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SPECTROPHOTOMETRIC METHOD FOR THE DETERMINATION OF SIMVASTATIN IN PHARMACEUTICAL DOSAGE FORMS

S. VIJAYA SARADHI*, G. DEVALA RAO[a], B. SITARAM[b], K. PRAVALLIKA[b], P. AMULYA CHOWDARY[b] and V. SINDHU[b]

Department of Biochemistry, P. B. Siddhartha College of Arts and Science,
VIJAYAWADA – 520010 (A. P.) INDIA.
[a]K.V.S.R. Siddhartha College of Pharmaceutical Sciences, VIJAYAWADA – 520010 (A. P.) INDIA
[b]Department of Chemistry, P. B. Siddhartha College of Arts and Science,
VIJAYAWADA – 520010 (A. P.) INDIA

ABSTRACT

A simple, sensitive and reproducible spectrophotmetric method has been developed for the determination of simvastatin in bulk and dosage forms. This method is based on the formation of colour species on binding of simvastatin with the ligand ferric nitrate and concentrated nitric acid to produce yellowish green colored solution (λ_{max} at 390 nm). Results of analysis were validated statistically and by recovery studies. This method is successfully employed for the determination of simvastatin in various pharmaceutical preparations.

Key words : Simvastatin, Spectrophotometric determination, Beer's law

INTRODUCTION

Simvastatin[1] is an example of antihyperlipedemic drug used in the treatment of obesity. Chemically, it is 2,2- dimethyl butanoic acid (1S, 3R, 7S, 8S, 8aR)-1 ,2 ,3, 7, 8, 8a- hexahydro-3-7-dimethyl –8-[2-[(2R, 4R)- tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-napthalenyl ester. Thorough survey of literature revealed only derivative spectrophotmetric[2], HPLC[3,4] and LC-MS[5] methods. Recently three methods have been reported by Vijaya Saradhi et al. regarding estimation of simvastatin in pharmaceutical dosage forms, which have also been reviewed.

This paper described the development of a simple and sensitive spectrophotometric

* Author for correspondence; Phone: 91-866-2441449, E-mail: spsree@yahoo.com

method for the routine quality control analysis of bulk dosage forms containing simvastatin in which the drug is treated with ferric nitrate (20 % w/v in distilled water) and concentrated nitric acid to form yellowish green chromogen. Then the absorbance is measured at 390 nm.

EXPERIMENTAL

Instrumentation

Spectral and absorbance measurements are made with Systronics UV-Visible double beam spectrophotometer model 2201.

Reagents

All the chemicals used were of analytical grade. All the solutions were freshly prepared with distilled water. Freshly prepared solution of ferric nitrate (20 % w/v) was used for this method.

Standard and sample solution of simvastatin

About 100 mg of simvastatin (bulk or formulation) was accurately weighed and dissolved in 100 mL of methanol in a volumetric flask to make a solution of 1 mg/mL standard solution. Further dilutions are made with distilled water only.

Assay procedure

Aliquots (1-5 mL) of standard simvastatin solution (100 µg/mL) were transferred to a series of 10 mL graduated tubes and the volume is made up to 5 mL with distilled water. To each tube, 4 mL of ferric nitrate and 0.4 mL of concentrated nitric acid was added. The contents were mixed thoroughly and kept at room temperature for 5 minutes. The absorbance of the coloured solution was measured at 390 nm against the reagent blank. The amount of simvastatin was computed from the calibration curve.

RESULTS AND DISCUSSION

The proposed method was based on reaction of simvastatin with ferric nitrate and concentrated nitric acid based on the formation of yellowish green colored chromogen. This reaction is a typical example of Schiff's base formation. The optical characteristics such as absorption maxima, Beer's law limits, molar absorptivity and Sandell's sensitivity for this method are presented in Table 1. The regression analysis using the method of least squares was made for the slope (a), intercept (b) and correlation coefficient (r) obtained

from different concentrations (Table 1). The precision and accuracy were found by analyzing six replicate samples containing known amounts of the drug and the results are su mmarized in Table 1.

Table 1. Optical characteristics, precision and accuracy of the proposed method

Parameters	Method
λ_{max} (nm)	390
Beer's law limit (µg / mL)	10-50
Sandell's sensitivity (µ g / cm^2 / 0.001 abs. unit)	1.302
Molar absorptivity (litre. $mole^{-1}.cm^{-1}$)	0.3214
Correlation coefficient (r)	0.9964
Regression Equation (Y)*	
Slope (a)	0.505
Intercept (b)	0.00081
% RSD **	0.36%
% Range of errors (95% confidence limits)	
0.05 Significance level	± 0.3018
0.01 Significance level	± 0.4465

*Y = a + bx, where Y is the absorbance and x is the concentration of simvastatin in µg/mL.

** For six replicates.

The accuracy of this method was ascertained by comparing the results obtained with the proposed and reference method in the case of formulations and is presented in Table 2. As an additional check on the accuracy of this method, adding known amounts of pure drug to pre-analyzed formulations recovery experiment were performed and percent recovery values obtained are listed in Table 2. Recovery experiment indicated the absence of interferences from the co mmonly encountered pharmaceutical additives and excipients.

Thus, the proposed method is simple and sensitive with reasonable precision and accuracy. This can be used for the routine determination of simvastatin in quality control analysis.

Table 2. Estimation of simvastatin in pharmaceutical formulations

Formulations	Labeled amount (mg / vial)	% Recovery by proposed method
Vial - 1	5	99.64
Vial - 2	5	99.44
Vial - 3	5	99.54
Vial - 4	5	100.3

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