Int. J. Chem. Sci. : 1 (3), 2003, 221–224

SPECTROPHOTEMETRIC METHODS FOR THE DETERMINATION OF SILDENAFIL IN TABLETS–PART II

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ABSTRACT

Three simple and accurate visible spectrophotometric methods for the quantitative determination of sildenafil in either pure from or in pharmaceutical formulations are proposed. Method A is based on the reaction of the drug with 2,6–dicloroquinone–4–chlorimide (DCQC: Gibb's reagent). Method B is based on the formation of yellow colored ion–pair association complex of the drug with acidic dye, tropaeolin '00' in acidic medium. The ion–pair complex formed is quantitatively extracted into chloroform under experimental conditions and estimated by spectrophotometry. The absorption maxima and Beer's law linearity ranges are, method A – 470 nm; 20–120 μg / mL; method B – 420 nm; 20–160 μg / mL. The optimum reaction conditions and other analytical parameters are statistically evaluated and by recovery studies. The results obtained are reproducible with coefficient of variation less than 1.0%.

Key words : Sildenfil, Spectrophotometric method

INTRODUCTION

Sildenafil (SDF) is chemically [(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. This paper describes two methods for the estimation of SDF in pharmaceutical formulations. Method A utilizes the oxidative coupling reaction of SDF with DCQC, the well known Gibb's reagent[7], to produce a chromophore with λ_{max} at 460 nm. Method B consists of extractive spectrophotometry of drug with acidic dye, tropaeolin '00'

resulting in chloroform extractable yellow ion–association complex with λ_{max} at 420nm. Extractive spectrophotometric procedures are normally adopted for the assay of drugs because of higher sensitivity, reproducibility and accuracy of the methods. Usually extractive methods have higher λ_{max}8 and less interference[9] from the associated impurities. 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.

EXPERIMENTAL

Instruments

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

Reagents

Aqueous solutions of DCQC (0.2% w/v) and tropaeolin '00' (0.1% w/v) were prepared in distilled water, filtered and used. Buffer solution of potassium hydrogen phthalate of pH 2.4–4.0 was prepared as per Briton and Robinson method[10]. pH 9.4 borate buffer was prepared by mixing 250 mL, 0.2 m boric acid with 160 mL, 0.2 m NaOH and diluted to 1000 mL with distilled water. The pH was adjusted to 9.4.

Preparation of standard drug solution

A standard drug solution of SDF containing 1mg / mL was prepared by dissolving 100 mg of pure drug in 100 mL distilled water. From this, working standard solutions were prepared by dilution with distilled water, method A–500 µg/mL; method B–200 µg/mL.

Preparation of sample drug solution

In each method, drug equivalent to 100 mg of SDF was dissolved in 50 mL distilled water, the contents are shaken, filtered and volume made up to 100 ml with distilled water to give 1mg/ mL solution. This solution was suitably diluted with distilled water as in standard drug solution preparation.

Assay Procedure

Method A

Aliquots of standard drug solutions 1.0–6.0 mL, 500 µg/mL were transferred into a series of 25 mL volumetric flask and 5.0 mL of pH 9.4 buffer solution was added. Then 2.0 mL of DCQC solution was added and the flasks were kept aside for 10 m and they were diluted to mark with distilled water. The absorbances of the colored solutions were measured at 460 nm during next 10 m against a reagent blank prepared simultaneously.

Method B

Aliquots of standard drug solutions 1.0–8.0 mL, 200 µg/mL were transferred into a series of separating funnels, 4.0 mL of buffer pH 2.4–4.0 and 2.0 mL of tropaeolin dye solution were added successively and the volume of aqueous phase was adjusted to 10 mL with distilled water and to each separating funnel, 10 mL of chloroform was added and the flasks were shaken for 5 m and layers were allowed to separate. The chloroform layers were collected and absorbance measured at 420 nm against the reagent blank prepared simultaneously. The amount of SDF present in sample solution was computed from the respective calibration curves.

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.

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 show good agreement.

Table 1. Optical characteristics and precision of the proposed methods

Parameter	Method A	Method B
$\lambda_{max\ (nm)}$	470	420
Beer's law Limit (µg/ mL)	20–120	20–160
Molar absorptivity ($Lmol^{-1}\ cm^{-1}$)	1.04×10^4	1.03×10^4
Sandell's sensitivity (mg cm^{-2} per 0.001 absorbance unit)	0.027	0.010
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 (%)**	0.323	0.781
% 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.

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	99.09 ± 0.10
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	99.09 ± 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).

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

ACKNOWLEDGEMENTS

The authors thank Sun Pharmaceuticals for providing the gift sample of Sildenafil. One of the authors, GVS is thankful to Bapatla Education Society, Bapatla for providing the necessary research facilities.

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Accepted : 2.5.2003