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A NOVEL UV- SPECTROPHOTOMETRIC METHOD DEVELOPMENT AND VALIDATION OF SIMVASTATIN IN BULK AND PHARMACEUTICAL DOSAGE FORMS

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ABSTACT

A simple, accurate and precise Area under curve spectroscopic method was developed and validated for the estimation of Simvastatin in bulk and Pharmaceutical dosage forms and has an absorption maximum between 236-246 nm in 0.1 M HCl. The Linearity was found to be in the concentration range of 2-12 µg/ml and the correlation coefficient was found to be 0.9999 and it has showed good linearity, reproducibility, precision in this concentration range. The regression equation was found to be Y = 0.0485 X + 0.0006. The % recovery values were found to be within 99.15 - 99.94 % showed that the method was accurate. The LOD and LOQ were found to be 0.018871 and 0.18871 µg/ml, respectively. The % RSD values were less than 2. The method has been validated according to ICH guidelines for linearity, accuracy, precision, robustness, ruggedness. Limit of detection and limit of quantitation. Proposed method was successfully applied for the quantitative estimation of Simvastatin in bulk and pharmaceutical dosage form.

KEY WORDS: Simvastatin, Area under curve Spectroscopy, 0.1M HCl, accuracy.

INTRODUCTION

Simvastatin Statins are a group of 3-hydroxyl–3- methylglutaroyl-coenzyme A (HMG-CoA) reductase inhibitors used in heterozygotic hypercholesteraemia and hyperlipidemia[1, 2].

Simvastatin (Figure 1) is a prodrug[2, 3] which is biotransformed in liver into an active form of simvastatin (β-hydroxyacid) by ring opening reaction of the lacton. Chemically, simvastatin is (1S,3R,7S,8S, 8aR)-8-[2-[(2R,4R)-4-hydroxy-2H-pyran-2-yl]ethyl]-3,7-dimethyl-1,2,3,7,8,8a hexahydronaphthalen-1-yl 2,2 dimethyl—butanoate. The inhibition of the HMGCoA causes a decrease in LDL, low density lipoprotein (20–40 %), triglycerides (10–20 %), while it increases HDL, high-density lipoprotein (5–15%) and LDL receptor expression[3, 4]. So, it is most commonly prescribed for the prevention of atherosclerosis and heart disease.

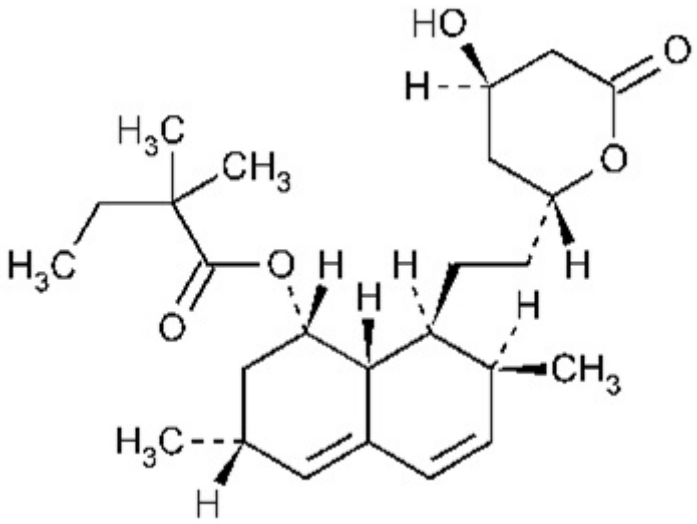

Figure.1: Chemical structure of Simvastatin.

Literature Survey revealed that the drug has been estimated by few UV spectrophotometric[5,6,7], HPLC methods[8,9], and Voltammetry[10,11] has been reported so far.

The aim of present work was to develop and validate a novel, rapid, simple, precise, and specific Area under curve spectroscopic method for estimation of Simvastatin in its bulk and pharmaceutical dosage form.

