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Validated Extractive Spectrophotometric Estimation of Tadalafil in Tablet Dosage Form

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Abstract: Two simple spectrophotometric methods have been developed for the estimation of tadalafil in both pure and tablet dosage form. Methods A and B are based on the formation of ion-pair complexes of the drug with dyes such as bromothymol blue (BTB) and bromocresol green (BCG) in acidic buffer solution followed by their extraction with chloroform to form yellow colored chromogen with absorption maxima at 420 nm and 415 nm respectively. Beer's law is valid in the concentration range of 10-50 mcg/mL for both the methods. These developed methods were validated for precision, accuracy, ruggedness and robustness. Statistical analysis proves that the methods are reproducible and selective for the routine analysis of the said drug.

Keywords: Extractive spectrophotometry, Tadalafil, Bromothymol blue, Bromocresol green, Validation

Introduction

Tadalafil is a phosphodiesterase type 5- inhibitor, used in the management of erectile dysfunction. Chemically tadalafil is hydro-2-methyl-6-[3,4-(methylene dioxy)phenyl] pyrazino-[1',2':1,6] pyrido[3,4-b] indole-1,4-dione (Figure 1). It is not official in any of the pharmacopoeias. It is listed in the Merck Index[1] and Martindale, The Complete Drug Reference[2]. Extensive literature survey revealed that the determination of the drug in pure and dosage forms are not official in any pharmacopoeia and therefore, require much more investigation. Several analytical methods that have been reported for the estimation of tadalafil in biological fluids or pharmaceutical formulations include liquid chromatography[3,4], Densitometry[5] and UV-visible spectrophotometry[6]. The proposed method is based on the ion-pair extractive spectrophotometry[7].

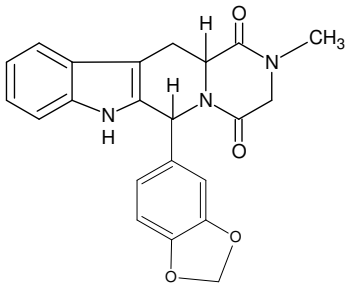

Figure 1. Chemical structure of tadalafil**.**

Experimental

A Schimadzu UV/VIS spectrophotometer (model 1201, Schimadzu, Japan) was employed for all the spectral measurements. All the chemicals used in the investigation were of analytical grade. The BTB solution of 0.04% w/v, the BCG solution of 0.04% w/v and phthalate buffer solution of pH 3.8 were prepared[8]. Standard solution of tadalafil was prepared by dissolving 50 mg in 50 mL and diluting 10 mL of this solution to 100 mL with methanol (100 mcg/mL). The method was extended for the determination of tadalafil in tablet dosage form. The tablet containing 10 mg strength was taken. Twenty tablets were weighed and powdered. The tablet powder equivalent to 25 mg of tadalafil was transferred into 25 mL volumetric flask containing 15 mL of methanol and flask was kept for ultrasonication for 5 min, then it was diluted up to the mark with methanol and the solution was filtered through Whatman filter paper No. 41. From the above solution 5 mL was pipetted out into a 50 mL volumetric flask and the volume was made up to the mark with distilled water. The final concentration of tadalafil was brought to 100 mcg/mL and used for the analysis.

In method A, aliquots of tadalafil ranging from 1-5 mL of standard solution were transferred into a series of separating funnel. To each separating funnel 1 mL of 0.04% w/v BTB solution and 1 mL of phthalate buffer solution of pH 3.8 were added and the volume of the aqueous layer was adjusted to 10 mL with distilled water. The aqueous layer was extracted twice with chloroform. The combined chloroform extracts were collected and diluted to 10 mL with chloroform. The absorbances were measured at 420 nm against the reagent blank prepared simultaneously. The amount of the drug in a sample was calculated from the calibration graph.

In method B, aliquots of tadalafil ranging from 1-5 mL of standard solution were transferred into a series of separating funnel. To each separating funnel 1 mL of 0.04% w/v BCG solution and 1 mL of phthalate buffer solution of pH 3.8 were added and the volume of the aqueous layer was adjusted to 10 mL with distilled water. The aqueous layer was extracted twice with chloroform. The combined chloroform extracts were collected and diluted to 10 mL with chloroform. The absorbance were measured at 415 nm against the reagent blank prepared simultaneously. The amount of the drug in a sample was calculated from the calibration graph.

