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A SIMPLE UV SPECTROSCOPIC METHOD DEVELOPMENT AND VALIDATION FOR THE QUANTIFICATION OF SIMVASTATIN IN BULK AND ITS FORMULATION

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ABSTRACT

A simple, rapid, accurate, precise, selective and economical UV Spectrophotometric method has been developed for estimation of Simvastatin in bulk and its dosage form. Ethanol 30% v/v was used as diluent for the study. The maximum absorption was monitored at 238 nm. The method exhibited linearity in the concentration range of 5-30µg/ml with correlation coefficient value 0.999. The accuracy of the method was checked at three different levels of 50%, 100% and 150 %. The % recovery was found to be 100.18%. The developed method was validated with respect to accuracy, precision, selectivity, specificity and robustness. All the parameters examined were within the acceptance limits.The above method was a cost-effective quality control tool for routine analysis of Simvastatin in bulk and its pharmaceutical dosage form.

KEYWORDS: Simvastatin, Spectroscopy, quality control, Accuracy, Precision, Robustness.

INTRODUCTION

Simvastatin is a lipid-lowering agent [1] that is derived synthetically from the fermentation of Aspergillus terreus.[2] It is a potent competitive inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A reductase (hydroxymethylglutaryl COA reductases), which is the rate-limiting enzyme in cholesterol biosynthesis. It may also interfere with steroid hormone production. Due to the induction of hepatic LDL receptors, it increases breakdown of LDL cholesterol.[1] Chemically it is, (1S,3R,7S,8S,8aR)-8-{2-[(2R,4R)-4-hydroxy-6-oxooxan-2-yl]ethyl}-3,7-dimethyl-1,2,3,7,8,8a-hexahydronaphthalen-1-yl2,2-dimethylbutanoate.[3] The chemical structure of Simvastatin was shown in Fig 1.

From extensive survey of literature on Simvastatin.[4-9] reveals that few reported works UV spectroscopy.[10-15] for the determination of Simvastatin pure drug and its pharmaceutical dosage form to the best of our knowledge. So the present emphasis was given to develop simple, selective, precise and accurate UV method for determination of Simvastatin in bulk and its tablet dosage form. The developed method to be validated in accordance to ICH Q2 (R1) guidelines.[16]
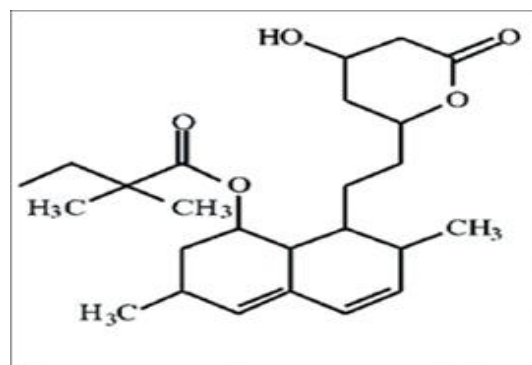

Figure 1: Chemical structure of Simvastatin.

MATERIALS AND METHODS

Chemicals and reagents
The reference sample of Simvastatin was procured as gift sample from MSN laboratories (Hyderabad, India). Tablet formulation [Simvotin], Solrex Formulation Pvt. Ltd was purchased from local pharmacy and used for the

study. Ethanol was acquired from Merck specialty's private ltd., Mumbai, India. All the reagents used were of analytical grade and distilled water was used as diluent for further preparations of the drug.

Instrument used
For the current study UV/VIS double beam spectrophotometer Shimadzu 1800 incorporated with UV probe software, having deuterium lamp.

Methodology
Selection of solvent
The selection of solvent was done based upon the drug solubility, stability and absorbance maxima of the compound in the particular solvent. 10 mg of simvastatin was weighed and solubility of this sample was checked in the 0.1N HCL, 0.01N NaOH, Methanol, Ethanol, Phosphate buffer pH6.8 and distilled water.From the reported studies as ethanol 30% v/vwas not used for the determination of simvastatin. Hence the current method was developed in 30%v/v ethanol.

