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SPECTROPHOTOMETRIC METHODS FOR THE DETERMINATION OF SILDENAFIL IN TABLETS–PART–I

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ABSTRACT

Two simple and sensitive spectrophotometric methods (A–B) in visible region have been developed for the determination of sildenafil. The reactions in both the methods (A–B) are stoichiometric oxidations when the drug is treated with an excess of oxidant (Nitrous acid (HNO_2), method A; N–Bromosuccinimide (NBS), method B. The unreacted oxidant is then estimated colorimetrically using an oxidisable dye (cresyl fast violet acetate (CFVA), method A; Celestine blue (CB), method B. Beer's law limits for methods A & B are 4 – 20 µg/mL and 8–40µg/mL, respectively. No interference was observed from tableting additives and the applicability of the methods was examined by analyzing tablets containing sildenafil.

Key words: Spectrophotometry, Sildenafil

INTRODUCTION

Sildenafil (SDF) chemically 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 for estimation of SDF is based on reaction of the drug with sodium nitroprusside forming a charge transfer complex. The second reported method is based on extraction spectrophotometry leading to chloroform soluble ion association complex with an acidic dye, alizarin red. Apart from being too general one, these procedures suffer from the disadvantage of low absorption maxima (470nm). More over the analytically useful functional groups in SDF namely amide and tertiary amino group have not been fully exploited.

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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 involving the oxidation of SDF. Both the methods are indirect procedures involving the addition of excess oxidant and determination of the unreacted oxidant by measuring the decrease in absorbance of dye as suggested by Sastry *et al.* HNO_2 / CFVA[7] and NBS / CB[8].

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

1. Sodium Nitrite ($NaNO_2$) (0.2%) – 200 mg in 100 mL distilled water
2. Cresyl fast violet acetate – (CFVA) (0.01%) – 10 mg dissolved in 100 mL distilled water.
3. N–Bromosuccinimide (NBS) (0.1%) – 100 mg dissolved in 100 mL distilled water and filtered, if necessary.
4. Celestine blue (CB) (0.2%) – 200 mg dissolved in 100 mL distilled water.
5. HCl (5M) – 217.5 mL of concentrated hydrochloric acid dissolved in 500 mL of distilled water.

Preparation of Standard Drug Solution

In method A, 100 mg of SDF was accurately weighed and treated with 10 mL of 1M $NaNO_2$ solution and the contents were mixed well and kept at room temperature for 10 min. Subsequently the solution was treated with 1M HCl for bringing down the pH to almost neutrality (6.5 – 7.0) and then diluted with distilled water to 100 mL to obtain a 1mg /ml HSDF stock solution. In method B, 100 mg of pure SDF was dissolved in 100 mL distilled water to get a stock solution of 1mg /mL. Working standard solutions (100 µg/mL for method A and 200 µg/mL for method B) were obtained by appropriate dilution of the stock solutions with distilled water and sample solutions for tablets were prepared exactly in the same manner as given under the standard solutions with prior filteration, if necessary before making up the final volume and analysed as described for pure samples.

Assay Procedure

Method A

To aliquots of hydrolysed solution of SDF (1–5 mL, 100 µg/mL) taken into a series of 25 mL volumetric flasks, 1.25 mL of 5.0 M HCl and 2.0 mL of $NaNO_2$ (20 µg/mL) were added and

the volume was made up to 15 mL with distilled water. After 3 min, 10.0 mL of CFVA was added, mixed thoroughly and the absorbences were measured after 5 min at 560 nm against distilled water. Blank experiment was carried out in a similar manner omitting the drug. The decrease in absorbance corresponding to consumed HNO_2, which in turn to drug concentration was obtained by subtracting the absorbance of the blank solution from that of the test solution. The amount of drug present was calculated from its calibration graph.

Method B

To aliquots of compound SDF solution (1.0–5.0 mL, 200 μg/mL) taken into a series of 25 mL calibrated flasks, 1.25 mL of 5.0 M HCl, 2.0 mL of NBS were added and the volume was made up to 20.0 mL in each flask. After 15 min, 5.0 mL of CB was added and mixed thoroughly. After 5 min, the absorbances were measured at 540 nm against distilled water. The blank (omitting drug) and the dye (omitting drug and oxidant) solutions were prepared in a similar manner and their absorbances corresponding to consumed NBS and in turn to drug concentration, were obtained by subtracting the decrease in absorbance of test solution (dye–test) from that of the blank solution (dye–blank). The amount of drug was calculated from its calibration graph.

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 method was followed. The excipients present in the formulation do not interfere in the estimation.

Table 1. Optical Characteristics and Precision of the Proposed Methods

Parameter	Method A	Method B
λ_{max} (nm)	560	540
Beer's law Limit (μg/mL)	4–20	8–40
Molar absorptivity (L mol^{-1} cm^{-1})	1.59×10^4	2.01×10^4
Sandell's sensitivity (mg cm^{-2}per 0.001 absorbance unit)	0.007	0.009
Regression equation (y = a + bC)* Slope (b)	7.3×10^{-4}	2.31×10^{-4}
Intercept (a)	6.1×10^{-4}	6.12×10^{-3}
Correlation coefficient (r)	0.9999	0.9999
Relative standard deviation (%)**	0.60	0.51
% Range of error (confidence limits – 95%)**	0.70	0.71

* 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 1 (A)	50	49.1	49.5	49.5	99.8	99.7
Tablet 2 (B)	100	99.3	99.2	99.3	99.2	99.6

*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 accuracy of the method was confirmed by comparing the results obtained by the proposed method with the reported spectrophotometric method. The results are summarized in Table 2. The results of the proposed method when compared with the reported method shows good agreement. The results indicate that the proposed method is simple, inexpensive, accurate and reproducible and can be used for the routine determination of SDF in bulk drugs and its dosage forms.

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