Results and Discussion

The absorption spectral analysis shows the λ max of tadalafil was found to be 420 nm for method A and 415 nm for method B. The calibration curve was obtained for a series of concentration in the range of 10-50 mcg/mL for both the methods Figure 2 & 3. They were found to be linear and hence, suitable for the estimation of the drug. The slope, intercept, correlation coefficient and optical characteristics are summarized in Table 1.

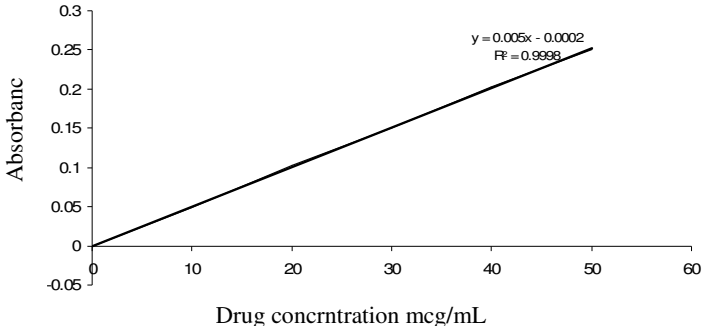

Figure 2. Calibration curve of tadalafil by method A

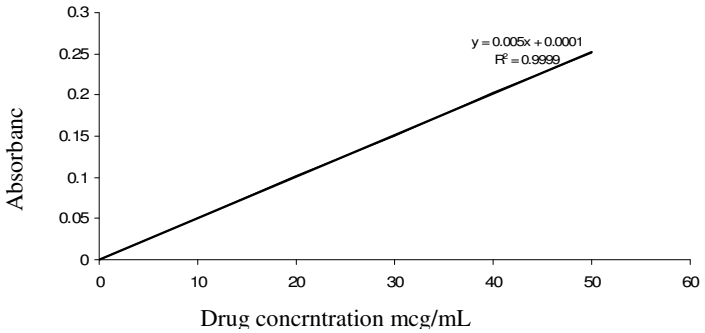

Figure 3. Calibration curve of tadalafil by method B

Table 1. Optical characteristics of the proposed methods.

Parameters	Values	
	Method A	Method B
Absorbance maximum, nm	420	415
Linearity range, mcg/mL	10-50	10-50
Correlation coefficient, r^2	0.9998	0.9999
Regression equation	Y=0.005 X - 0.0002	Y=0.005 X +0.0001
Slope	0.005	0.005
Intercept	0.0002	0.0001
Limit of detection, mcg/mL	2.23	2.36
Limit of quantitation, mcg/mL	6.63	6.98

Regression analysis of Beer's law plot revealed a good correlation. The effects of various excipients generally present in the tablet dosage form of tadalafil were investigated. The results indicated that they did not interfere in the assay in amounts far in excess of their normal occurrence in it. The proposed methods were validated as per the ICH guidelines[9-11]. The precision was measured in terms of repeatability, which was determined by sufficient number of aliquots of a homogenous sample. The %RSD was found and lying with in ±2.0. This showed that the precision of the methods are satisfactory. The recovery technique was performed to study the accuracy and reproducibility of the proposed methods. For this, known quantities of the tadalafil solution were mixed with definite amounts of pre-analyzed formulations and the mixtures were analyzed. The total amount of tadalafil was determined by using the proposed methods and the amount of added drug was calculated by the difference.

The %RSD was less than ±2.0. This showed that the recoveries of tadalafil by the proposed methods are satisfactory and the results are shown in Table 2. Ruggedness and Robustness were determined and the %RSD values were calculated from precision study was less than ±2.0. Limit of detection (LOD) and limit of quantitation (LOQ) were determined by the proposed methods.

Table 2. Summary of validation parameters.

