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NOTE

Simultaneous Estimation of Simvastatin and Ezetimibe in Tablet Formulations

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An accurate and economical procedure for the simultaneous estimation of simvastatin and ezetimibe in tablet formulation has been developed. The method involves the solving of simultaneous equations. Simvastatin has absorbance maxima at 242 nm in chloroform and ezetimibe has absorbance maxima at 248 nm in chloroform. Both these drugs obey Beer's law in concentration ranges employed for the present method. The result of analysis has been validated statistically by recovery studies.

Key Words: Simvastatin, Ezetimibe, Simultaneous estimation.

Simvastatin, chemically 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. It is a lipid-lowering agent derived synthetically from fermentation product of *Aspergillus terreus*. It is an inactive lactone, whereas chemically ezetimibe is 1-(4-fluorophenyl)-3(R)-[3-(4-fluorophenyl)-3(S)-hydroxypropyl]-4(S)-(4-hydroxyphenyl)-2-azetidinone, belongs to a class of lipid-lowering compounds that selectively inhibits the intestinal absorption of cholesterol and related phytosterols.

Few reports were found for the analysis in formulation in individual form particularly for simvastatin and ezetimibe[1-7], but no methods were reported for their estimation simultaneously by spectrophotometric methods. So this work presents a simple, accurate, reproducible and economical method for the simultaneous estimation[8,9] of these two compounds in tablet formulations.

Shimadzu double beam spectrophotometer (model: UV PharmaSpec 1700) with matched quartz cells corresponding to 10 mm path length was used in present studies. Simvastatin, ezetimibe and chloroform of analytical grade.

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Preparation of standard stock solution: Standard stock solutions of simvastatin and ezetimibe were prepared by dissolving 100 mg each in chloroform in volumetric flasks and the volume was made up to 100 mL using chloroform to get a final concentration of 1 mg/mL. Further dilutions were made to get concentrations of 6 mcg/mL, respectively. Two solutions were scanned at the range of 240 to 280 nm and the λ_{max} of simvastatin and ezetimibe suitable for simultaneous estimation found to be at 242 and 248 nm, respectively.

Dilutions were made to get concentrations 2-10 µg/mL for simvastatin and 2-12 µg/mL for ezetimibe, respectively. Calibration curves were plotted for each drug using absorbance *vs.* concentration. The standard plots were constructed from different concentrations of each compound in the fixed concentration (10 mcg/mL) of the other. The correlation coefficients were 0.9997 (n = 5) and 0.9967 (n = 6) for simvastatin and ezetimibe, respectively. The slope and intercept for simvastatin were 0.1478 and 0.0272 and for ezetimibe were 0.1008 and 0.1378, respectively as determined by the method of least squares.

Preparation of tablet sample solution: 20 Tablets containing combination of simvastatin and ezetimibe were weighed and average weight was calculated and ground to fine powder. A quantity of powder sample equivalent to 100 mg of simvastatin and 100 mg of ezetimibe was taken in a volumetric flask and dissolved in chloroform. The solution was filtered through a Whatmann filter paper No. 10 and the volume was made up to 100 mL using chloroform. Further dilutions were made to get 6 mcg/mL of simvastatin and 6 mcg/mL of ezetimibe using chloroform. The absorbance of diluted solution at different wavelengths *i.e.* 248 nm (λ1) and 242 nm (λ2) were taken and A1 and A2 were determined. The two drugs were determined by solving the simultaneous equations.

Calculations: A set of equations[8] were used as given below:

$$A1 = ax1 \times Cx + ay1 \times Cy \quad (1)$$

$$A2 = ax2 \times Cx + ay2 \times Cy \quad (2)$$

where Cx and Cy are concentrations of simvastatin and ezetimibe respectively, ax1 and ax2 are the molar absoptivities of simvastatin at λ1 and λ2; ay1 and ay2 are the molar absorptivities of ezetimibe at λ1 and λ2. A1 and A2 are the absorbance of diluted formulation at λ1 and λ2. The molar absorption co-efficients were found to be 566.74 and 649.45 mol^{-1} cm^{-1} for simvastatin at λ1 and λ2 and 523.4 and 494.75 mol^{-1} cm^{-1} for ezetimibe at λ1 and λ2, which are the means of independent determinations (n = 5).

The precision of the method was calculated by conducting recovery studies. Recovery studies were carried out and the results were found satisfactory. The per cent recovery ± SD ranges from 99.9 ± 0.25 to 98.09 ± 0.15 for simvastatin and 98.12 ± 0.45 to 100.14 ± 0.41 for ezetimibe

which are satisfactory with the label claim. The brand used to recovery studies was Simvotin EZ™ 10 manufactured by Ranbaxy Laboratories limited. The label claim is 10 mg of simvastatin and 10 mg of ezetimibe. The recovery studies indicate the non-interference of the tablet excipients used[10]. The present method can be successfully employed for the determination of simvastatin and ezetimibe simultaneously in tablet formulations.

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