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Simultaneous derivative and multicomponent spectrophotometric determination of Simvastatin and Ezetimibe in tablets

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Abstract

Two new, simple, accurate and economical spectrophotometric methods have been developed for simultaneous estimation of simvastatin and ezetimibe in two component tablet formulation. The methods employed are first order derivative spectrophotometry using zero crossing techniques and multicomponent analysis both the drugs obey the Beer's law in the concentration range employed for these methods. The results of analysis are validated statistical evaluation and recovery studies.

Key words: Simvatatin, derivative spectrophotometry, multicomponent spectrophotometry, Ezetimibe.

INTRODUCTION

Simvastatin is a lactone that inhibits the enzyme HMG Co Enzyme A, which is responsible for the conversion of Hydroxy Methyl Glutaryl to cholesterol, used in the treatment of type I and type II hyperlipedemia[1]. Ezetimibe, having azetidinone ring structure, inhibits the absorption of cholesterol and reduces the blood cholesterol level it also decrease the excessive accumulation of cholesterol in blood vessels. Chemically simvastatin (SIM)[1] is Butanoic acid-2,2-dimethyl-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester,[1S-1α,3α,7β,8β(2S,4S)8αβ)] and ezetimibe (EZM)[2] is (3R,4S)-1-(4-fluoro phenyl)-3-[(3S)-3-(4-fluoro phenyl)-3-hydroxyl propyl)]-4-(4-hydroxy phenyl)-2-azetidinone. SIM is official in Indian Pharmacopoeia and EZM is official in USP. By the literature survey HPLC, Stability Indicating HPLC, LC-MS methods have been reported for the estimation of EZM while UV, HPLC and LC-MS methods have been reported for EZM[3-8]. A combination

of SIM and EZM Is use to treat the patient suffering from hyperlipedemia and Primary Hypercholesterolaemia.[10]

RESULTS

The assay values for tablets by both the methods were in the range of 99.08-99.47% and 99.12 – 99.35% for SIM and EZM, respectively. The results obtained were comparable with the corresponding labeled amounts (Table-1). The recovery study were carried out the both the brands by standard addition methods by standard addition method. The results of recovery study for both the drugs for both the methods were in the range of 99.11-99.25% and 99.31-99.46 %. The statistical analysis was performed on the results of nine determinations at three different concentration levels. The Standard deviation and relative standard deviation was used to check the accuracy of method. Intraday and interday precision was used to check the precision of method. *ANOVA* test was carried out to check the analysis of variance the P value was found to be 0.351 which is >0.5 so it is considered as non significant.

Table-1 Assay results of Simvastatin and Ezetimibe in marketed formulations

Brand	Parameters	% label claim				%Recovery			
		Method 1		Method 2		Method1		Method2	
		SIM	EZM	SIM	EZM	SIM	EZM	SIM	EZM
1SIMAS-EZ	Mean SD RSD	99.15 0.18 0.002	99.29 0.076 0.001	99.22 0.13 0.003	99.35 0.054 0.003	99.11 0.25 0.002	99.22 0.016 0.003	99.24 0.31 0.003	99.21 0.080 0.001
2.STARSET-EZ	Mean SD RSD	99.26 0.21 0.002	99.32 0.064 0.001	99.12 0.20 0.005	99.18 0.024 0.003	99.19 0.31 0.004	99.21 0.018 0.002	99.29 0.36 0.002	99.31 0.015 0.003

Method-1 is first order derivative method and method-2 is multicomponent method. Values of recovery are mean of nine estimations at three different concentration levels, SD is standard deviation and RSD is relative standard deviation.

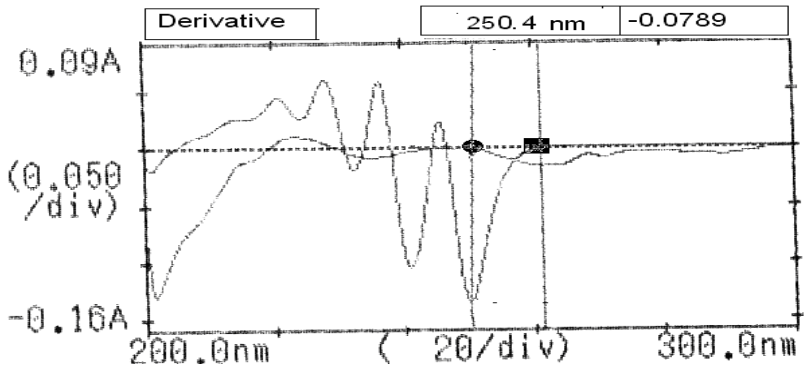

Figure :1 First order derivative overlain spectra of Simvastatin and Ezetimibe. Zero crossing for ezetimibe (●) and for simvastatin (■)

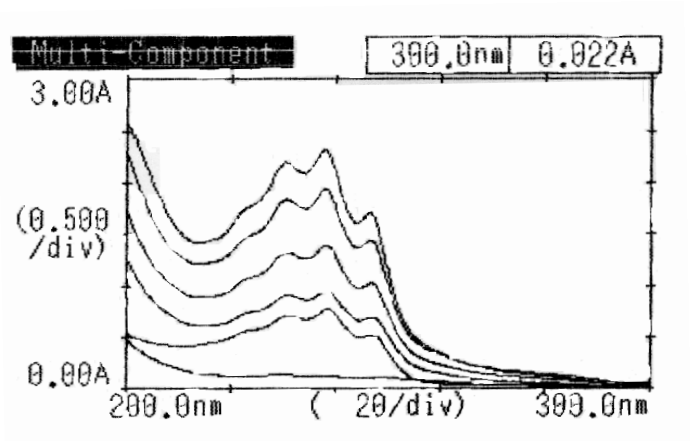

Figure :2 Multicomponent overlain spectra of Simvastatin and Ezetimibe

MATERIALS AND METHODS

Simultaneous estimation of SIM and EZM using derivative spectrophotometric method and multicomponent method has been developed in the present investigation. Instrument involved is the UV/VIS double beam spectrophotometer; model shimadzu 1601 with spectral band width of 2nm and wavelength accuracy of 0.5 nm with automatic wavelength correction and a pair of 10mm matched quartz cells. Gift samples of SIM and EZM were obtained from sun pharmaceuticals ltd, Baroda. Standard stock solutions were prepared by dissolving 10mg of each in 100 ml of methanol (E.Merck)

