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Research Article

SPECTROPHOTOMETRIC METHODS FOR ESTIMATION OF SIMVASTATIN IN BULK DRUG AND ITS DOSAGE FORM

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ABSTRACT

Simple, accurate, precise, sensitive and highly selective spectrophotometric methods were developed for the estimation of simvastatin. The estimation of simvastatin was carried out by various solvents like methanol (method I) at 236 nm, 2-propanol (method II) at 230nm and conc.H_2SO_4 (method III) at 415 nm. And these methods were found to be linear in the range of 1-6µg/ml, for method I and II and 10-60µg/ml for method III. And Beers law range were found to be 1-15µg/ml, 1-15µg/ml, and10-250µg/ml, and with mean recovery of 97.5 %, 97.5 % and 103.5 % of simvastatin for methods I, II and III respectively. The developed method was validated according to ICH guidelines and it found to be accurate and precise Thus the proposed method can be successfully applied for simultaneous determination of simvastatin and in routine analysis work.

Keywords: Simvastatin, Spectrophotometric, Validation, Beer's law.

INTRODUCTION

Simvastatin (SIM) 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, is a lipid-lowering agent that is derived synthetically from fermentation products of Aspergillus terreus [1] After oral ingestion SIM, which is an inactive lactone, is hydrolyzed to corresponding b-hydroxy acid leading to the inhibition of 3-hydroxy 3-methyl glutaryl – coenzyme A. (HMG- CoA) reductase, responsible for catalyzing the conversion of HMG CoA to mevalonate, which is an early and rate limiting step in cholesterol biosynthesis[2] Ezetimibe (EZ), 1-(4-Fluorophenly) – 3 (R) - [3-(4-fluorophenyl) - 3 (S) hydroxyl propyl]-4 (S) – (4-hydroxy phenyl) – 2 azetidinones is a therapeutically beneficial drug that works by inhibiting the protein transporters on small intestinal brush border, which brings about this active transport of cholesterol. In addition, it also inhibits phytosterol absorption[3]. This distinct mechanism of action results in a synergistic cholesterol lowering effect when used together with statins that inhibits cholesterol synthesis by liver [4].SIM may be determined by several methods including gas chromatography–mass spectrometry (GC–MS)[5], liquid chromatography with UV detection (LC–UV)[6-8]. Literature survey revealed that there

is few UV-visible methods have been reported.

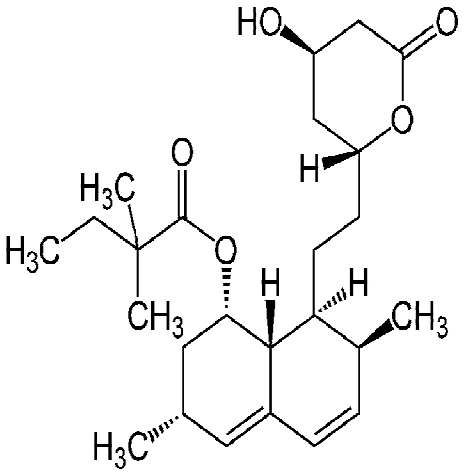


Fig.1: Chemical structure of simvastatin

EXPERIMENTAL

Instrumentation

The present work was carried out on Elico SL164 UV- visible spectrophotometer having double beam detector configuration. The absorption spectra of reference and test solution were carried out in a 1 cm quartz cell over the range of 200-800 nm.

Chemicals

All chemicals of analytical grade used as it is.

Preparation of standard solution

A stock solution of 1 mg/ml was prepared in methanol. This solution is diluted with methanol to obtain required concentrations.

Preparation of sample solutions

20 tablets were weighed and powdered; an amount equivalent to 100mg of simvastatin was weighted and transferred to the 100ml volumetric flask. To it 50 ml of methanol was added and shake until the drug is dissolved. The solution was filtered and made up to 100ml with methanol. This solution was suitably diluted to obtain the required concentration. The same procedure is followed in other methods with respective solvents.

PROCEDURE

Aliquots of working standard solution of simvastatin 1-6ml (100µg/ml) were transferred into a series of 10ml volumetric flask. The volumetric flasks are made up to the volume with the respective solvents (i.e. methanol (method-I), 2-propanol (method-II), conc.H2SO4 (method-III).

Then the absorbance of the samples are measured spectrophotometrically at 236nm for method using methanol, at 240nm for method using 2-propanol and at 415nm for method using conc.H_2SO_4 against a reagent blank.

