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DEVELOPMENT OF UV SPECTROPHOTOMETRIC METHOD FOR THE ESTIMATION OF EZETIMIBE FROM TABLET FORMULATION

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ABSTRACT

Simple and sensitive spectrophotometric method has been developed for the quantitative estimation of Ezetimibe from pharmaceutical tablet dosage form. The method was developed are based on the solubility of Ezetimibe in acetate buffer pH 4.5 containing 0.45% SLS. The drug showed maximum absorbance at 232 nm. Linearity was obeyed in concentration range of 5-30 µg/mL. The results of analysis were validated statistically and by recovery studies.

Key words: Ezetimibe, Acetate buffer pH 4.5, UV Spectrophotometric method.

INTRODUCTION

Ezetimibe is an anti-hyperlipidemic agent used to lower cholesterol levels[1-3] and official in USP. It is chemically (3R, 4S)-1-(4-Fluoro phenyl)-3-[(3S)-3-(4-floro phenyl]-3-hydroxyl propyl]-4-(4-hydroxy phenyl)-2-azetidinone[4]. It acts by binding to a critical mediator of cholesterol absorption, the Niemann-Pick C1-Like 1 (NPC1L1) protein on the gastrointestinal tract epithelial cells as well as in hepatocytes. Ezetimibe is in a class of lipid-lowering compounds that selectively inhibits the intestinal absorption of cholesterol and related phytosterols. Ezetimibe, administered alone is indicated as adjunctive therapy to diet for the reduction of elevated total-C, LDL-C and Apo B in patients with primary hypercholesterolemia. It is also used in combination therapy with HMG-CoA reductase inhibitors. It causes a reduction of hepatic cholesterol stores and an increase in clearance of cholesterol from the blood. This distinct mechanism is complementary to that of HMG-CoA reductase inhibitors.

Various spectrophotometric[5-7], HPLC[8-10] and LC-MS[11-14] methods have been reported for the determination of Ezetimibe in pure and pharmaceutical formulations.

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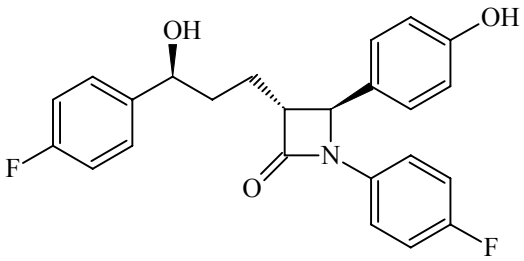

Fig. 1: Chemical structure of Ezetimibe

EXPERIMENTAL

Apparatus

A Shimadzu UV/Visible double beam spectrophotometer (Model 1700) with 1 cm matched quartz cells were used in present study for spectral and absorbance measurements.

Reagents and materials

All reagents used were of analytical grade and doubly distilled water was used throughout the investigation.

- Acetate buffer (pH 4.5): It was prepared according to USP 2009.
- Standard stock solution: Ezetimibe (100 mg) was transferred to a 100 mL volumetric flask containing sufficient quantity of the pH 4.5 acetate buffer (containing 0.45% SLS) to dissolve it and sonicate for 10 minutes. The volume of solution was made upto 100 mL with pH 4.5 acetate buffer.

Developed method

A series of ezetimibe solution ranging from 5 to 30 μg/mL were prepared from standard solution. Different aliquots (0.5, 1.0, 1.5 2.0, 2.5 and 3 mL) of a standard ezetimibe (1000 μg/mL) solution were transferred into a series of 100 mL calibrated flasks and all were made upto the mark with acetate buffer pH 4.5 (containing 0.45% SLS) and absorbance was measured at 232 nm against blank. A calibration curve was constructed for ezetimibe by plotting absorbance versus concentration. A representative UV spectrum and calibration curve in acetate buffer pH 4.5 are represented in Fig. 2 and 3, respectively. The optical characteristics such as Beer's law limit, molar absorptivity were calculated and summarized in Table 1. Regression equation, correlation coefficient, slope and intercept are also shown in Table 1.

