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Zero order and first order derivative method development and validation of Gliclazide in its bulk and pharmaceutical dosage form

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ABSTRACT

First-derivative spectrophotometry, applying the peak-zero method, was developed for the determination of Gliclazide in tablets. The solutions of standard and sample were prepared in 0.1N NaOH. Quantitative determination of the drug was performed at 226 nm,217nm for zero order and first order respectively and was evaluated for the parameters specificity, linearity, precision, and accuracy. The specificity test showed that there was no interference from excipients commonly found in the commercial pharmaceutical formulation at 226 nm and 217nm. The standard curve showed a correlation coefficient of 0.99992 for zero order spectroscopy and 0.99999 for first derivative method. Precision was demonstrated by a standard deviation value of 0.838.The recovery test resulted in an average of 100.48%, and 100.64% for zero order and first order respectively which confirmed the accuracy of the method.

Keywords: Gliclazide, First Derivative Spectroscopy, Validation.

INTRODUCTION

Gliclazide is an oral hypoglycemic (anti-diabetic drug) and is classified as a sulfonylurea. Gliclazide binds to the beta cell sulfonyl urea receptor (SUR1)[1]. This binding subsequently blocks the ATP sensitive potassium channels. The binding results in closure of the channels and leads to a resulting decrease in potassium efflux leads to depolarization of the beta cells. This opens voltage-dependent calcium channels in the beta cell resulting in calmodulin activation, which in turn leads to exocytosis of insulin containing secretorty granules[2].Selective and sensitivie analytical method for quantitative determination of drugs and their metabolites are essential for successful evaluation of clinical pharmacology, pharmacokinetics (PK), bioavailability (BA) and bioequivalence (BE) studies [3].Gliclazide is known to possess low

aqueous solubility [4]. Large inter- and intraindividual responses following administration of sulphonylurea (glibenclamide etc.) reparations have also been reported [5-7]. Such variations are undesirable and may expose susceptible patients to the danger of hypoglycaemia or other associated hazards when a patient's therapy is changed from one preparation to another.The objective of this investigation was to device a simple, precise, rapid and economical method for the estimation of Gliclazide in bulk drug and the tablet formulation[8-9].

MATERIALS AND METHODS

Pure drug was procured from Actavis Pharma,Chennai;INDIA.Tablets of one brand procured from the local market were analyzed by the proposed method. In this method, the tablets were crushed and dissolved in 0.1 N NaOH and diluted further. Sufficient amounts of the samples were withdrawn and their absorbances were noted at 226 nm against reagent blank.

Instrument, Chemicals, Reagents

Shimadzu 1700 U.V visible spectrophotometer with 1cm matched quartz cells, and 0.1 N NaOH was used as a solvent for the experiment.

Experimental:

Gliclazide Stock Solution

An accurately weighed quantity of about 10mg of Gliclazide was taken in 100ml volumetric flask, dissolved in sufficient quantity of 0.1N NaOH, sonicated and diluted to100ml with the same so as to get the concentration of 100µg/ml.

Sample solution of pharmaceutical formulation (Tablet)

Sample solution: Twenty tablets of Gliclazide were weighed and powdered in glass mortar. Amount equivalent to 10 mg was transferred to 100 ml volumetric flask, dissolved in sufficient quantity of 0.1 N NaOH, sonicated and made up the volume with same to obtain concentration of 100µg/ml. This solution was then filtered through Whitman filter paper # 41. Further dilutions were made from this stock solution to get required concentration.

Aliquots of 0.5 to 5 ml portions of standard solution of both pure drug and tablet were transferred to a series of 10 ml volumetric flask and volume in each volumetric flask was adjusted to 10 ml with solvent. The absorbances of resulting solutions were measured at required wavelength against reagent blank and calibration curve was constructed.

Zero order spectroscopic method

Determination of λ_{max}

The standard solution of Gliclazide (50µg/ml) was scanned at different concentrations in the range of 200-400 nm and λ_{max} was found to be 226 nm against reagent blank.

Calibration curve for Gliclazide

The absorbances were recorded for 05-50µg/ml at 226 nm (λ_{max}). From this calibration curve was plotted.

First order derivative method

The standard solution of Gliclazide (50µg/ml) was scanned at different concentrations in the range of 200-400nm and the first order derivative spectra showed a sharp peak at 217.0 nm against reagent blank.

Calibration Curve for Gliclazide

The absorbances were recorded for 05-50µg/ml at 217nm in derivative mode. From this calibration curve was plotted.