VALIDATION

Validation of the developed method was done according to ICH guidelines

Linearity

The linearity of the method is its ability to elicit test results that are directly proportional to the concentration of the analyte in samples. The calibration curve was taken in the range of 4-14 µ/ml at the respective λmax for method I and Method II, and 10-60 µg/ml. The correlation coefficient of the linearity were found for three methods and reported in table No.1

Precision and Accuracy

The precision of an analytical method is determined by assaying a sufficient number of aliquots of a homogeneous sample to be able to calculate statistically valid estimate of % Relative Standard Deviation (%RSD). Intermediate precision was done to express within laboratory variation, on different days. Five replicates of 12 µg/ml concentration of the working standard mixture and sample solution were analyzed %RSD was found to be less than 2%. Accuracy were determined for three methods and results were reported in table no.2

Specificity

Results of tablet solution showed that there is no interference of the excipients when compared with the working standard solution. Thus, the method was said to be specific.

RESULT AND DISCUSSIONS

The optimum conditions for methods I, II and III have been established by varying the parameters one at a time and keeping the other parameters fixed and observing the effects of products on the absorbance of the sample and colored species. Beer's law limits, molar absorbivity, Sandal's sensitivity, % range of error and % relative standard deviation are summarized in Table I. The regression analysis using the method of least squares was made for the slope (b), intercept (a) and correlation coefficient (r)obtained from different concentrations are given in Table I The results showed that these methods have reasonable precision.

To evaluate the validity and reproducibility of the methods, known amounts of pure drug were added to the previously analyzed pharmaceutical dosage forms and the mixtures were analyzed by the proposed methods. The percentage recoveries are given in Table - 2. The interference studies revealed that the common excipients and other additives that are usually present in the injection dosage forms did not interfere at their regularly added levels.

Table 1: Optical regression characteristics, precision and accuracy of the proposed methods

Parameter	Method -I	Method - II	Method - III
λmax(nm)	236nm	240nm	415nm
Beer's law limits (μg.ml^{-1})	0.5-15μg/ml	0.5-15μg/ml	10-250μg/ml
Molar absorbivity (lit . mole^{-1},cm^{-1})	125.4x10^{3}	137.94 x 10^{3}	8.36x10^{3}
Sandell's sensitivity (μg.cm^{-2}/0.001 abs.unit)	0.0033	0.00303	0.05
Regression equation (y*=a+bx) slope (b)	0.0601	0.0662	0.00398
Intercept (a)	2.7 x10^{-4}	-1.9 x10^{-4}	1.3 x10^{-4}
Correlation Co-efficient (r)	0.995	1.05	0.994
R.S.D.	0.488	0.85	0.491
Range of error** (confidence limits) 0.05 level	0.041	0.0714	0.041
0.01 level	0.60512	1.054	0.60884

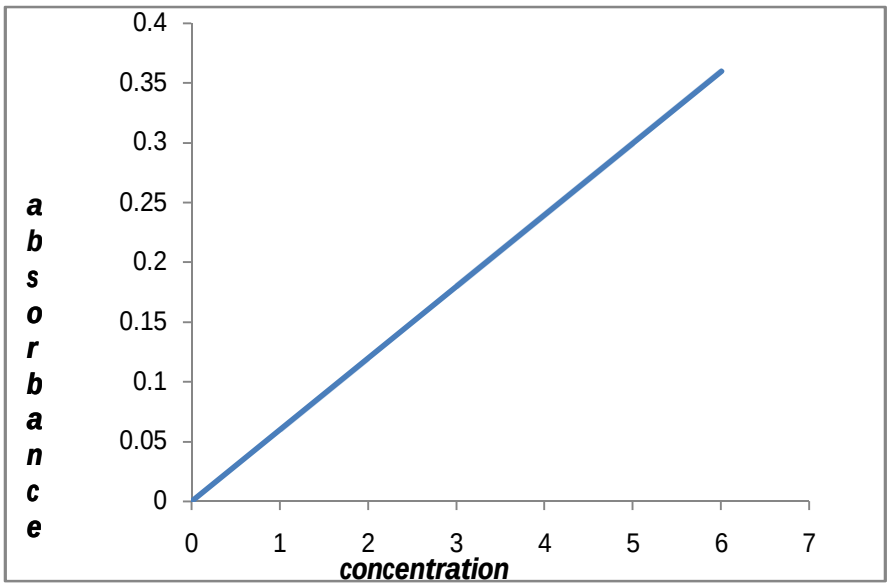
Y = a+ bx where x is the concentration of simvastatin μg/ml and Y is the absorbance at the respective λ max.
**Average of six determinations considered.