First order derivative spectroscopy[10] offers, a useful approach for the analysis of drugs in multicomponent mixtures. In the present work, derivative methods employs zero crossing wavelengths of SIM and EZM at 261.0 nm and 250.4 nm , respectively. Calibration curves were plotted between amplitudes observed at 1^{st} order (key no.2) for both the drugs at both the wavelengths against the concentrations, in the range of 5-40 µg/ml. Estimation of these drugs was done by solving the regression equations

$$Y=0.0020x + (-0.0001)\_ \_ \_ (1)\ Y= 0.0007 + (-0.0001)\_ \_ \_ \_ (2).$$

For multicomponent method six mixed standards and two sampling wavelengths as 247.0 (λ_{max} for SIM) and 232.5 nm (λ_{max} for EZM) were satisfactory to serve the purpose of experiment six mix standards solutions of SIM and EZM were prepared in the concentration ratio of 1:1 containing (6, 10, 14, 18, 22, 26 µg/ml of EZM and SIM) concentration were estimated by the multi-component mode of an instrument.

Twenty tablets of Brand 1(SIMVAS –EZ Micro lab, Mumbai label claim SIM 10 mg and EZM 10 mg) and Brand 2 (STARSAT-EZ Lupin Pharmaceuticals , Pune label claim SIM 10 mg and EZM 10 mg), were weighed average weight was determined and finally powdered. An accurately weighed powdered sample, equivalent to average weight of one tablet was transferred to a beaker, dissolved in methanol, filtered through whatmann filter paper no.1 into 100 ml volumetric flask and the volume was made up to the mark with same solvent. Necessary dilutions were made with methanol to give final concentration of 10 µg/ml of SIM and EZM the

absorbances were measured at 261.0 nm and 250.4 nm at derivative mode and 247.0 nm and 232.5 nm at multicomponent mode of an instrument.

The first order derivative overlein spectra for both the drugs showed the wavelengths of zero crossing as 261.0 nm and 250.4 nm for SIM and EZM respectively.(Fig.1). absorbances were measured at both the wavelengths. Calibration curves were plotted and regression analysis was carried out. Both the drugs obeyed linearity individually and in mixture with in the concentration range of 5-40 µg/ml with co-relation coefficient (r^2= 0.9993) concentrations were calculated by solved equation no 1 and 2. Analysis of both the brands was performed under multicomponent mode of an instrument. For quantitative estimation, absorbance were measured at λ_{max} of both the drugs viz. 247.0 nm and 232.5 nm respectively for SIM and EZM.

CONCLUSION

By observing the validation parameters like accuracy, precision, range, raggedness, specificity, linearity and range both the mentioned methods found to be specific, sensitive, accurate, and precise and reproducible[11-13].

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REFERENCES

[1] Eugenia, M., Cathy, D. and Robert, M., In, Pharmacology Principles and Applications, **2003**, 606.
[2] Budawari, S., Eds. The Merck Index, 13th Edn., Merck & Co., Inc., Whitehouse Station, NJ, **2003**, 618, 8618.
[3] Sistla, R., Tata, V.S., Kashyap, Y.V., Chandrasekar, D., and. Diwan, P.V., *J.Pharm. Biomed. Anal.* **2005**, Sep 15, 39(3-4), 517-522.
[4] Singh, S., Singh, B., Bahuguna, R., Wadhwa, L., Saxena, R., *J Pharm Biomed Anal*., **2006**, Jun 7, 41(3), 1037-40.
[5] Shuijun, Li., Gangyi, Liu., Jingying, Jia., Xiaochuan, Li., Chen, Yu., *J Pharm Biomed Anal*. Vol.40, 987-992
[6] Wang, L, Asgharnejad, M., *J Pharm Biomed Anal*., **2000**., Jan.21(6)., 1243-8.
[7] Carlucci, G., Mazzeo, P., Biordi, L., Bologna, M., *J Pharm Biomed Anal.*, **1992** Sep., 10(9)., 693-7.
[8] Bae, C. K., Eunmi, B. , J. S. P., Yun K. S., Chong K. K., *J. Liq. Chro. Rel. Tech* , Vol. 27(19), **2004**, 3089 – 3102.
[9] Michael, H., Davidson, M.D., Darbie, Michael, M.S., Strony, M.D., Musliner., MD, *American J. of Cardiology*, Vol.97, **2006**, 223-228.
[10] Kalsi, P.S., In ; Spectroscopy of organic compound, 5th Edn., New age International Publishersw, New delhi, 7.
[11] ICH, Q2A, Text on Validation of Analytical Procedures, International Conference on Harmonization, Geneva, October **1994**, 1-5.

[12] ICH, Q2B, Validation of Analytical Procedures: Methodology, International Conference on Harmonization, Geneva, November, **1996**, 1-8.
[13] Haider, S.I., In; Pharmaceutical Master Validation Plan, Lucie press, **2002**, 2.