Figure 1:Spectra of Gliclazide in zero order

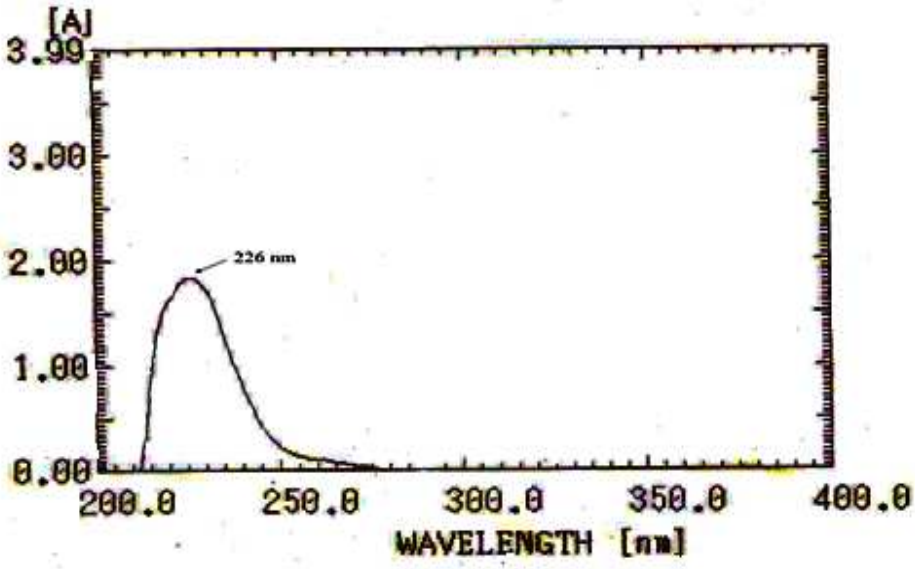

Figure 2: Calibration Curve for Gliclazide

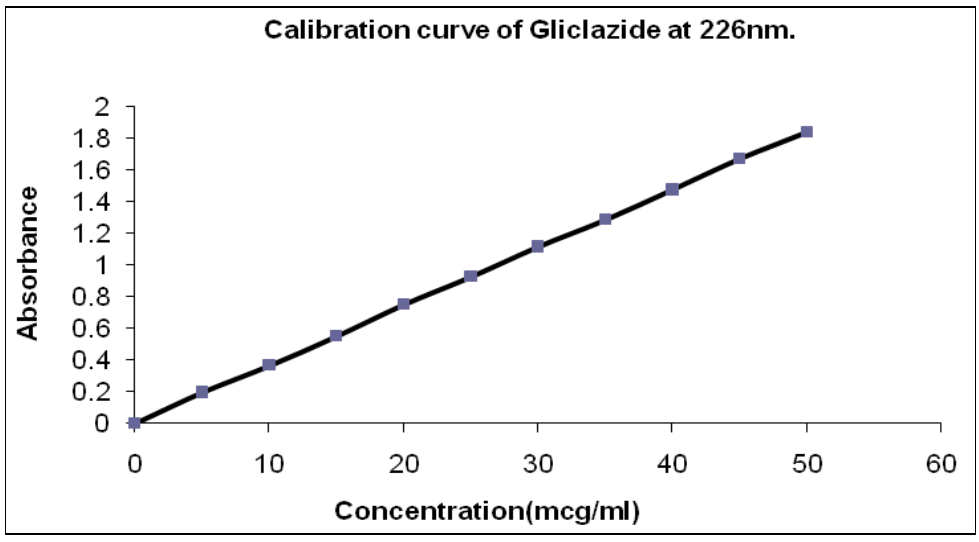

Figure 3: First Order Derivative Spectra of Gliclazide

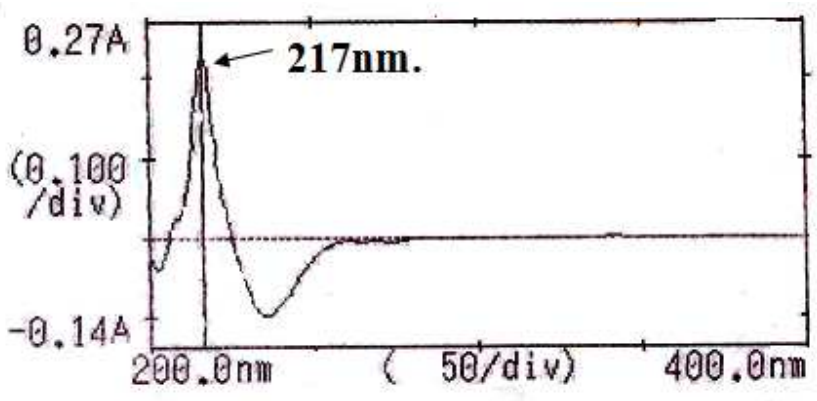

Figure 4: Calibration Curve for Gliclazide

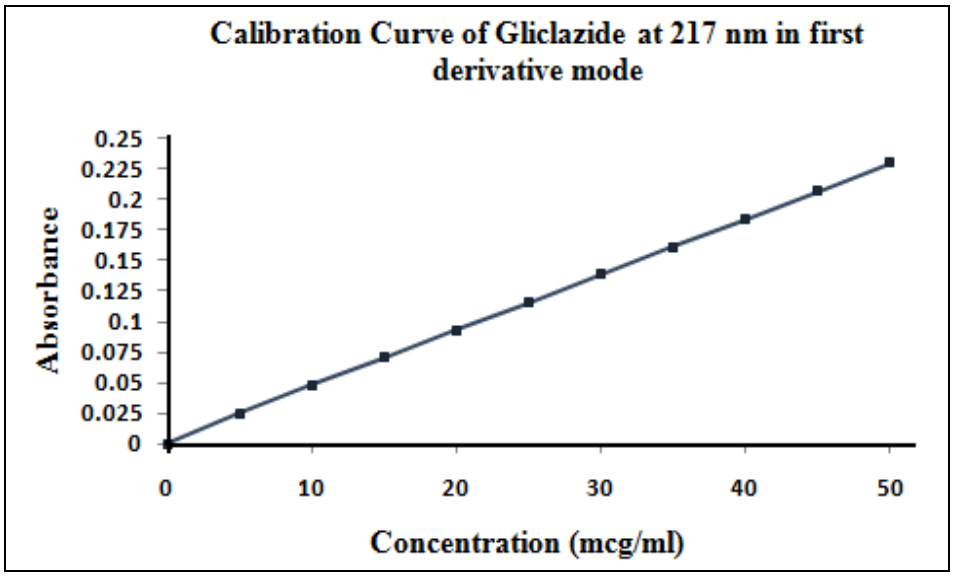

Table 1: Optical Characteristics and Precision

Following are the parameters obtained during the experiment:

Parameters	values
Absorption maxima (nm)	226
Beer's law limit (mcg/ml)	05-40
Correlation coefficient	0.99992
Molar absorptivity (lit/mole/cm)	1.1898×10^{4}
Sandell's sensitivity(mcg/sqcm/0.001)	0.0272
Slope (m)	0.036789
Intercept	0.0054
% COV	0.632
Standard error	0.00194
LOD (µg/ml)	0.40
LOQ (µg /ml)	1.30

Table 2: Results of analysis

Sr.No	Tablet	Label claim (mg/tablet)	Estimated (mg/tablet)	% Estimated	% Recovery*
1	Glizid-40	40	39.92	99.80	100.48

Table 3:Statistical analysis of results

Sr.No	Tablet	SD*	COV (%)*	SE*
1	Glizid-40	0.740	0.7365	0.302

** Mean of six readings*

SD-Standard deviation, COV-Coefficient of Variation, SE- Standard Error.

Table 4:Optical Characteristics and Precision

Following are the parameters obtained during the procedure.

Parameters	values
Absorption maxima (nm)	217
Beer's law limit (mcg/ml)	05-50
Correlation coefficient	0.99999
Molar absorptivity (lit/mole/cm)	0.1466×10^{4}
Sandell's sensitivity(mcg/sqcm/0.001)	0.22068
Slope (m)	0.00453
Intercept	0.00253
% COV	0.302
Standard error	0.000143
LOD (µg /ml)	0.25
LOQ (µg /ml)	0.80

Table 5: Results of analysis

Sr.No	Tablet	Label claim (mg/tablet)	Estimated (mg/tablet)	% Estimated	% Recovery*
1	Glizid-40	40	39.75	99.375	100.64

Table 6: Statistical analysis of results

Sr.No	Tablet	SD*	COV (%)*	SE*
1	Glizid-40	0.838	0.833	0.342

** Mean of six readings*

SD-Standard deviation, COV-Coefficient of Variation, SE- Standard Error.

Method Validation:

