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SPECTROPHOTOMETRIC METHODS FOR THE DETERMINATION OF SILDENAFIL IN TABLETS : PART-III

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ABSTRACT

Two simple and sensitive spectrophotometric methods for the determination of sildenafil in bulk and pharmaceutical dosage forms are described. The methods involve formation of charge transfer complexes of the drug with chloranilic acid (method A) and chloranil (method B). The absorption maxima and Beer's law linearity range for method A are 430 nm; 10-60 mg/mL and for method B are 540 nm; 20-120 mg/mL, respectively. When pharmaceutical preparations containing sildenafil (tablets) were analysed, the results obtained by the proposed methods are in good agreement with the labeled amounts. Recovery is 98-101%.

Kcy words : Spectrophotometric, Sildenafil.

INTRODUCTION

Sildenafil (SDF) is [(1-[4-ethoxy-3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-H-pyrozolo-[4,3-d]pyrimidin-5-yl) phenyl sulphonyl] – 4 - methyl piperazine[1]. It is indicated for the treatment of erectile dysfunction in men[2]. It is a new drug and is not official in any of the pharmacopoeia. Literature survey revealed the presence of two reverse phase HPLC[3,4] methods and two visible spectrophotometric[5,6] methods for its estimation. The first reported spectrophotometric method is based on oxidative coupling reaction of the hydrolysed SDF with metol and iodine. The second reported method is based on the diazotization of the drug with sulfanilic acid in presence of sodium hydroxide. The functional groups of the drug have not been fully exploited. Hence as a part of our continuing efforts to develop simple and selective visible spectrophotometric analytical procedures for bulk drugs and their formulations, attention was focused on SDF molecule, keeping in view the relative lack of such methods for its estimation. This paper presents two procedures for the estimation of SDF using chloranilic acid

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(3,6-dichloro-2,5-dihydroxy benzoquinone) and chloranil are described. Both the methods involve the formation of colored charge-transfer complexes. The formation of outer complexes or electron donor-acceptor (EDA) complexes between quinones and amines is well known. This famous reaction forms the basis for both the methods.

EXPERIMENTAL

Instruments

An Elico SL 171 spectrophotometer with 1 cm matched quartz cell was used for absorbance measurements. Elico L1-120 digital pH meter was used for pH measurements.

Reagents

a) Chloranilic acid (CDH, 0.1%) -100 mg of the reagent was dissolved in 80 mL of chloroform and 20 mL of isopropyl alcohol.

b) Chloranil (BDH, 0.1%) -100 mg of the reagent was dissolved in 100 mL of 1,4-dioxane.

Chloroform, 1,4-dioxane and dimethyl formamide were obtained from Qualigens.

Preparation of standard drug solution

A standard drug solution of SDF containing 1 mg/mL was prepared by dissolving 100 mg of pure drug in 100 mL distilled water. The free base released after mixing 50 mL of the above stock solution of SDF and 5 mL of 10% NaOH solution was extracted in a separating funnel with 3 x 15 mL portions of chloroform and combined chloroform layer was brought upto 50 mL with chloroform to obtain 1 mg/mL of SDF in free base form. This free base stock solution was further diluted stepwise with chloroform to obtain a working standard solution of SDF of 100 mg/mL (method A) and 200 mg/mL (method B), respectively.

Preparation of sample drug solution

Two brands of commercial tablets were analyzed by the proposed methods. In each method drug equivalent to 100 mg of SDF was dissolved in 100 mL distilled water and treated with 5 mL of 10% NaOH and extraction carried out with chloroform as mentioned in the preparation of standard drug solution. The amount of SDF present in the sample drug solution was found out by carrying out the procedure as mentioned in the standard drug assay and computed from standard calibration curve.

Assay procedure

Method A

Aliquots of standard drug solution, 1-6 mL (100 mg/mL, drug in the free base form) were taken in a series of 10 mL volumetric flasks and 2 mL of chloranilic acid was added and the

flask were kept aside for 5 min and the volume was made upto 10 mL with chloroform in each flask and the absorbance was measured at 535 nm against a reagent blank. The amount of SDF present in the sample drug solution was obtained from the calibration plot.

Method B

Aliquots of standard drug solution, 1-6 mL (200 mg/mL, drug in the free base form) were taken in a series of 10 mL volumetric flasks and 1 mL of chloranil was added and the volume in each flask was made upto 10 mL with dimethyl formamide. It was heated for 15 min at 65°C, Then cooled for 30 min, the absorbance was recorded at 620 nm against a reagent blank. The amount of SDF present in the sample drug solution was obtained from the calibration plot.

RESULTS AND DISCUSSION

The optical characteristics and absorption parameters together with the regression equation for the calibration plot are given in Table 1. In order to confirm the suitability of the proposed method, recovery experiments were carried out by adding a known amount of SDF to the previously analyzed samples and proposed methods were followed. The excipients present in the formulations do not interfere in the estimations.

Table 1. Optical characteristics and precision of the proposed methods.

Parameter	Method A	Method B
λmax (nm)	430	540
Beer's law Limit (mg/ mL.)	10-60	20-120
Molar absorptivity ($Lmol^{-1}$ cm^{-1})	3.92×10^4	8.14×10^4
Sandell's sensitivity ($mg\ cm^{-2}$ per 0.001 absorbance unit)	0.010	0.0480
Regression equation (y = a + bC)*		
Slope (b)	0.035	0.010
Intercept (a)	0.0018	0.0015
Correlation coefficient (r)	0.9999	0.9998
Relative standard deviation (%)**	0.31	0.71
% Range of error (confidence limits - 95%)**	0.139	0.653

* Y = a + bC, where C is concentration of analyte and Y is absorbance unit,
** average of six determinations.

The accuracy of the methods was confirmed by comparing the results obtained by the proposed methods with the reported spectrophotometric method. The results are summarized in Table 2. The results of the proposed methods, when compared with the reported method shows good agreement.

Table 2. Assay of SDF in pharmaceutical formulations by the proposed methods

Drug*	Label Claim mg/tablet	Amount found by Proposed Methods ** (mg)		Reference Method[6] (mg)	% Recovery by proposed methods ***	
		Method A	Method B		Method A	Method B
Tablet	25	24.8	24.9	24.8	99.08 ± 0.12	99.9 ± 0.1
Tablet	50	49.8	49.8	49.8	99.09 ± 0.18	99.09 ± 0.19
Tablet	100	99.9	99.7	99.8	99.08 ± 0.12	9.09 ± 0.13

* Drugs from different pharmaceutical companies.
** Average ± standard deviation of 6 determinations;
*** Recovery of 10 mg added to the preanalysed pharmaceutical dosage forms (average of 3 determinations).

Chemistry of colored species

Amines are good electron donors and quinones are good electron acceptors[7-11]. Since both the donor and acceptor are often very reactive, chemical reaction can occur between them. The complexes are usually characterized by an intermolecular charge-transfer absorption band, which often appears in the visible region. The energy of the band for a given complex agrees well with the electron donating and accepting properties of the two components[12]. Chloranilic acid has been used for the determination of metal ions[13,14] and alkaloids[15]. Substituted quinones like chloranil[16] has been used in the study of amines.

The proposed methods are simple, accurate and reproducible and can be used for routine determination of SDF in bulk and in pharmaceutical formulations.

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