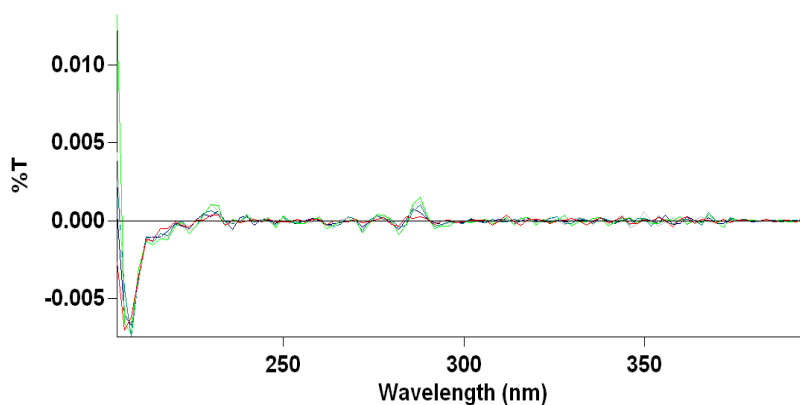


Fig. 3: Overlain of third order derivative spectrum of GLZ.

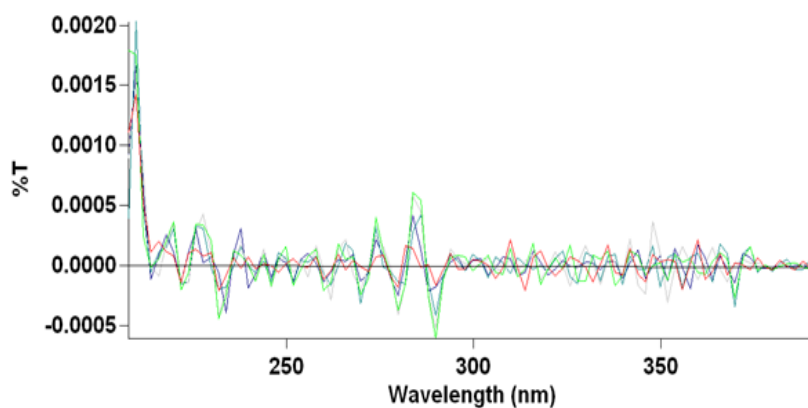


Fig. 4: Overlain of fourth order derivative spectrum of GLZ.

Study of Derivative Spectrum

The zero order overlay spectrum of GLZ was converted into first, second, third and fourth order spectra. As the first order overlain spectrum did not show satisfactory result for the proper selection of zero crossing point of GLZ, the second, third and fourth order overlain spectra were selected to show zero crossing point (ZCP) which assisted the present method of estimation.

Derivative spectroscopic method

The working standard solutions ranging from 2 µg/ml to 10 µg/ml were scanned from 200-400 nm. For the second, third and fourth order derivative spectra the ZCPs were obtained at 219 nm, 204 nm and 213 nm respectively, whose amplitudes were plotted against the corresponding concentrations to give calibration curves with good regressions as shown in figures 5, 6 and 7. The derivative spectra of GLZ obtained for the overlain spectrum in second, third and fourth order derivative spectroscopy are shown in figures 2, 3 and 4 respectively.

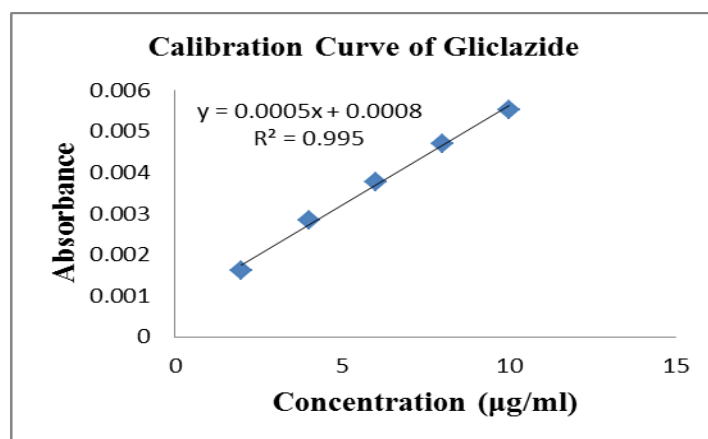


Figure 5: Linearity of Gliclazide by second order derivative spectroscopy.

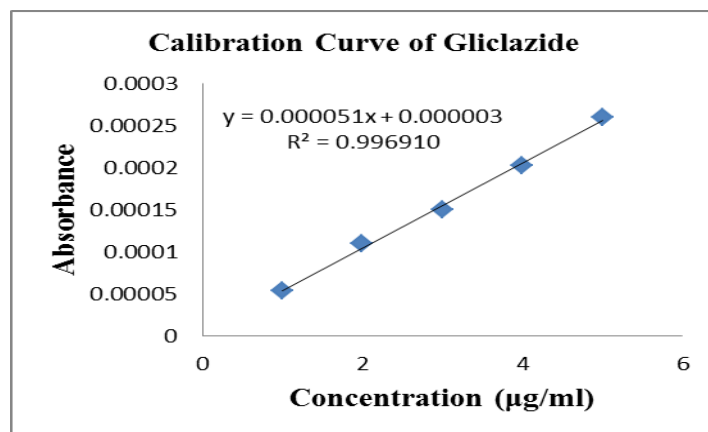


Figure 6: Linearity of Gliclazide by third order derivative spectroscopy.