Table 2: Assay of simvastatin in Pharmaceutical formulation

Formulation	Labeled amount in mg	Amount found by proposed MethodM_I	Amount found by proposed Method M_{II}	Amount found by proposed Method M_{III}	%Recovery* proposed by methods M_I	%Recovery* proposed by methods M_{II}	%Recovery* proposed by methods M_{III}
Tablet-I	10	10.13	9.67	9.6	101.3	96.7	96
Tablet-II	10	9.67	9.47	10.9	96.7	94.7	109
Tablet-III	10	9.47	10.13	10.4	94.7	101.3	104

R. Reference was UV method developed in the laboratory.
*Recovery amount is the average of six determinations

Fig. 2: calibration curve for method I



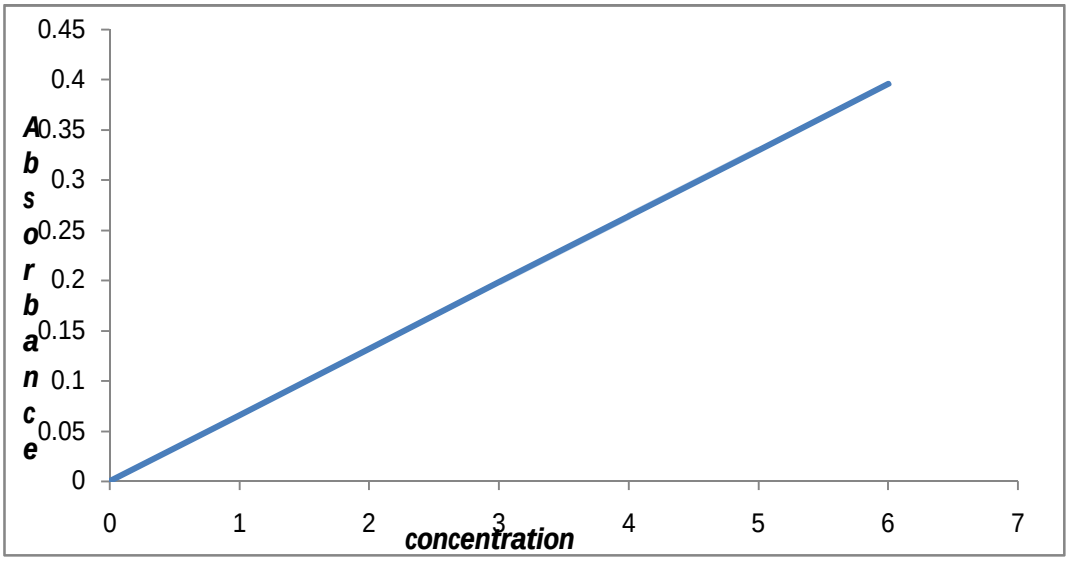


Fig .3: calibration curve for method II

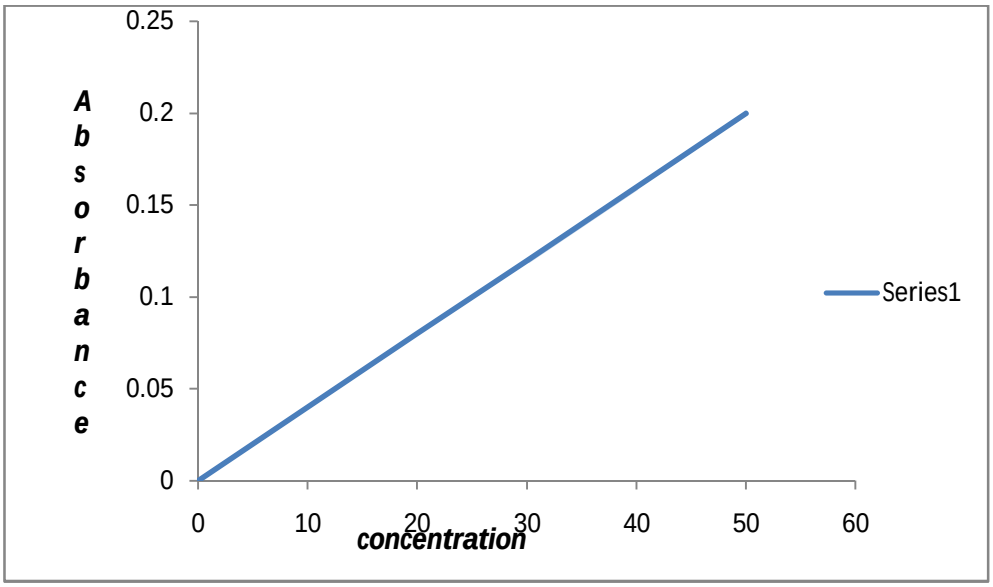


Fig. 4: calibration curve for method III

CONCLUSIONS

The proposed spectrophotometric methods were accurate, precise and reliable for the measurement of SIM in dosage form. The developed spectrophotometric method was validated for estimation of SIM using linearity, range, accuracy and precision. The RSD for all parameters was found to be less than one, which indicates the validity of method and assay results obtained by this method are in fair agreement. The developed method can be used for routine quantitative estimation of SIM in pharmaceutical Preparation.

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