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SIMULTANEOUS SPECTROPHOTOMETRIC ESTIMATION OF EZETIMIBE AND ATORVASTATIN IN PHARMACEUTICAL DOSAGE FORM

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ABSTRACT

One simple, sensitive, accurate, precise, rapid and economical method is developed for the estimation of ezetimibe and atorvastatin in two components solid dosage form. The method is based on area under curve method. Ezetimibe has absorbance maxima at 232.5 nm and atorvastatin has absorbance maxima at 246.5 nm in methanol. The linearity was obtained in the concentration range 5-30 μg/mL for both ezetimibe and atorvastatin. In this method, the concentrations of the drugs were determined by using area under curve method. Concentration of the drugs were determined by using range of wavelengths at 230-235 nm and 244-249 nm for atorvastatin and ezetimibe in methanol. The results of analysis have been validated statistically and by recovery studies.

Key words: Ezetimibe, Atorvastatin, AUC- Area under curve.

INTRODUCTION

Atorvastatin (ATV) is chemically [R, R]-2-(4- fluorophenyl)-β, δ-dihydroxy 5- (1-methylethyl)-3-phenyl-4-[(phenyl amino) carbonyl]-1H-pyrrole-1-heptanoic acid and ezetimibe (EZE) is (3*R*,4*S*)-1-(4-fluorophenyl)-3-((3*S*)-3-(4-fluorophenyl)-3-hydroxypropyl)-4-(4-hydroxyphenyl)-2-azetidinone. Ezetimibe and atorvastatin both are used as antilipidemic agents. Literature survey reveals that HPLC[1-4], electrochemical methods[5], and a tandem MS[6-8] method for estimation of atorvastatin in pharmaceutical dosage form and from human plasma are reported. Similarly, survey of literature for ezetimibe revealed

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several methods based on HPLC[9-10] for estimation of ezetimibe in pharmaceutical dosage form. However new method has been developed for estimation of these drugs in combined dosage form. This paper presents a simple rapid, reproducible and economical method for simultaneous estimation in tablet dosage form.

EXPERIMENTAL

Material and methods

Instruments and reagents

A Jasco model V-530 double beam UV-Vis Spectrophotometer with spectral width of 2 nm wavelength accuracy of 0.5 nm and a pair of 10 mm matched quartz cells were used to measure the absorbance of resulting solutions. A Shimadzu analytical balance, an ultra sonic cleaner, ezetimibe (Glenmark Pharmaceuticals Ltd., Mumbai) and atorvastatin (BAL Pharma, Bangalore) and methanol were used in the study.

Preparation of standard drug solutions

The standard stock solutions of EZE and ATV were prepared by dissolving 10 mg of each drug in 10 mL volumetric flask separately using methanol. Final working standard solutions of 10 μg/mL of each EZE and ATV were prepared by diluting 0.1 mL of the above solution to 10 mL with methanol.

Procedure

Method: Area under curve method

Working standard solutions were scanned in the entire range of 200-400 nm to determine the λmax of both the drugs. The λmax of EZE and ATV were found to be 232.5 nm and 246.5 nm, respectively. Six standard solutions having concentrations 5, 10, 15, 20, 25, 30 μg/mL for both; EZE and ATV were prepared in methanol using the final working standard solution (10 μg/mL). The absorbances of resulting solutions were measured at 232.5 nm and 246.5 nm and calibration curves were plotted at these wavelengths. The absorptivity coefficients of these two drugs were determined by using calibration curve equation. Two simultaneous equations were formed using these absorptivity coefficient values.

$$C_x = \frac{X^{P}_{230-235} \text{ x } AUC_{244-249} - X^{P}_{244-249} \text{ x } AUC_{230-235}}{X^{A}_{244-249} \text{ x } X^{P}_{230-235} - X^{A}_{230-235} \text{ x } AUC_{244-249}} \quad \ldots(1)$$

$$C_y = \frac{X^A_{244-249} \text{ x } AUC_{230-235} - X^A_{230-235} \text{ x } AUC_{244-249}}{X^A_{244-249} \text{ x } X^P_{230-235} - X^A_{230-235} \text{ x } X^P_{244-249}} \quad \ldots(2)$$

Where, C_x and C_y are concentrations of EZE and ATV, respectively in g/100 mL in sample solution. $AUC_{230\text{-}235}$ and $AUC_{244\text{-}249}$ are range of absorbance of the sample solution containing EZE and ATV at 230-235 nm and 245-249 nm, respectively.