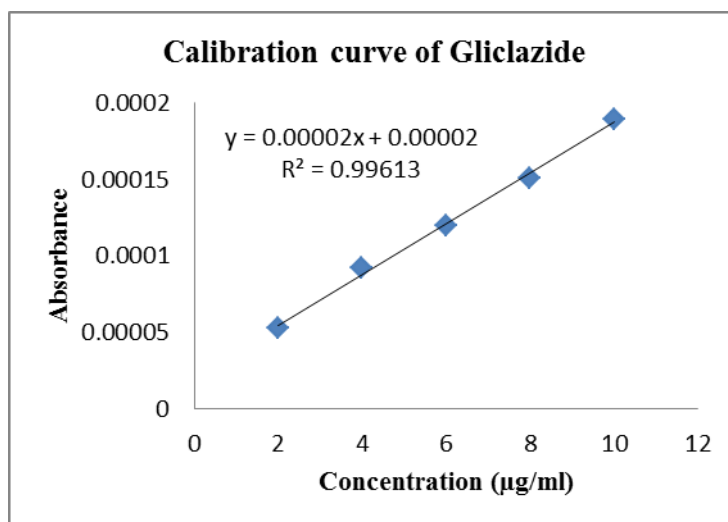


Figure 7: Linearity of Gliclazide by fourth order derivative spectroscopy.

Analysis of marketed formulation

Twenty tablets (Diazone, label claim 80 mg) were made into a fine powder and mixed well. An accurately weighed quantity of the powder equivalent to 10 mg of GLZ was transferred into a 10 ml volumetric flask. Sufficient quantity of methanol was added and sonicated for 20 minutes to allow complete dissolution. The volume was made up to the mark and the solution was then filtered through whatmann filter paper no.40. From the above solution 0.1ml was taken and made up to 10ml with methanol to obtain 10 µg/ml solution. It was then analyzed and percent recovery was determined as summarized in Table 1.

Table 1: Analysis of marketed formulation.

Parameters	Analysis of Marketed Formulation		
	Second Order	Third Order	Fourth Order
Drug Content (%)	98.65	99.05	100.03
± S.D	0.31	0.51	0.43
% R.S.D	0.42	0.60	0.49

RESULTS AND DISCUSSION

The analytical method was validated with respect to parameters such as linearity, precision, limit of detection (LOD), limit of quantitation (LOQ) and accuracy as per ICH guidelines.

Linearity

Standard stock solution was diluted with methanol so as to get the working standard solutions in the concentration range of 2-10 µg/ml and their corresponding absorbances were recorded at 219, 204 and 213 nm respectively. The linearity was calculated by the least square regression method as shown in Table 2.

Table 2: Results of Linearity Study.

Parameter	2 nd Order	3 rd Order	4 th Order
Linearity	2-10 µg/ml	2-10 µg/ml	2-10 µg/ml
λ_{\max} nm	219 nm	204 nm	213 nm
Regression Equation $Y=mx+c$	$Y=0.0005x+0.0008$	$Y=0.000025x+0.000003$	$Y=0.00002x+0.00002$
Correlation Coefficient R^2	0.995	0.996	0.996
Slope(m)	0.0005	0.000025	0.00002
Intercept (c)	0.0008	0.000003	0.00002

Accuracy

To check the accuracy of the proposed method, recovery studies were carried out by applying standard addition method. A known amount of standard GLZ, corresponding to 80, 100 and 120% of the label claim was added to pre-analyzed sample of the tablet. The recovery studies were carried out in triplicate at each level and are shown in Table 3.

Table 3: Recovery Study Data.

Sl.no	Amount of tablet powder (mg)	Amount of pure drug added (mg)	Amount recovered \pm SD	% Recovery	% RSD
1.	10	8	17.95 \pm 0.060	98.70	0.33
		10	19.94 \pm 0.09	99.20	0.45
		12	21.94 \pm 0.131	99.04	0.59

Precision

To check the intra-day and inter-day variation of the method, solutions containing 2, 4 and 6 µg/ml of GLZ were subjected to the proposed spectroscopic method of analysis and the recoveries obtained were noted as shown in Table 4.

Limit of detection (LOD) and Limit of Quantitation (LOQ)

LOD and LOQ were calculated based on the standard deviation of the analytical response and the slope of the calibration curve using the equations $LOD = 3.3 \sigma/S$ and $LOQ = 10 \sigma/S$, where σ is the SD of the response and S is the slope of the calibration curve and the LOD, LOQ values are shown in Table 4.

Table No. 4: Results of Validation Studies of the Proposed Method.

Parameter	2 nd Order	3 rd Order	4 th Order
Limit of detection ($\mu\text{g/ml}$)	0.165	0.132	0.525
Limit of quantitation($\mu\text{g/ml}$)	0.5	0.4	0.9
Precision (n=3)%RSD	0.36	0.38	0.42
	0.16	0.41	0.56
	0.34	0.49	0.51
Inter-day	0.24	0.33	0.39
	0.16	0.42	0.51
	0.40	0.42	0.49

CONCLUSION

The present article describes application of second order, third order and fourth order derivative spectroscopy for the estimation of Gliclazide in tablet dosage forms. The developed method was found to be novel, simple, accurate, precise and rapid for the estimation of Gliclazide. The method is economical and do not require any sophisticated instruments contrast to chromatographic methods. Hence it can be effectively applied for the routine analysis of Gliclazide in bulk and in pharmaceutical dosage forms.

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