Spectrophotometric Estimation of Sildenafil Citrate in Tablets

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Accepted 27 December 2005
Revised 4 March 2005
Received 3 July 2004

Two simple, accurate, rapid and sensitive methods have been developed for the estimation of sildenafil citrate in health care medicines. The method A is based on reduction of ferric ions to ferrous ions by the drug, which further in presence of potassium ferricyanide as oxidizing agent produces blue colored complex measured at 715 nm against reagent blank. The chromogen obeyed linearity over the range of 10 to 70 μg/ml of drug. The method B is based on reduction of ferric ions to ferrous ions by the drug, which further in presence of potassium dichromate as oxidizing agent produces greenish blue colored complex measured at 700 nm against reagent blank. The chromogen obeyed linearity over the range of 50 to 130 μg/ml of drug.

Sildenafil citrate[1,2] which is used in the therapy of erectile dysfunction, chemically is 1-[[3-(4,7-dihydro-1-methyl)-7-oxo-3-propyl-1H-pyrazolo[4,3-d]-pyrimidin-5-yl)-4-ethoxy phenyl]sulfonyl)-4-ethylpiperazine citrate. Literature survey reveals determination of sildenafil citrate by HPLC[3-5], liquid chromatographic[6] methods and no colorimetric method for determination of sildenafil citrate in health care medicines. The present work describes two simple colorimetric methods for the estimation of sildenafil citrate in tablet formulations. The estimation is based on reduction of ferric ions in its salt to ferrous ions by the drug which further in presence of oxidizing agents like of potassium ferricyanide (method A) and potassium dichromate (method B) produce blue (715 nm) and greenish blue colored complex (700 nm), respectively (fig.1).

A Systronics spectrophotometer 106 with 1cm-matched cuvettes was used for spectrophotometric estimation. Ferric nitrate reagent (5% in 5% nitric acid solution), potassium ferricyanide (0.3% in distilled water) and potassium dichromate (0.3% in distilled water) were freshly prepared. The standard drug solution (500 μg/ml) was prepared by dissolving 50 mg of sildenafil citrate in methanol and final volume was made to 100 ml with the same.

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Ten tablets of sildenafil citrate (each tablet containing 50 mg and 100 mg of drug) were weighed and powdered in a glass mortar. The amount equivalent to 50 mg of sildenafil citrate was transferred to separate 100 ml volumetric flask, dissolved and prepared in the same way as standard solution. One milliliter of standard solution was transferred to ten separate test tubes, in which ferric nitrate reagent (0.2 to 2.0 ml for method A and 0.1 to 1.0 ml for method B), 2 ml of potassium ferricyanide (method A) and potassium dichromate (method B) were added. The test tubes were heated on boiling water bath for 1.5 min for reaction to complete and then cooled. The volume in each test tube was adjusted to 10 ml with distilled water. The absorbance of the solution in each test tube was measured at 715 nm (method A) and 700 nm (method B) against reagent blank.

One mililitre of standard solution was transferred to ten separate test tubes in which ferric nitrate reagent (0.4 ml for method A and 0.2 ml for method B) 0.3 to 3.0 ml of complexing agent (potassium ferricyanide for method A and potassium dichromate for method B) were added. Then the same procedure was followed as mentioned in optimization of ferric nitrate.

Drug reagent complex solutions were prepared as mentioned above with ferric nitrate (0.4 ml for method A and 0.2 ml for method B), 2.7 ml potassium ferricyanide (method A) and 2.2 ml potassium dichromate (method B).

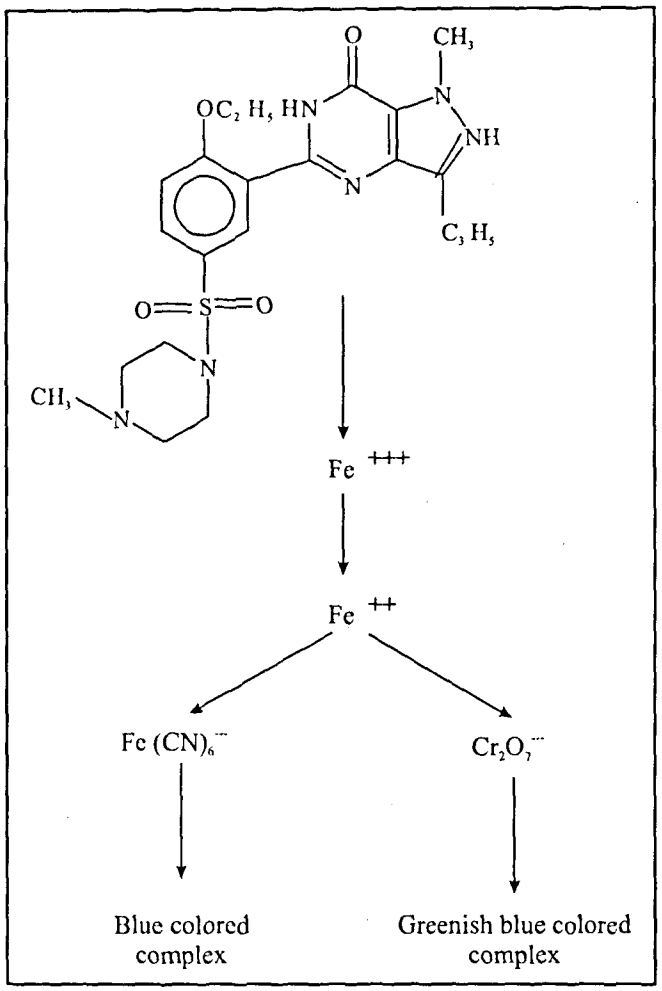

Fig. 1: Proposed mechanism for reaction of sildenafil citrate with reagents.

