A validated method for development of atovaquone as API and tablet dosage forms by UV spectroscopy

Abstract

A simple new spectrophotometric method has been developed for estimation of Atovaquone in bulk and tablet dosage form. Atovaquone is estimated to be 251 nm in methanol. The Beer's law is obeyed in the concentration range of 1–10 μg/mL of the drug. The slope and intercept values are 0.111 and 0.012, respectively. Results of analysis of this method have been validated statically and by recovery studies. The method is applied to the marketed tablet formulation. A result of the analysis of tablet formulation, given as a percentage of label claim ± standard deviation, is 99.14 ± 0.66. The precision and accuracy has been examined by performing recovery studies and found to be 100.09 ± 1.14. The developed method is simple, sensitive, and reproducible, and can be used for the routine analysis of Atovaquone in bulk and tablet dosage form.

Key words: Atovaquone, methanol, pharmaceutical preparation, UV Spectrophotometnric method

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INTRODUCTION

Atovaquone [Figure 1] is a potent hydroxyl naphthoquinone with approved use in the USA, Canada and several European countries for the treatment of *Pneumocystis carinii* pneumonia[1-3] in acquired immunodeficiency syndrome (AIDS) patients intolerant to trimethoprim/sulfamethoxazole. Its potent antiprotozoal activity against *Plasmodium*, *Pneumocystis* and *Toxoplasma*[4-6] had prompted further investigations including clinical trials for treatment of *T. gondi* encephalitis in AIDS patients.[7] A previous study of atovaquone disposition in humans yielded no evidence of metabolites.[5] To date, the assays published for atovaquone are limited to complex gas chromatographic methods and high-performance liquid chromatography (HPLC) methods with multiple sample preparation and extraction procedures.[8-14]

EXPERIMENTAL

Apparatus

Shimadzu 1800 double beam spectrophotometer with Shimadzu UV PC software was used for all the spectrophotometric measurements and treatment of data. Zero-order absorption spectra were traced in 1 cm quartz cells over the range of 200–400 nm. Satodius balance with having 0.1 mg sensitivity was used for weighing the samples. Class'A' volumetric glass wares were used.

Materials and reagents

Atovaquone was gift sample from Glen Mark Pharmaceutical Ltd., Mumbai and used without further purification. Methanol AR Grade was procured from Rankem Chemicals. All the solvents used in spectrophotometric analysis were of analytical reagent grade.

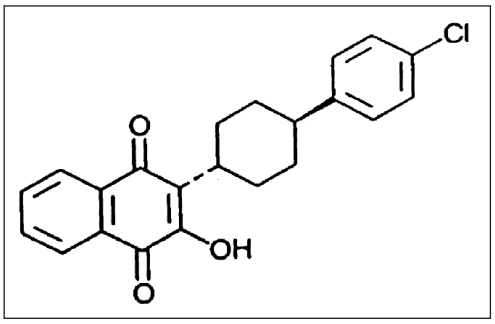

Figure 1: Chemical structure of atovaquone trans-2-[4-(4-chloro-phenyl) cyclohexyl]-3-hydroxy-1,4-naphthoquinone

Procedure

Preparation of standard stock solution

About 10 mg of the drug was accurately weighed and transferred to a 100 mL volumetric flask and dissolved in about 25 mL of methanol. The volume was then made up to the mark with methanol. Ten milliliters of this drug solution was transferred to a 100 mL volumetric flask and further diluted up to the mark with methanol. This solution contained 10 µg of drug per milliliter of the solution.

Determination of wavelength of maximum absorbance

Five milliliters of stock solution of Atovaquone was transferred to a 10 ml volumetric flask. It was diluted up to the mark with methanol. The absorbance of the final solution was scanned in the range of 200–400 nm, against methanol as the blank. Atovaquone showed absorbance maxima at 251 nm [Figure 2]. The drug followed linearity in the concentration range of 1–10 µg/mL (Y = 0.111 x + 0.012, R^2 = 0.9990) [Figure 3].

Preparation of calibration curve for Atovaquone

Stock solutions of atovaquone (1–10 ml) were pipetted out in to a series of 10 volumetric flask of 10 ml. The volume in each volumetric flask was made up to the mark with methanol and the mixer was shacked. That produced the concentration range of 1–10 µg/ml of Atovaquone. The absorbances of solutions were measured at 251 nm against methanol as blank [Figure 2].

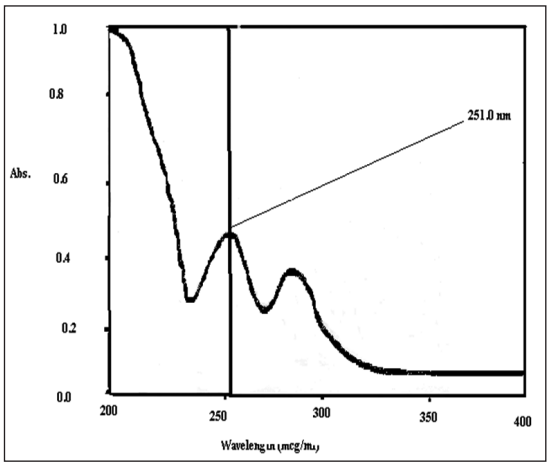

Figure 2: UV-Spectrum of Atovaquone

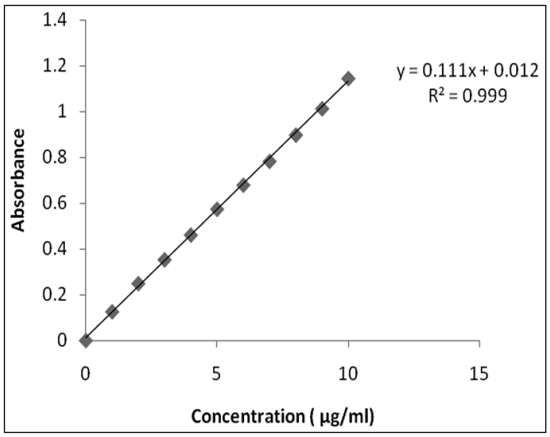

Figure 3: Calibration curve of Atovaquone at 251 nm

Table 1: Optical characteristics, regression equation and coefficient of the method

Data	Results
Maximum wavelength (λmax)	251 nm
Beer's law limit	1–10 µg/mL
Molar absorptivity (1 mole-1 cm-1)	9.454 x 103
Regression equation	Y = 0.111 x + 0.012
Slope	0.111
Intercept	0.012
Correlation coefficient (r)	0.9990
Accuracy (% Recovery) (n = 6)	100.09
Precision (% RSD)	
Intraday (n = 3)	1.09
Inter day (n = 3)	1.14

RESULTS AND DISCUSSION

Linearity

Under the experimental conditions described, the graph obtained for UV spectroscopy showed linear relationship. Regression analysis using the method of least-squares was made for the slope, intercept and correlation coefficient values. The regression equations of calibration curves was Y = 0.111 x + 0.012 (R^2 = 0.9990) for the UV spectroscopy. The range was found to be 1–10 µg/ml for UV spectrophotometric methods. The statistical parameters given are the regression equation calculated from the calibration

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