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NOTE

Spectrophotometric Estimation of Glibenclamide

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Two simple and sensitive spectrophotometric methods are developed for the quantitative estimation of glibenclamide in pure and pharmaceutical formulations. Both methods are based on the formulation of coloured oxidative coupling product with *p*-N,N-dimethyl phenylene diamine (DMPD) and chloramine-T (CAT) or 2,6-dichloroquinone chlorimide (DCQC) exhibiting maximum absorption at 535 and 530 nm respectively.

Key Words: Spectrophotometric estimation, Glibenclamide.

Glibenclamide (GBC)[1] is an antidiabetic agent and belongs to the class sulfonyl urea. Chemically it is 10[4-[2-(5-chloro-2-methoxy benzamide ethyl] benzene sulphonyl]-3-cyclohexyl urea. A few methods were reported for the estimation of GBC. The methods so far reported are HPLC[2], UV[3] and colorimetry[4].

A Systronic UV-Visible spectrophotometer-117 with 10 mm matched quartz cells was used for spectral and absorbance measurements. All the chemicals were of analytical grade and all the solutions were prepared in triply distilled water.

Preparation of standard and sample solutions

The stock solution (1 mg/mL) was prepared by dissolving 100 mg of pure glibenclamide in 10 mL of methanol, 10 mL of (1 : 1) methanolic HCl (5 N) was added and refluxed by keeping in water bath for 1 h. The solution was cooled, the excess of HCl was removed by vacuum and the residue was washed with methanol 3–4 times. Then the residue was dissolved in 10 mL of 0.01 NaOH and diluted to 100 mL with distilled water. This solution was further diluted with distilled water to obtain the working standard of HGBC solution of concentration 50 μg/mL.

Assay procedures

Method A: An aliquot of HGBC solution (0.5–2.5 mL, 50 μg/mL), 1.0 mL of *p*-N,N-dimethyl phenylene diamine dihydrochloride (0.05%) solution and 1.0 mL of chloramine-T (0.02%) solution were taken in 10 mL volumetric flasks; the flasks were kept aside for 10 min and made up to the mark with distilled water. The absorbance was measured at 535 nm against a reagent blank within 30 min and the amount of the drug was estimated from a calibrated graph.

Method B: Aliquots of HGBC solution (0.5–2.5 mL, 50 μg/mL) were introduced into a series of 10 mL calibrated tubes, 1 mL of 2,6-dichloroquinone-chlorimide (0.2%) was added to each tube, mixed well and the total volume in each tube was adjusted to 8.0 mL with isopropanol. Then the tubes were heated on a boiling water bath for 10 min, cooled and made up to the volume with isopropanol. The absorbance was measured at 530 nm against a reagent blank within 60 min. The amount of HGBC was then determined from the calibration curve.

Beer's law limits, Sandell's sensitivity, molar extinction coefficient, per cent relative standard deviation (calculated from eight measurements containing 3/4th of the amount of the upper Beer's law limits), correlation coefficient, % range of error (0.05 and 0.01 confidence limits) and detection limits are given in Table-1.

TABLE-1
OPTICAL CHARACTRISTICS AND PRECISION OF THE PROPOSED METHODS FOR GBC

Parameter	Method A	Method B
λ_{max} (nm)	535	530
Beer's law limits (μg/mL)	2.5–12.5	2.5–12.5
Detection limits (μg/mL)	1.131	0.072
Molar absorptivity (L $mol^{-1}cm^{-1}$)	2.43×10^4	2.18×10^4
Sandell's sensitivity (μg cm^{-2}/0.001 absorbance unit)	0.020	0.023
Regression equation (Y = a + bC):		
Slope (b)	4.87×10^{-2}	4.42×10^{-2}
Intercept (a)	1.80×10^{-3}	1.00×10^{-4}
Correlation coefficient (r)	0.9999	0.9999
Relative standard deviation (%)*	0.323	0.642
% Range of error (Confidence limits)*:		
0.05 level	0.270	0.536
0.01 level	0.399	0.794

* Average of eight determinations.

p-N,N-dimethyl phenylene diamine dihydrochloride reacts initially with chloramine-T to produce highly reactive and less stable *p*-benzoquinone diamine derivative, which may further react with the phenolic coupler (HGBC) by electrophilic attack in the most nucleophilic site on the benzene ring of the coupler (*i.e.*, *p*-position to the phenolic hydroxyl; if *p*-position is blocked, *o*-position to the phenolic hydroxyl). The resulting leucodye is oxidized to indodye.

The highly reactive 2,6-dichloroquinone-chlorimide (DCQC) reacts with phenolic coupler (HGBC) by electrophilic site on the benzene ring of the coupler (*i.e.*, *p*-position to the phenolic hydroxyl; if *p*-position is blocked, *o*-position to the phenolic hydroxyl) to form coloured indophenol.

Pharmaceutical formulations of glibenclamide were analyzed by the proposed methods. The results obtained by the proposed and reported methods were presented in Table-2. To evaluate the validity and reproducibility of the method, known amounts of pure drug were added to previously analyzed samples and the mixtures were analyzed by the proposed method. Interference studies revealed that the excipients present in the pharmaceutical preparations do not interfere in the proposed method.

TABLE-2
ASSAY AND RECOVERY OF GLIBENCLAMIDE IN DOSAGE FORMS

Method	Sample	Labelled amount (mg)	Methods		Proposed method % recovery
			Reported method[R] (mg)	Proposed method (mg)	
A	Tablets I	5	5.00	4.99	100.5
	Tablets II		5.01	5.02	99.78
B	Tablets I	10	10.0	10.01	100.2
	Tablets II		10.0	10.03	100.2

[R] Reference was the UV method developed in our laboratory.

The results indicate that the proposed method is simple, sensitive and can be used for the routing determination of glibenclamide in pharmaceutical preparations.

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