Parameters	Method A		Method B	
Label claim, Tablet, mg	10	10	10	10
Amount found ± SEM[a]	10.04±0.026	10.03±0.020	10.05±0.022	10.06±0.021
Precision, RSD, %	0.983	0.823	0.786	0.974
% Recovery ± SEM[a]	100.3±0.74	100.8±0.53	100.8±0.54	99.8±0.64
Recovery, RSD, %	0.79	0.88	0.98	0.81

[a]*Mean of six determinations, SEM indicates standard error mean, RSD indicates relative standard deviation.*

Conclusion

Thus it can be concluded that the methods developed in the present investigation are simple, sensitive, accurate, rapid and precise. Hence, the above said methods can be successfully applied for the estimation of tadalafil in tablet dosage form.

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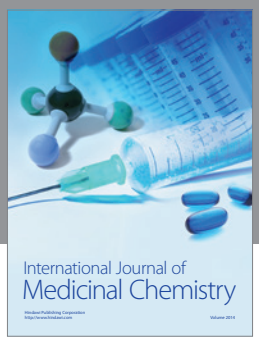

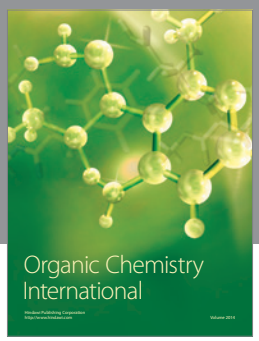

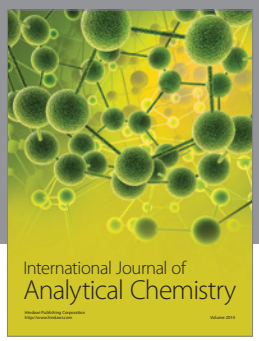

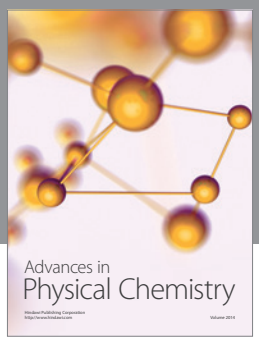

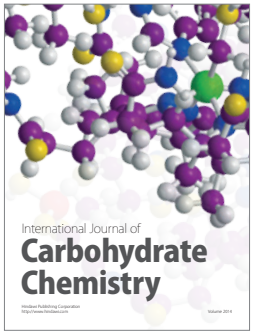

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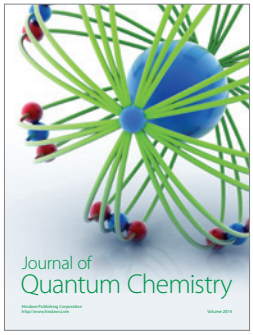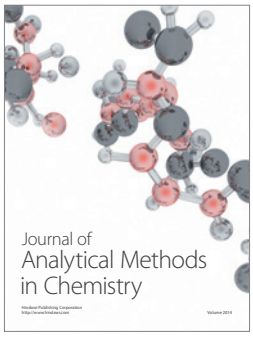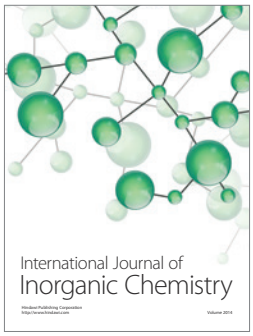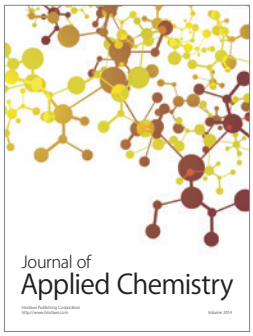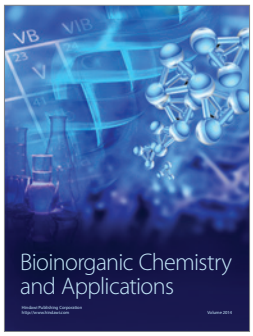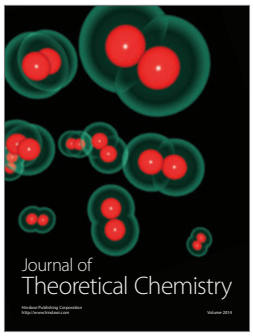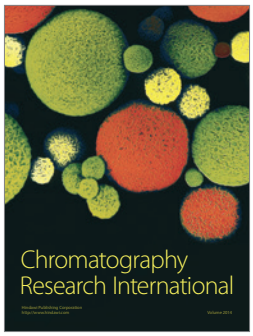
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