International Journal of Pharmaceutics & Drug Research
ISSN: 2347-6346
Available online at http://ijpdr.com

Original Research Article

SIMPLE COST EFFECTIVE STABILITY INDICATING AND ECOFRIENDLY METHOD FOR THE ESTIMATION OF GLICLAZIDE IN MARKETED FORMULATION BY UV AND HPLC

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***Article History:**

Received: 18/04/2023
Revised:01 /05/2023
Accepted: 22/05/2023

ABSTRACT

This study comprehensively deals with development of a novel and efficient analytical method for the determination of Gliclazide using hydrotopy & stability indicating HPLC. All the methods for examining different parameters were performed according to standard procedure. The correlation coefficients of Gliclazide were found to be 0.999. At 80 & 100% recovery level the % recovery was observed to be 99.00±0.514 & 98.37±1.451 respectively while for 120% recovery level maximum recovery of 99.37±0.406 was seen. The % RSD for 80,100 & 120 recovery level was estimated to be 0.519, 1.475 & 0.409 respectively. The % RSD value was found to be 0.071, 0.301, 0.039, 0.053 for repeatability, day to day, analyst to analyst and reproducibility indicating that the method is precise. The system suitability parameters revealed that hat tailing factor & retention time have value of 0.987±0.020 & 4.204±0.003. The no. of theoretical plates were noted to be 2358.333± & 67.669. Result of linearity of Gliclazide revealed slope & intercept as 50.23 & 9.691. Further at 80, 100 & 120 % recovery level the % Mean±SD was observed to be 98.95±1.159, 99.30 ±0.590 & 99.25±0.485 respectively. Results of precision shown that repeatability, day to day & analyst to analyst variation have % Mean±SD of 99.342±0.240, 99.542±0.071& 99.403±0.074. The robustness of method was calculated as 99.539±0.054. The LOD & LOQ was estimated to be 0.85 & 2.35. The tablet formulation analysis revealed that in 60 mg label claim drug, about 59.78 mg of drug was found. The % Assay & % RSD was noted to be 99.63 & 0.110 respectively. The maximum degradation of drug which is 13.17% with minimum drug recovery of 86.65 was seen in acidic conditions. Thus the proposed approach effectively solubilize Gliclazide & prevents degradation of drug products.

Keywords: Gliclazide, Hydrotropy, Solubility, UV, HPLC, Stability

INTRODUCTION

Diabetes is one of the top causes of death worldwide, with around 422 million (8.5% of the global population) currently diagnosed. It is a multifactorial, chronic, and progressive metabolic condition characterised by chronic hyperglycemia caused by abnormalities in carbohydrate, lipid, and protein metabolism. Persistent hyperglycemia is linked to long-term organ damage, dysfunction, and failure, particularly in the eyes, kidneys, nerves, heart,

and blood vessels (Kumar *et al*., 2020; King *et al*., 1998).

Gliclazide is an antihyperglycemic medication taken orally that is used to treat non-insulin-dependent diabetic mellitus (NIDDM). It has been classed variously based on its pharmacological qualities, with gliclazide designated as a first-generation sulfonylurea due to the presence of a sulfonamide group capable of releasing a proton and the presence of one aromatic group. Gliclazide, on the other hand, is classified as a second-generation sulfonylurea with a higher potency and a shorter half-life based on its pharmacological efficacy. However, as a BCS class 2 medication, it is weakly soluble (Campbell *et al*., 1991; Sarkar *et al*., 2011).

The phenomena of hydrotropic solubilization is the rise in aqueous solubility of poorly water soluble and insoluble medicines. Hydrotropy is one of the approaches that have been used to improve aqueous solubility. The most frequent hydrotropic agents used to improve medication water solubility are sodium salicylate, sodium benzoate, urea, nicotinamide, sodium citrate, and sodium acetate (Patil *et al*., 2021; Asnani *et al*., 2012). This work will explore use of hydrotropic agents, such as urea, nicotinamide, or sodium benzoate, to enhance the solubility of Gliclazide in the aqueous phase. Help in optimization of the concentration of the hydrotropic agent to achieve the maximum solubilization of Gliclazide & the development of a simple, cost-effective, and rapid spectrophotometric or spectrofluorimetric method to quantify Gliclazide in the presence of the hydrotropic agent. It will assist in validation of the hydrotropic method in terms of linearity, precision, accuracy, and robustness as per ICH guidelines.

Next important step is to check the stability of Gliclazide. High performance liquid chromatography (HPLC) is an essential analytical method for determining the stability of pharmaceutical products. HPLC procedures should be capable of separating, detecting, and quantifying the numerous drug-related degradants that can occur during storage or production, as well as detecting and quantifying any drug-related impurities added during synthesis. Forced degradation studies of new chemical entities and medicinal products are required to aid in the development and demonstration of the specificity of such stability indicating methodologies. Forced degradation studies can be performed to determine the breakdown pathways and degradation products that may arise during storage, as well as to aid in formulation, development, manufacturing, and packing (Shah *et al*., 2012; Ngwa,2010). Thus, this study comprehensively deals with Development of a novel and efficient analytical method for the determination of Gliclazide using hydrotopy & stability indicating HPLC.

