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Development and validation of uv spectroscopy method for simvastatin in pH 6.8 phosphate buffer

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ABSTRACT

The aim of present work is to develop and validate simple, sensitive and specific Spectrophotometric method for the determination of simvastatin, a hypolipidemic drug in pure form and in pharmaceutical formulations.UV-Spectrophotometric method, which is based on measurement of absorption of U.V. The maximum wavelength in solvent system employed for determination of simvastatin was estimated at 233 nm in pH 6.8 phosphate buffer. The linearity range was found to be 0.01- 0.08 µg/mL(R^2=0.999). The developed method was validated with respect to linearity, accuracy (recovery), precision and specificity. The optimum conditions for analysis of the drug were established. The drug obeyed the Beer's law and showed good correlation. Beer's law was obeyed in concentration range 0.01-0.08µg/ mL The method was found to be simple, accurate, precise, economical and robust. This method has been statistically validated and is found to be precise and accurate.

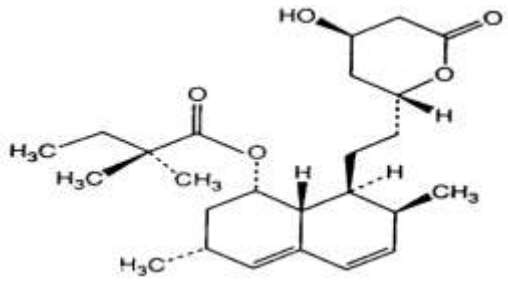
Keywords: Dimethylsulphoxide, Simvastatin, UV-Spectroscopy, pH 6.8 phosphate buffer, Validation.

INTRODUCTION

Simvastatin

Simvastatin[1] (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, shown in figure-1[2]is a lipid-loweringagent that is derived syntheticallyfrom fermentation products of *Aspergillus-terreus*[3]. After oral ingestion SIM, which is an inactive lactone, is hydrolyzed to corresponding β-hydroxy acid form[4] leading to the inhibition of 3-hydroxy 3-methylglutaryl – coenzyme A. (HMG-CoA)reductase, responsible for catalyzing the conversion of HMG CoA tomevalonate, which is an

early and rate limiting step in cholesterol biosynthesis[5]. Simvastatin is rapidly absorbed from the gastrointestinal tract after oral administration but undergoes extensive first-pass metabolism in the liver. It is inactive lactone prodrug and hydrolyzed in the gastrointestinal tract to the actives of hydroxy derivative.



Structure of simvastatin

Several methods were reported for the determination of SIM individually in plasma samples by HPLC[6] with simvastatin acid[7][8][9] and with metoprolol[10] by LC-MS/MS. The available methods are used either for the determination of SIM individually or for determination of these analytes along with it metabolites or with other drugs. The aim of our work was developed a simple, sensitive, rapid, economical and validated analytical method for the quantification of SIM in pH 6.8 phosphate buffer.

Present work focuses on the development of rapid and simple analytical method for quantification of SIM respectively. Further this method was applied for *Invitro* dissolution studies. The developed method may also be expected to provide a support for carrying out of the dissolution studies.

MATERIALS AND METHODS

INSTRUMENTS USED

The work was performed by using UV-Visible single beam spectrophotometer of Aquamateplus i.e., from Thermo scientific corporation. The absorption spectra analysis for the reference and test solutions were carried out in a quartz cell of the measured length of 1 cm over the specific λ_{max} at 200-400nm.

pH meter of ELICO® Li 120 was used for measuring of pH of the prepared pH 6.8 phosphate buffer.

CHEMICALS USED

Simvastatin was received from the Mylan pharmaceuticals, Hyderabad as the gift sample. The drug received was having the accurate purity of 99.99% w/w and was used for the analysis without the purification of the drug simvastatin. Dimethylsulphoxide (DMSO), potassium dihydrogen phosphate and sodium hydroxide were purchased from Loba chemie Pvt.Ltd. Mumbai. The chemicals and the reagents used for the analysis of the work is of the analytical grade. Simvotin® tablets of 10 mg manufactured by Ranbaxy are chosen for the estimation of drug content by this developed method.

PREPARATION OF PRIMARY STANDARD STOCK SOLUTION

Accurately weighed 10 mg of simvastatin and transferred into 100 mL volumetric flask and the volume was made up to the mark with DMSO to get 100 ug/mL solution.

PREPARATION OF SECONDARY STANDARD STOCK SOLUTION

1mL of primary standard stock solution was diluted up to 10 mL in a volumetric flask using DMSO as a solvent to get 10 µg/mL solution.

DETERMINATION OF λ MAX

1 mL of secondary standard stock solution was diluted up to 10 mL in a volumetric flask using pH 6.8 phosphate buffer as a solvent to get the 1 µg/mL solution. Spectrum of this solution was run from 200-400nm range in UV spectrophotometer. λ max of simvastatin was found at 233nm.

PROCEDURE FOR CONSTRUCTION OF CALIBRATION CURVE

Aliquots of 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7 and 0.8 mL were withdrawn from above prepared 1µg/ml of drug

solution and diluted to 10 mL in 10 mL volumetric flask with pH 6.8 phosphate buffer so as to get 0.01, 0.02, 0.03, 0.04, 0.05, 0.06, 0.07, 0.08 µg/ mL Absorbance of each solution was measured by UV spectrometer at 233 nm using pH 6.8 phosphate buffer as blank.

STUDY OF LINEARITY

An aliquot of concentration of 0.01-0.08 µg/mL were prepared and absorbance were measured as per the developed method to confirm the linearity[10][11]. The calibration curve was constructed for the obtained absorbance values of simvastatin and its concentrations at λ max of 233nm and linearity was evaluated by linear regression equation. The slope intercept and correlation coefficient values are recorded.