The absorbance of solution is measured at 715 nm (method A) and 700 nm (method B) at the interval of 15 min for 2.5 h.

Aliquots (0.2 ml to 1.4 ml for method A and 1.0 to 2.6 ml for method B) of standard solution were transferred to series of 10 ml corning test tubes. To each test tube, ferric nitrate reagent (0.4 ml for method A and 0.2 ml for method B), 2.7 ml potassium ferricyanide (method A) and 2.2 ml potassium dichromate (method B) were added. The test tubes were heated on a boiling water bath for 1.5 min for reaction to complete and then cooled. The volume of each test tube was adjusted to 10 ml with distilled water. The absorbance of the solution in each test tube was measured at 715 nm (method A) and 700 nm (method B) against reagent blank and the calibration curve was constructed. The linearity range was found to be 10 to 70 μg/ml and 50 to 130 μg/ml for method A and method B, respectively. One millilitre sample solution for method A and 2.2 ml for method B were treated similarly and absorbance values were recorded at 715 nm and 700 nm, respectively. The amount of sildenafil citrate was determined by the respective calibration curve.

To test the accuracy and reproducibility of the proposed methods, the recovery experiments were performed by adding known amount of drug to the pre-analyzed formulation, re-analyzing the mixture by proposed methods and the results are shown in Table 1. The recovery was performed at 0, 50, 100, 150, 200 and 250 % levels for method A and 50, 100, 150, 200 and 250 % levels for method B. The percentage recoveries ranged between 99.97 to 101.4 and 100.7 to 102.0 for method A and method B, respectively.

The estimation is based on reduction of ferric ions in its salt to ferrous ions by the drug which further in presence of oxidizing agents like of potassium ferricyanide (method A) and potassium dichromate (method B) produce blue (715 nm) and greenish blue colored complex (700 nm), respectively.

It was found that ferric nitrate reagent (0.4 ml for method A and 0.2 ml for method B), 2.7 ml potassium ferricyanide and 2.2 ml potassium dichromate were necessary for the achievement of maximum color intensity. However the absorbance decreased with higher and lower amounts of ferric nitrate reagent, potassium ferricyanide and potassium dichromate solution. It was found that 10-15 min are required to complete the reaction i.e. to form the stable chromogen. The chromogen was stable for further 75 min for method A and method B. However absorbance values decreased after 75 min.

Pure sildenafil citrate spiked with common excipients such as starch, talc, lactose and magnesium stearate was assayed and it was found that the assay result was unaffected by the presence of such excipients. In the sildenafil citrate tablet it was noticed that the excipients did not interfere in the absorbance.

The calibration curve yielded coefficient of correlation (r) 0.9997 over the Beers range of 10 to 70 μg/ml and 0.9994 over the Beers range of 50 to 130 μg/ml for method A and method B respectively. The regression equation was found to be y=0.02x-0.12 for method A and y=0.01x+0.02 for method B. The molar absorptivity and sandell's sensitivity are 1.32×10^4 l/mol.cm and 4.96×10^{-2} μg/cm^2/0.001 (method A) and 0.37×10^4 l/mol.cm and 0.18×10^{-2} μg/cm^2/0.001 (method B) which indicate that the methods are sensitive. The percent coefficient of variation (% CV) calculated from

TABLE 1: ANALYSIS OF TABLET SAMPLES

Formulation	Label claim (mg)	Method	Percent estimated*	Percent recovery*	Standard Deviation
		A	99.69	100.78	0.5187
	50				
Tablet 1		B	99.56	101.68	0.7393
(Caverta,		A	99.55	99.97	0.5433
Ranbaxy)	100				
		B	99.69	100.78	0.6051
		A	99.78	101.43	0.9225
	50				
Tablet 2		B	100.08	100.21	0.5879
(Penigra, Cadila)		A	99.93	100.47	0.1798
	100				
		B	100.40	101.43	0.7638
		A	99.20	100.32	0.4983
	50				
Tablet 3		B	98.93	101.96	0.2025
(Alcegra, Alembic)		A	99.70	100.02	0.6013
	100				
		B	98.35	101.96	0.9173

*Mean of five determinations

5 replicate readings (absorbance values) at concentration 30 μg/ml of sildenafil citrate was found to be 0.3348 (method A) and 0.1937 (method B), which is less than 2 % so the methods are precise.

In a replicate analysis (n=5) of three brands of sildenafil citrate tablets each of 50 mg and 100 mg by proposed methods, the percentages of drug in the tablets were found to be in the range of 99.20–99.93 for method A and 98.35 to 100.40 for method B (Table 1). The low values of SD ranged from 0.1798 to 0.9225, %CV 0.1800 to 0.9246 and 95% confidence limit of 0.1888 to 0.9683 for method A and SD ranged from 0.2025 to 0.9173, %CV 0.5874 to 0.9326 and 95% confidence limit of 0.5017 to 0.9628 for method B, obtained indicate that the methods are precise.

To confirm the accuracy and precision of the proposed methods, the recovery experiments were carried out. The percentage recoveries were found to be in the range of 99.97 to 101.43 and 100.71 to 101.96 for method A and method B respectively (Table 1), which also indicates non-interference from the formulation excipients.

ACKNOWLEDGEMENTS

Thanks are extended to The Principal, Govt. College of Pharmacy, Karad and Head, Department of Chemical Technology, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad for their invaluable assistance and encouragement. We are also grateful to R & D (F) Lupin Aurangabad for providing us gift sample of sildenafil citrate.

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