MATERIALS AND METHODS

Chemicals

Urea, PEG, methanol, ethanol, Distilled water, hydrochloride acid were obtained from Merk india. All solvents & reagents used were of analytical grade.

Method I: Based on the solubility, stability and spectral characteristics of the drug 2M Urea + 2% PEG 4000 + 2% PEG 6000 in the ratio of (2:1:1 v/v/v) was selected as hydrotropic agent. Presence of hydrotropic agent do not shows any significant interference in the spectrophotometric assay thus further confirming the applicability and reproducibility of the developed method.

Linearity

Linearity was established by least squares linear regression analysis of the calibration curve.

Recovery studies

Recovery studies were carried out by applying the method to drug sample to which known amount of Glipizide at three concentration levels of 80, 100 and 120 % were added.

Precision

The precision of the analytical method was studied by multiple sampling of the homogenous sample. The precision was done by measuring the absorbance for six times.

Method II: Stability indicating method development for the estimation of Gliclazide using RP-HPLC. The RP-HPLC method was developed for estimation of Gliclazide in formulation by isocratically using 10mM KH_2PO_4: Methanol in the ratio of 20:80 v/v, Prontosil C-18 column (4.6 x 250mm, 5µparticle size) column as stationary phase and chromatogram was recorded at 254nm. Then developed method was validated by using various parameters.

System Suitability

The system suitability parameter was carried out to verify that the analytical system was working properly and could give accurate and precise result. The six replicates of reference standard Gliclazide 10µg/ml were injected separately and chromatogram were recorded.

Linearity

The linearity of analytical method was carried out to check its ability to elicit test results that are proportional to the concentration of analyte in sample within a given range. Different levels of standard solutions were prepared and injected into the HPLC and the chromatogram was recorded.

Specificity

Specificity of the method was carried out to assess unequivocally the analyte presence of the components that might be expected to be present, such as impurities, degradation products and matrix components.

Accuracy

The validity and reliability of proposed methods were assessed by recovery studies. The recovery of added standards (80%, 100% and 120%) was found at three replicate and three concentrations level.

Precision

Precision was determined by repeatability and Intermediate precision of drug. Repeatability result indicates the precision under the same operating condition over short interval time. The intermediate precision study is expressed within laboratory variation on different days and analyst to analyst variation by different analyst. The value of SD and %RSD are less than 2 indicate the precision of method.

Robustness

The robustness of developed method was checked by changing in the deliberate variation in solvent. This study demonstrates the resilience of the analytical technique, which is a measure of a method's ability to remain unaffected by minor but deliberate modifications in method parameters. Robustness (Table 5) was investigated utilising mobile phase composition, mobile phase pH, flow rate, column temperature, wave length, and injection volume at 100% test concentration (100 lg/mL).

LOD & LOQ

The terms LoD and LoQ stand for limit of detection and limit of quantitation, respectively. LoD is the smallest concentration of an analyte in a test sample that we can easily distinguish from zero, whereas LoQ is the smallest concentration of an analyte in a test sample that we can determine with acceptable reproducibility and accuracy. LOD = 3.3 / S, whereas the limit of quantification (QL, or quantitation limit) is LOQ = 10 / S. Here, S is the slope of the calibration curve and is the standard deviation of the response.

Assay of tablet formulation

The results of the analysis of synthetic mixture were reported. The assay value of drugs was close to 100, SD and % RSD are less than 2 indicate the no interference of excipient in the estimation of drugs.

Forced degradation studies

According to ICH guidelines stability testing is necessary to classify the stability characteristics of active ingredients. Forced degradation studies were carried out to determine the method's stabilityindicating power. Bilastine raw material, finished product, and placebo were subjected to acidic, basic, peroxide, thermal, and photolytic stress experiments at 0.5 mg/ml in the diluent.

Method I

Table 1: Results of Linearity of GLZ

S. No.	Parameter	Results of Linearity
1	Working λ_{max}	230nm
2	Beer's law limit (µg/ml)	2-10
3	Correlation Coefficient (r^2)*	0.999
4	Slope (m)*	0.060
5	Intercept (c)*	0.003

Table 2: Results of Recovery Studies on Marketed Formulations

Recovery Level %	% Recovery (Mean±SD)*	% RSD
80	99.00±0.514	0.519
100	98.37±1.451	1.475
120	99.37±0.406	0.409

Table 3: Results of validation (%R.S.D.)