MATERIALS AND METHOD

Instrument

UV-Visible double beam spectrophotometer, SHIMADZU (model UV-1800) with UV probe software. All weights were taken on analytical balance.

Chemicals

Simvastatin pure form was obtained as gifted sample from pharma industry and its pharmaceutical dosage form Simvastatin Tablets labelled claim 10 mg were purchased from local pharmacy.

Solvent

0.1M HCl (prepared by dissolving 8.5ml in 1000ml of distilled water).

Selection of analytical wavelength

Appropriate dilutions were prepared for drug from the standard stock solution and the solution were scanned in the wavelength range of 200-400 nm. The absorption spectra thus obtained were derivatized from AUC method which illustrated in Fig.2.

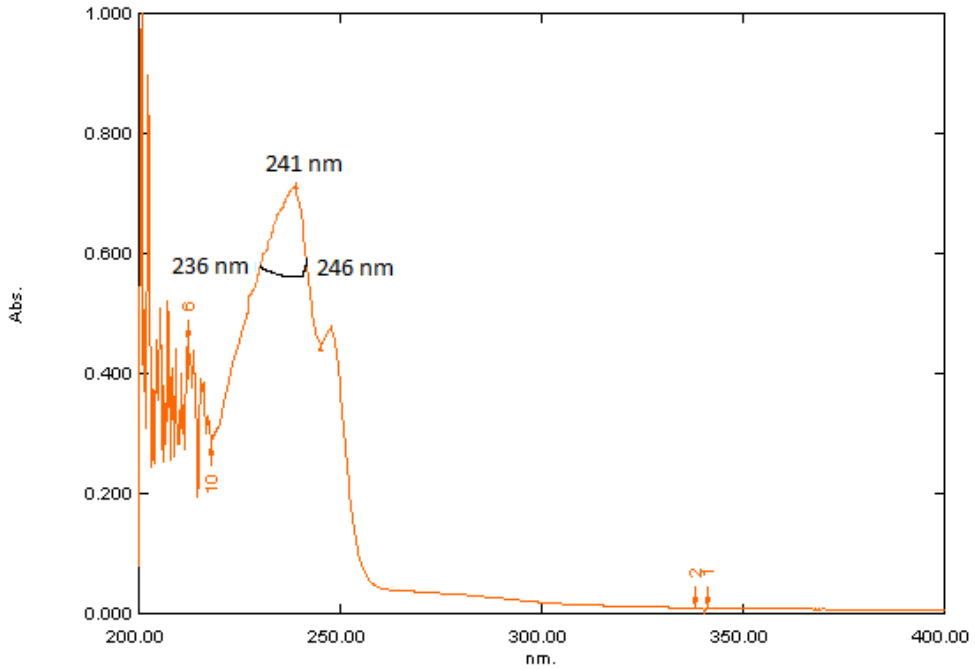

Fig.2: Typical Zero order spectra of Simvastatin showing Area Under Curve [AUC] from 236nm to 246 nm.

Preparation of Standard stock solution

Accurately weigh 100mg of Simvastatin was transferred into 100ml volumetric flask and dilated with 0.1M HCl up to the mark. From this pipette out 10ml into 100ml volumetric flask and diluted with 0.1M HCl up to the mark, from this solution pipette out 0.2, 0.4, 0.6, 0.8, 1.0,and 1.2 ml into 10ml individual volumetric flask and add 0.1M HCl up to the mark, this gives 2, 4, 6, 8, 10, and12 µg/ml concentrations.

Preparation of Sample solution

Twenty tablets were weighed and powdered, the tablet powder equivalent to 100mg of Simvastatin was transferred into100ml volumetric flask then it was diluted with 0.1M HCl and made up to mark and the solution was filtered through. Whatmans filter paper no.41. From this pipette out 10 ml in a 100ml volumetric flask and make up the volume up to the mark with 0.1M HCl. From this solution pipette out 0.3 ml into 10ml volumetric flask and make up the volume with 0.1M HCl, this gives 3µg/ml concentrations.