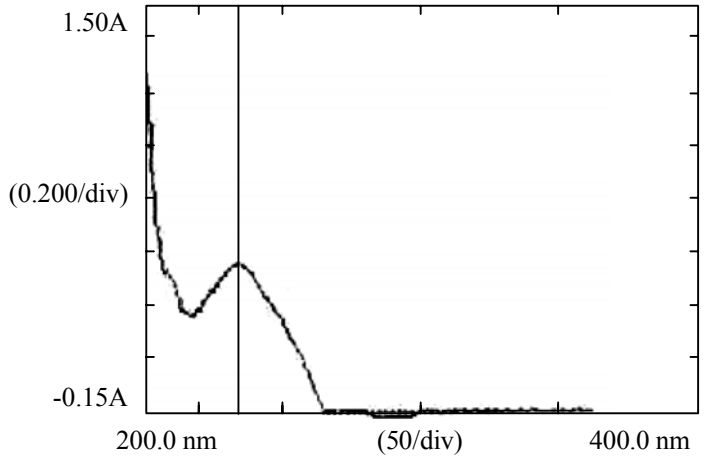

Fig. 2: Spectra of Ezetimibe in acetate buffer pH 4.5

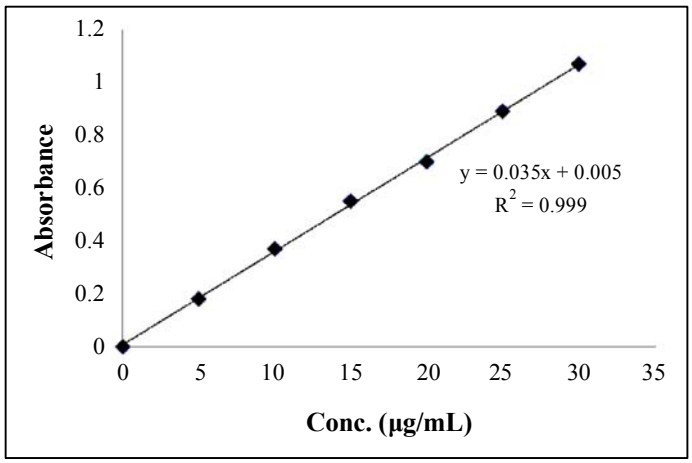

Fig. 3: Calibration curve of Ezetimibe in acetate buffer pH 4.5

Table 1: Quantitative parameters of spectrophotometric method

Parameters	Result
λ_{max} (nm)	232
Beer's law limits (µg/mL)	5-30
Molar absorptivity (l mol^{-1} cm^{-1})	14.97 x 10^3
Regression equation	y = 0.035x + 0.005

Cont…

Parameters	Result
Slope	0.035
Intercept	0.005
Correlation coefficient (r^2)	0.999

Analysis of tablet formulation

Ezetimibe tablets each containing 10 mg of ezetimibe was procured from the market. Twenty tablets were weighed accurately and average weight per tablet was determined. The tablets were powdered and powder equivalent to 10 mg of Ezetimibe was accurately weighed and dissolved in about 20 ml acetate buffer pH 4.5. The solution was sonicated for about 10 min and filtered using Whatman filter paper no. 41; residue was washed with 20 mL acetate buffer pH 4.5. Filtrate and washing were transferred to a 50 mL calibrated volumetric flask and acetate buffer was added upto the mark. The 5 mL of above filtrate was diluted to 50 ml with acetate buffer pH 4.5. Absorbance was measured at 232 nm wavelength against reagent blank and the concentration of the drug in sample solution was determined from calibration curve. Process was repeated five times for two different samples of marketed formulations. Results of analysis are reported in Table 2.

Recovery studies

Recovery studies were carried out for the above developed method by addition of known quantity of standard drug solution to pre analyzed sample of tablet at three different concentration levels (80%, 100% and 120%). The concentration of drug in final dilution was determined after addition of known concentration of pure drug and determined the percentage recovery after deduction of concentration of drug in original tablet sample. Results of recovery studies are reported in Table 2.

Table 2: Results of analysis of tablet formulation and recovery studies

Method	Brand	Label claim (mg/Tablet)	% Label claim estimated*	S.D.	% Recovery**
UV	A	10	98.97	0.286	100.12
	B	10	99.46	0.358	99.74

*Average of six determinations

** Average of recovery studies at three different concentration levels

UV: Ultraviolet Spectroscopy

RESULTS AND DISCUSSION

A U.V. method has been developed for the quantitative estimation of Ezetimibe from tablet formulation. The developed method are based on the solubility of Ezetimibe in acetate buffer having pH 4.5. The results of analysis from tablet formulation were within the permissible limits and the results of recovery studies reflect nil interference from excipients. The developed method was found to be simple, accurate and economical, hence can be used for routine analysis of Ezetimibe from pharmaceuticals.

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