Preparation of standard stock solution
The standard stock solution of Simvastatin was prepared by transferring accurately weighed 50mg of drug to 50ml volumetric flask and dissolving it with ethanol 30% v/v to get a concentration of 1000µg/ml. The solution was diluted accordingly to a concentration of 1000µg/ml and was kept as the stock solution. From the stock solution various dilutions were carried with distilled water to get working standard solutions of concentration 5-30µg/ml. These aliquots are scanned at its analytical wavelength.

Preparation of sample solution
Weight equivalent to 25 mg of drug simvastatin tablet dosage form and transfer into 25 ml volumetric flask and dissolve in 30%v/v ethanol, the contents were sonicated for 5 min to enhance solubility of the drug and then finally made up to the volume. From this aliquot of 20 µg mL-1 was prepared and used.

Method Validation
Linearity and Range
Linearity data for the spectrophotometric method was obtained at an absorption maximum of 238 nm as shown in figure 2 by using sixconcentrations in the range of 5–30µg/ml. A calibration curve was obtained by plotting absorbance against concentration by considering six observations as shown in figure 3. The regression of Simvastatin concentration over its absorbance was found to be y=0.0222x+0.0399 and R^2 as 0.9997(where y is the absorbance and x is the concentration of simvastatin). The linearity data was shown table no 1.

Accuracy
The accuracy of the proposed method was tested by recovery studies at different replicate levels in triplets for 50%, 100% and 150%.The sample solutions were prepared by adding a known amount of pure drug to the pre-analysed formulation.The mean percent recovery was calculated and was reported in the tableno 2.

Precision
The intra-day precision was performed by analysing six replicate standard solutions on the same day, and inter-day precision was performed by analysing a series of standard solutions for six consecutive days using the proposed UV method. The precision value of inter and intra-day were found to be 0.885 and 1.394% respectively which was found to be within limits i.e. < 2.

Detection and Quantification limits
Limit of detection (LOD) represents the lowest amount of analyte in the sample which can be detected. Limit of quantification (LOQ) represents the lowest amount of analyte, which can be quantitatively determined. The above parameters are calculated based on the standard deviation of the response and the slope. The standard deviation was calculated based upon the calibration curve. LOD = 3.3σ/SLOQ = 10σ/S. The LOD and LOQ values for simvastatin were 0.9825µg/ml and 2.9772µg/ml respectively.

Robustness
Robustness is defined as the measure of its capacity to remain unaffected by small but deliberate variation in method parameters, and it provides an indication of its reliability during normal range. Robustness was studied using six replicates of the sample at a concentration level of 20µg/ml (for UV).The % Relative standard deviation of Assay values between two analysts should be not more than 2.0%. From the observation it was found that the % RSD was within limit at all variable conditions.

RESULTS AND DISCUSSION

The method was validated in terms of linearity, precision, accuracy, LOD, LOQ and robustness. Detection wavelength was selected at 238 nm.Linearity response was observed in 5-30µg/ml having R^2=0.9997. The precision results show % RSD as less than 2, each level clearly that the method is precise enough for the analysis of Simvastatin. The accuracy of the method was checked by recovery studies. The developed method was validated in accordance with ICH Q2 (R1) guidelines and overall summary of validation parameters were tabulated in Table 3.The uv spectra and overlay spectra of Simvastatin were shown in figure 2 & 3.
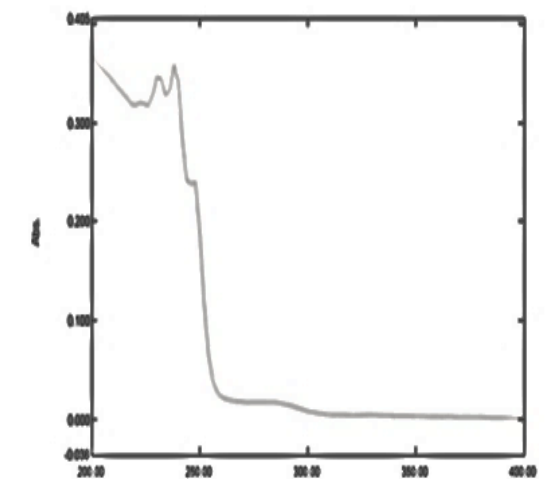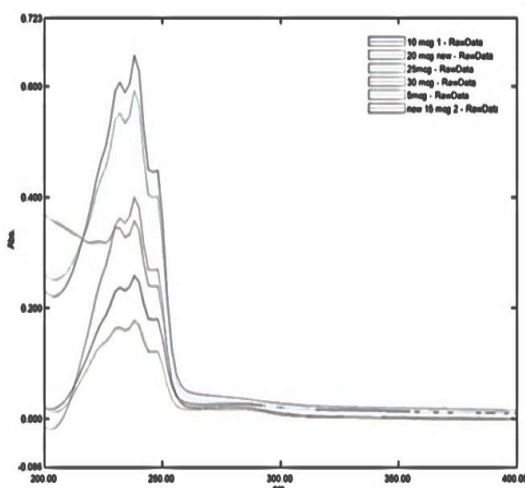
Figure 2: UV spectra of Simvastatin.