PRECISION

The precision[11][12] of the assay was determined by repeatability and reported as %RSD. For this 0.03µg/mL concentration was taken and measured six times in a day and same was measured in the next day. The %RSD was calculated.

ACCURACY

The accuracy of method was evaluated through standard addition method [11][12]. In this known amount of standard simvastatin was added in pre-analysed sample. This was done for 0.03 µg/mL concentration taking it as a 100% for three times. It was done for 80%, 100% & 120% and the recovery studies were performed and finally the %RSD was calculated.

ROBUSTNESS

It is a study of small but deliberate variations in method parameters[11][12] such as absorption maxima,pH and ratio of mobile phase solvents. In this present work the absorption maxima was decreased and increased by 2nm and carried the process for 0.03 µg/mL solution for 6 times. The %RSD was calculated.

RUGGEDNESS

It is the study[11][12] of degree of reproducibility of test results obtained by the variety of conditions like different analysts, reagents, laboratories, days, equipment etc.The present work was performed bythe change of analyst. Then nearly same results were obtained which are similar to that of first analyst.

ASSAY OF SIMVASTATIN IN MARKETED PRODUCT

Simvotin 10 tablets manufactured by Ranbaxy laboratories limited was selected and analyzed for simvastatin using the newly developed and validated method. 0.03µg/mL of simvastatin was taken as a reference standard solution. 10 tablets were accurately weighed and powdered equivalent to average weight of tablet was accurately weighed and transferred to 100mL DMSO. 1 mL of this solution was diluted up to 10 mL in a volumetric flask using pH 6.8 phosphate buffer as a solvent and blank. From this 0.3 mL was withdrawn and diluted to 10 mL in 10 mL volumetric flask with pH 6.8 phosphate buffer. Absorbance of this solution was measured by UVspectrometer at 233 nm.

RESULTS AND DISCUSSION

A simple, selective, accurate, precise spectroscopic method for estimation of simvastatin in bulk and pharmaceutical dosage form has been developed and validated. The linearity range was in the concentration range of 0.01-0.08µg/ mL (r2=0.999). it indicated that the concentrations of simvastatin had good linearity. The assay of simvastatin was found to be 98.56%. it indicated that by the precision of method was confirmed by the repeatable analysis of solution. The % RSD was found to be 0.631 and 0.771% respectively for intra and interday precision. It indicated that method had good precision. The procedure for accuracy was repeated for 3 times by taking 0.03µg/ mL as 100%. The recovery was calculated for 80%, 100% and 120%. The % RSD was found to be 1.157%. Because the % RSD were below 2 the method developed is highly accurate and,precise.

Figure 1: Calibration curve of simvastatin in pH 6.8 phosphate buffer

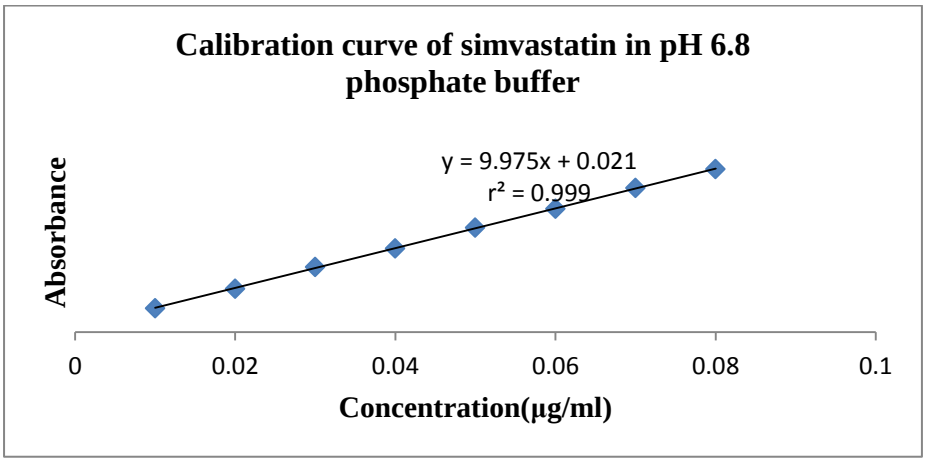


TABLE 1: PRECISION OF DEVELOPED METHOD

S.No	Intraday precision	% RSD	Inter day precision	% RSD
1	0.382		0.377	0.771
2	0.383	0.631	0.378	
3	0.380		0.375	
4	0.386		0.382	
5	0.385		0.381	
6	0.386		0.382	

TABLE 2: ACCURACY DATA OF DEVELOPED METHOD

Conc. (µg/mL)	Spike level	Mean absorbance	Amount found (mg)	% Recovery	Mean % RSD	Total Mean % RSD
0.03	80%	0.582	0.0534	98.88	0.334	
0.03	100%	0.645	0.0594	98.66	0.806	0.436
0.03	120%	0.711	0.0655	98.78	0.168	

TABLE 3: ROBOUSTNESS OF DEVELOPED METHOD

S.NO	231nm	%RSD	235nm	%RSD
1	0.316		0.315	
2	0.317		0.316	
3	0.315	0.500	0.317	0.360
4	0.318		0.317	
5	0.314		0.318	

CONCLUSION

The proposed method is simple, accurate, precise,specific and selective for estimation of simvastatin in bulk and pharmaceutical dosage forms. The method is economical, rapid and do not require any sophisticated instruments in contrast to chromatographic method. Hence it can be effectively applied for routine analysis of simvastatin in bulk and marketed formulation.

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