Parameter		Mean±SD	% RSD
Precision (%R.S.D.)*	Repeatability	98.425±0.070	0.071
	Day to Day	96.869±0.270	0.301
	Analyst to Analyst	98.955±0.038	0.039
	Reproducibility	98.542±0.052	0.053

Table 4: Results of system suitability parameters

Parameters	% Mean±SD*
No. of Theoretical Plates	2358.333±67.669
Tailing Factor	0.987±0.020
Retention time	4.204±0.003

Method II

Table 5: Results of linearity of Gliclazide

Parameter	Gliclazide
Concentration (µg/ml)	5-25
Correlation Coefficient (r^2)*	0.999
Slope (m)*	50.23
Intercept (c)*	9.691

Table 6: Results of recovery study

% Level	% Mean±SD*
80%	98.95±1.159
100%	99.30±0.590
120%	99.25±0.485

Table 7: Results of precision

Parameter	% Mean±SD*
Repeatability	99.342±0.240
Day To Day	99.542±0.071
Analyst to Analyst	99.403±0.074

Table 8: Results of Robustness

Parameter	% Mean±SD*
Robustness	99.539±0.054

Table 9: Results of LOD and LOQ

Name	LOD (µg/ml)	LOQ (µg/ml)
Gliclazide	0.85	2.35

Table 10: Analysis of tablet formulation

	Gliclazide *
Label Claim (mg)	**60mg**
% Found (mg)	59.78
% Assay	99.63
% RSD	0.110

Table 11: Results of Forced degradation studies of GLZ

Stress conditions	Drug recovered (%)	Drug decomposed (%)
Standard drug	99.82	0
Acidic hydrolysis	86.65	13.17
Alkaline hydrolysis	92.23	7.59
Oxidative degradation	90.45	9.37
Thermal degradation	90.85	8.97

RESULTS AND DISCUSSION

The Linearity was established by least squares linear regression analysis of the calibration curve. The calibration curve was linear over the concentration range of 2-10µg/ml and correlation coefficients were found to be 0.999 for Gliclazide and the slope & intercept was noted to be 0.060 & 0.003 respectively.

Recovery studies were carried out by applying the method to drug sample to which known amount of Gliclazide at three concentration levels of 80, 100 and 120 % were added. At 80 & 100% recovery level the % recovery was observed to be 99.00±0.514 & 98.37±1.451 respectively while for 120% recovery level maximum recovery of 99.37±0.406 was seen. The % RSD for 80,100 & 120 recovery level was estimated to be 0.519, 1.475 & 0.409 respectively. The precision of the analytical method was studied by multiple sampling of the homogenous sample. The precision was done by measuring the absorbance for six times. The % RSD value was found to be 0.071, 0.301, 0.039, 0.053 for repeatability, day to day, analyst to analyst and reproducibility indicating that the method is precise.

The system suitability parameters revealed that hat tailing factor & retention time have value of 0.987±0.020 & 4.204±0.003. The no. of theoretical plates were noted to be 2358.333± & 67.669. Result of linearity of Gliclazide revealed slope & intercept as 50.23 & 9.691.

Further at 80, 100 & 120 % recovery level the % Mean±SD was observed to be 98.95±1.159, 99.30 ±0.590 & 99.25±0.485 respectively. Results of precision shown that repeatability, day to day & analyst to analyst variation have % Mean±SD of 99.342±0.240, 99.542±0.071 & 99.403±0.074. The robustness of method was calculated as 99.539±0.054. The LOD & LOQ was estimated to be 0.85 & 2.35.

The tablet formulation analysis revealed that in 60 mg label claim drug, about 59.78 mg of drug was found. The % Assay & % RSD was noted to be 99.63 & 0.110 respectively. The data from forced degradation studies revealed that acidic hydrolysis leads to maximum degradation of drug which is 13.17% with minimum drug recovery of 86.65. Secondly, Oxidative degradation plays major contribution in degradation with 9.37% of drug decomposed & 90.45% recovered. In case of higher temperature about 8.97% of drug was totally decomposed & 90.85% was recovered. The minimum degradation of 7.59% was seen in alkaline conditions with 92.23% drug recovery.

CONCLUSION

Gliclazide was successfully analysed using UV Visible Spectrophotometry. The developed method improves the solubility of both water-insoluble drugs, and there was no involvement of urea in the estimation, so we investigated that two UV spectroscopy techniques were established to be simple, accurate, inexpensive, and quick for concurrent estimation of Gliclazide bulk and tablet dosage forms. Using these spectroscopy techniques, multiple dose forms comprising Gliclazide may be easily analysed.

Further a method for determining Gliclazide in tablets that indicates stability was successfully established. The approach demonstrated adequate linearity, accuracy,

precision, sensitivity, selectivity, and durability. Gliclazide was found to be highly stable, with the greatest deterioration in acidic solution. It was demonstrated that the proposed approach effectively separated Gliclazide from its principal degradation products generated under acidic conditions. The approach also offers the advantage of using an aqueous system rather than potentially harmful organic solvents, as well as requiring fewer sample preparation procedures.

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

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