Table 1: Results of calibration curve at 238 nm for Simvastatin.

S. No.	Concentration (μg/ml)	Absorbance±Std dev
1	5	0.155±0.004
2	10	0.261±0.005
3	15	0.369±0.008
4	20	0.481±0.004
5	25	0.593±0.007
6	30	0.710±0.006

Regression value must be not more than 0.999. Llinearity of Deferiprone within 5-30μg/ml with regression value of 0.9997.
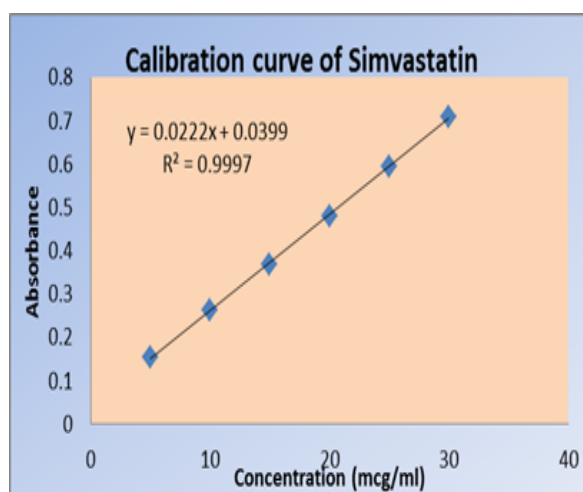

Figure 4: Linearity curve for Simvastatin.

Figure 3: Overlay UV spectra of Simvastatin.

Table 2: Determination of Accuracy results for Simvastatin.

S. No.	Spike Level	Absorbance	μg/ml Added	μg/ml Found	% Recovery
1	50 %	0.261	4.96901	5.06198	101.874
2	100 %	0.481	19.876	19.7934	99.5842
3	150 %	0.71	44.7211	44.3182	99.0991

The mean % recovery was found to be 100.18%.

Table 3: The total Summary of Optical characteristics and Other Parameters.

S. No.	Parameters	Results
1.	Beer's-Lambert's range (μg/ml)	5-30
2.	Regression equation (y)	Y = 0.022x - 0.0399
3.	Slope (b)	0.022
4.	Intercept (a)	0.0399
5.	Correlation coefficient (r^2)	0.999
6.	Intraday precision (% RSD)	0.88
7.	Interday precision (% RSD)	1.39
8.	Accuracy (% mean recovery)	100.18
9.	Limit of detection (μg / ml)	0.982
10.	Limit of quantification (μg / ml)	2.977
11.	Assay of tablets (%Purity)	99.38

*$Y = bx + a$ where x is the concentration of Simvastatin in mcg / ml and Y is the absorbance at the respective λ_{max}.

CONCLUSION

A novel, precise, accessible, reliable and reproducible method for estimation of Simvastatin in bulk and tablet dosage form using UV method was developed and validated as per ICH guidelines. The wide range of linearity establishes a further scope of promoting the proposed methods for estimation of Simvastatin. The RSD values for all the validation parameters were found to be within the limit, indicating that the proposed UV method was trusts worthy. This method hassample scope and application in industry for estimation of Simvastatin.

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