Method validation: The method is validated according to the ICH guidelines.[12, 13, 14]

RESULTS AND DISCUSSION

Method: Area under curve Spectroscopy

Linearity

The working standard solution were diluted serially with 0.1MHCl to obtain the range of 2-12 µg/ml. a calibration curve for Simvastatin was obtained by measuring the absorbance between 236 - 246 nm and absorbance values are shown in Table.1 and Calibration graph were presented in Fig.3. Statistical parameters like slope, intercept, coefficient of correlation, and Sandel sensitivity were determined and presented in Table.2.

Table.1: Results of calibration curve at 241 nm by Area under curve Spectroscopy.

Sl. no	Concentration in (µg/ml)	Absorbance between 236-246 nm
1	2	0.094
2	4	0.193
3	6	0.292
4	8	0.388
5	10	0.485
6	12	0.579

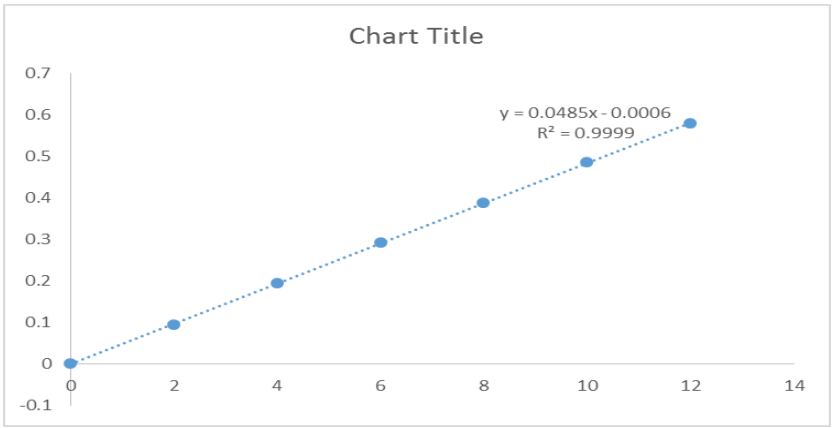

Fig.3: Linearity curves for Simvastatin by Area under curve Spectroscopy.

Table no.2: Regression parameters for Simvastatin by Area under curve Spectroscopy.

Regression parameters	Simvastatin
Range	2-12 µg/ml
Range to measure AUC nm	236-246 nm
Regression equation	Y=0.0485x+ -0.0006
Slope (b)	0.0485
Intercept(a)	0.0006
Correlation coefficient (r^2)	0.9999

Precision

Precision of the method was studied as intra-day and inter-day precision. Intra-day precision was determined by analyzing the 2, 4, 6, 8, 10 and 12µg/ml concentration for three times in same day. Inter-day precision was determined by analyzing the same concentration of solution daily for three days. Precision results are shown in Table.3.

Table. 3: Determination of precision results for Simvastatin by Area under curve Spectroscopy.

Concentration (µg/ml)	Intra-day Absorbance ±SD**	%RSD	Inter-day Absorbance ±SD**	%RSD
2	0.093± 0.0015	1.64	0.098 ± 0.001528	1.55
4	0.193±0.0026	1.37	0.197±0.001	0.507
6	0.290±0.0052	1.82	0.298±0.002082	0.698
8	0.390±0.0020	0.533	0.397±0.002	0.503
10	0.486±0.0015	0.319	0.497±0.00321	0.646
12	0.579±0.0025	0.434	0.596±0.002	0.335

Accuracy

To assess the accuracy of the proposed method, recovery studies were carried out at three different levels i. e, 50%, 100% and 150%. In which the formulation concentration was kept constant and varied pure drug concentration. Accuracy results were shown in Table.4.