Specificity- Pure Gliclazide was spiked with common excipients and assayed by proposed method. It was found that the assay results were unaffected by the presence of such excipients.

Linearity- Linearitywas observedin the range of 05-40 µg/ml and 05-50 µg/ml, for zero order and first order derivative methods respectively. The calibration curve yielded coefficient of correlation (r) 0.99992, 0.99999 for zero order and first order derivative methods respectively.

Sensitivity- High Molar absorptivity and low Sandell's sensitivity for the respective method reveals that all these methods are highly sensitive.

System precision-%COVcalculated from 6 replicate readings (absorbance values) at concentration (20µg/ml) confirm the precision of the method.

Assay results- One marketed formulation of Gliclazide tablets were analysed by proposed methods, the percentage of drug present in the tablet was determined and presented in the table. Assay results obtained are within limit.

Accuracy–The low values of S.D and %COV indicates that method is precise. % recovery was found to be within limit indicates the noninterference from the formulation excipients.

RESULTS AND DISCUSSION

All the methods Zero order and First order derivative methods for the estimation of Gliclazide in tablet dosage were found to be simple, accurate and reproducible. Beer- Lambert's law was obeyed in the concentration range of 5-40 µg/ml for zero order and 5-50 µg/ml for first order derivative methods. The accuracy of the method was assessed by recovery studies at three different levels i.e. 50%, 100%, 150%. The values of standard deviation were satisfactory and the recovery studies were close to 100%. The %RSD value is ≤ 2 indicates the accuracy of the method.

CONCLUSION

Both these methods i.e. zero order and first order derivative methods were found to be simple, sensitive, precise and reproducible. These methods can be used for routine quality control analysis of Gliclazide in bulk and in pharmaceutical formulations.

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