The concentration of C_x and C_y can be obtained as

$$C_y = \frac{215.67 \text{ x } AUC_{230-235} - 186.52 \text{ x } AUC_{244-249}}{215.67 \text{ x } 212.5 - 186.52 \text{ x } 186.6} \quad \ldots(3)$$

$$C_x = \frac{215.5 \text{ x } AUC_{244-249} - 186.6 \text{ x } AUC_{230-235}}{215.67 \text{ x } 212.5 - 186.52 \text{ x } 186.6} \quad \ldots(4)$$

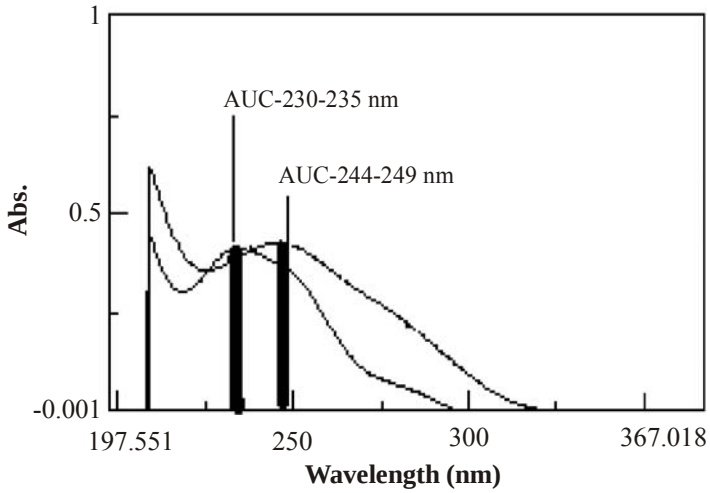

Fig. 1: Overlain spectra of AUC of ezetimibe (230-235 nm) and atorvastatin (244-49 nm)

Estimation of ezetimibe and atorvastatin in tablet

An accurately measured quantity of tablet powder equivalent to 10 mg of ezetimibe and 10 mg of atorvastatin are transferred to a 100 mL volumetric flask and dissolved in 50 mL methanol and sonicated for 10 min. The solution was filtered through Whatman filter paper No. 41 and residue was washed thoroughly with methanol. The filtrate and washings were combined in a 100 mL volumetric flask and diluted to the mark with methanol. The

solution was further diluted with the same solvent to get a final concentration of 10 μg/mL for both the drugs. The samples were determined using equations (1) and (2).

Table 1: Estimation of ezetimibe and atorvastatin in tablet

Method name	Label claim* mg/tab		Amount found* mg/tab		Percentage of label claim		Standard deviation		Coefficient of variation		Standard error	
	EZE	**ATV**	**EZE**	**ATV**	**EZE**	**ATV**	**EZE**	**ATV**	**EZE**	**ATV**	**EZE**	**ATV**
AUC	10	10	9.73	9.77	93.7	97.7	0.336	0.426	0.345	0.437	0.150	0.190

*Average of five determinations; AUC – Area Under Curve Method

Table 2: Recovery study data

Method name	Level of % recovery	% Recovery found		Standard deviation		Coefficient of variance		Standard error	
		EZE	**ATV**	**EZE**	**ATV**	**EZE**	**ATV**	**EZE**	**ATV**
AUC	**50**	99.79	97.43	0.0942	0.3399	0.0944	0.3488	0.0544	0.1964
	100	98.68	97.93	0.0849	0.2054	0.0861	0.2098	0.0820	0.1342
	150	97.09	97.13	0.0648	0.133	0.0667	0.1369	0.0374	0.0768

*Average of three determinations; AUC – Area Under Curve Method

The analysis procedure was repeated five times with tablet formulations. The result of analysis of tablet formulation is shown in Table 1. To study the accuracy and precision of above proposed method, recovery studies were carried out by addition of known amount of standard drug solution of EZE and ATV to preanalysed formulation. The resulting solution was then analyzed by proposed methods. Results of recovery studies were found to be satisfactory and Placebo study was also carried out without the drug substance. The results of recovery studies are shown in the Table 2.

RESULTS AND DISCUSSION

The proposed method was found to be simple, sensitive, accurate, precise, economical and rapid for routine simultaneous estimation of ezetimibe and atorvastatin. The value of standard deviation and coefficient of variation were satisfactory and recovery studies were indicative of the accuracy of the proposed method. In area under curve method, two range of wavelengths of respective absorbance i. e. 230-235 nm for EZE and 244-249

nm for ATV were used for the analysis of drugs. The criteria for obtaining maximum precision by this method was calculated and found to be outside the range of 0.1-2. The primary requirement for developing a method for analysis is that the entire spectra should follow the Beer's Law at all wavelengths, which was fulfilled in case of both these drugs. The validation parameters were studied at all the two range of wavelengths for both by this method. Accuracy was determined by calculating the % recovery and precision was calculated as repeatability (Standard deviation and relative standard deviation) and inter and intraday variation (% CV) for both the drugs. This method was successfully used to determine the amount of EZE and ATV present in tablet. The results obtained are in agreement with the corresponding labeled amount (Table I). Placebo study shows that the additives usually present in the pharmaceutical formulations did not interfere with determination of EZE and ATV.

CONCLUSION

The method described in this paper for the simultaneous estimation of ezetimibe and atorvastatin was found to be simple, sensitive, accurate, precise, rapid and economical and hence, this method could be successfully employed for the routine analysis of EZE and ATV in their combined dosage form.

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