Table. 4: Determination of accuracy results for Simvastatin by Area under curve Spectroscopy.

Spiked levels	Amount of sample (µg/ml)	Amount of standard (µg/ml)	Amount recovered(µg/ml)	% Recovery ±SD**	%RSD
50	3	1.5	4.13	99.61%±0.0107	0.0618
100	3	3	5.95	99.15%±0.0035	0.0035
150	3	4.5	7.46	99.94%±0.0056	0.0056

**Average of six determinations

Ruggedness

Ruggedness was determined between different analysts of 6 µg/ml concentration. The value of %RSD was found to be less than 2 and the results were shown in Table.5.

Analysts	**Analyst-1**	**Analsst-2**
Mean	0.289	0.294
Standard Deviation	0,00503	0.00401
% RSD	1.74	1.37

Limit of detection and Limit of Quantitation

The LOD and LOQ of the present method were calculated based on standard deviation of the Response and slope of linearity curve. LOD and LOQ values of Simvastatin were found to be 0.018871 µg/ml and 0.18871µg/ml.

CONCLUSION

Thus, the developed method was found easy, simple, accurate, precise, selective and economical for the routine estimation of Simvastatin in bulk and pharmaceutical dosage form.

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REFERENCES

1. Yang H, Feng Y, Luan Y. Determination of Simvastatin in human plasma by liquid Chromatography-mass spectrometry. J Chromatogr B Analyt Technol Biomed Life Sci. 2003; 785: 369–375.
2. Kumar AD, Sujan DP, Vijayasree V, Rao JVLNS. Simultaneous determination of simvastatin and ezetimibe in tablets by HPLC. E.J.Chem. 2009; 6(2): 541-5443.
3. Veronin MA, Nguyen NT. Comparison of simvastatin tablets from the US and international markets obtained via the Internet. Ann Pharmacother. 2008; 42(5): 613-20.
4. Patel BN, Sharma N, Sanyal M, Shrivastav PS. Simultaneous determination of simvastatin and simvastatin acid in human plasma by LC-MS/MS without polarity switch: application to a bioequivalence study. J Sep Sci. 2008; 31(2): 301-13.
5. Millership JS, Chin J. Determination of Simvastatin in tablet formulation by derivative UV spectroscopy. J. Anal. Chem. 2010; 65(2): 164-68.

6. Wang L, Asgharnejad M. Second-derivative UV spectrometric determination of simvastatin in its tablet dosage form. J. Pharm. Biomed. Anal. 2000; 21: 1243-1248.
7. Shrikanth B S, Archana H G, Prathap S K, Prajusha K P. Method Development and Validation of Simvastatin in Bulk and Pharmaceutical Dosage Forms by Using UV-Spectrophotometric Method. Imperial Journal of Interdsciplinary Research. 2017; 3(5): 1419-1422.
8. Ali A, Nameh ESM, Shawabkeh RA. High-perfromance liquid chromatographic determination of simvastatin in medical drugs. J. Anal. Chem. 2006; 61: 63-66.
9. Madan J, Thakkar V, Dwivedi A, Singh, S. Ion-pairing RP-HPLC analytical method for estimation of Simvastatin and its hydroxyl acid. J. Sci. Ind. Res. 2007; 66: 371-76.
10. Nigovi B, Lovri SK, Devi D. Rapid Voltammetric Identification and Determination of Simvastatin at Trace Levels in Pharmaceuticals and Biological Fluid. Croat. Chem. Acta 2008; 81(3): 453-459.
11. Coruh O, Ozkan SA. Determination of the antiperlipidemic simvastatin by various voltammetric techniques in tablets. Die. Pharmazie. 2006; 61: 285-290.
12. ICH, Q2A Text on Validation of Analytical Procedures; 1994.
13. ICH, Q2B Validation of Analytical Methodology; 1996.
14. ICH, Q2 (R1) Validation of Analytical Procedures: text and methodology; 2005.