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Development and Validation of UV/Visible Spectrophotometric Method for the Estimation of Simavastatin in Bulk and Pharmaceutical Formulations

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ABSTRACT

Simavastatin is an antihyperlipedemic drug used in the treatment of atherosclerosis a cardiovascular disorder A simple, sensitive, accurate and reproducible UV/visible spectrophotometric method was developed for the determination of Simavastatin in bulk and pharmaceutical dosage forms. The solvent used was distilled water and wavelength corresponding to maximum absorbance for the drug was found at 238 nm. Drug obeyed beer's law in the concentration range of 10 – 60µg/ml. with a correlation coefficient of 0.999. The linear regression equation obtained was y=0.0565x+0.0249, where y is the absorbance and x is the concentration of the pure drug solution. The method was validated for several parameters such as Linearity, Accuracy, Precision and Robustness as per the ICH guidelines. The % recovery value which is close to 100% indicates reproducibility of the method and absence of interference of the excepients present in the formulation. The authors conclude that the proposed spectrophotometric method for the estimation of Simavastatin can be used for routine analysis of Simavastatin in bulk as well as in tablet dosage form.

Keywords: Simavastatin, Spectroscope Absorbance

INTRODUCTION

Simvastatin belongs to a class of drugs called HMG-CoA reductase inhibitors commonly called statins that derived synthetically from fermentation products of Aspergillus terreus. [1] It is chemically known as (1S, 3R, 7S, 8S, 8aR)-8-{2-[(2r, 4r)-4-hydroxy-6-oxotetrahydro2H-pyran-2yl]-ethyl}-3, 7-dimethyl-1, 2, 3, 7, 8.8a hexahydronapthalen-1-yl-2, 2dimethylbutanoate (Fig. 1). All statins act by inhibiting 3-hydroxy-3methylglutarylcoenzyme. A HMG-CoA reductase, the rate limiting enzyme of the HMGCoA reductase pathway, the metabolicpath way responsible for the endogenous production of cholesterol mainly used for the treatment of dyslipidaemia and the prevention of cardiovascular diseases. Simvastatin is prodrug which is converted into its β- hydroxy which inhibits HMG CoA reductase(3-hydroxy-3-methyl glutarylCoenzyme A) enzyme, responsible for catalysing the conversion of HMG CoA to mevalonate a rate limiting step in the synthesis of cholesterol in liver. [2] The drug is officially listed in US pharmacopeia, British pharmacopeia and European pharmacopeia. Simvastatin can be estimated by UV spectrophotometry [3-10, 18, 19], Derivative Ratio spectrophotometry [11-13], Stability Indicating RP-UPLC [15], Stability Indicating RP-HPLC [14-17] , RP-HPLC [19-30], Stability indicating HPTLC [31], HPTLC [32-34] and LC-MS/MS [35] alone or in combination with other drugs. Two official methods utilizing HPLC Gradient methodology are reported in European Pharmacopoeia (EP) [36] United State Pharmacopoeia (USP) [37].

Because of cost-effective and minimal maintenance, UV spectrophotometry is always preferred at small scale industries. Literature survey reveals that so far many UV spectrophotometric methods have been reported for the estimation of Simvastatin in alone or

in combination with other drugs. But out of them only few methods included single estimation of Simvastatin. Therefore the main objective of the proposed methods were to develop simple, new and economic UV spectrophotometric methods for the estimation of Simvastatin in bulk and tablet dosage form and validate as per ICH guidelines.

MATERIALS AND METHODS

Chemicals and Reagents

The pure API sample of Simvastatin was obtained as free gift samplefrom Gen Pharma Ltd; Pune respectively while solvent such as methanol used were of spectroscopy grade (E. Merck India) and double distilled water used for whole experiment. The marketed combined pharmaceutical dosage form ofSimvastatin (10 mg) i.e. Simvas (Micro Labs, India)was purchased from local market.

Instrumentation

A UV-shimadzu1600 spectrophotometer, and 1-cm quartz cell was used for Spectral and absorbance measurements.

Preliminary solubility studies of drug

1 gm of Simvastatin was weighed and solubility was checked in 10 ml water, methanol, 0.1N NaOH and 0.1 N HCl. The drug was found to be freely soluble in methanol and practically poorly soluble in water, 0.1N NaOH and 0.1 HCl. Therefore methanol was selected as diluent and Simvastatin was also found to be stable in methanol for 48 hours in stability studies.

Preparation of standard stock solutions

Transfer 2.5 mg of pure Sitagliptin phosphate and Simvastatin in separate 25 ml of volumetric flask containing methanol as diluent and then sonicated for 15 minutes and final concentration of this stock solution being 100mcg per ml.

Determination of λmax

By appropriate dilution of standard stock solutions of Simavastatin in distilled water containing 20µg/ml of Simavastatin, dilutions were made and scanned on Shimadzu 160A a visible double beam spectrophotometer in the range of 200- 800 nm against distilled water as blank. Wavelength of maximum absorption was determined for drug. Simavastatin showed maximum absorbance at 304 nm.

Method validation

The method was validated for several parameters like Linearity, Accuracy, Precision, Robustness according to ICH guidelines5,6.

RESULT AND DISCUSSION

Linearity

The linearity of the analytical method was its ability to elicit test results which are directly proportional to analyte concentration in samples within a given range. To establish the linearity of the proposed method, various aliquots of the standard solution of the drug were prepared from stock solution and analysed. The calibration graphs were obtained by plotting the absorbance versus the concentration data and were treated by linear regression analysis. The drug showed linearity in the range of 20 – 100µg/ml. with a correlation coefficient of 0.9992. The slope, intercept, correlation-coefficient and optical characteristics are summarized in Table 1and 2 and Figure 1.

Accuracy

Accuracy of the proposed method was determined using recovery studies. Accuracy was determined by spiking known amounts of the analyte into the placebo formulation (F1, F2 and F3) across the specified range of the analytical procedure to obtain 40, 50 and 60 µg/ml (80, 100 and 120%). At each level, solutions were prepared in triplicate and the accuracy was evaluated in terms of percent recovery. (Table 3)

Percent Recovery was calculated using the formula

[%Recovery = 100 x Mean Experimental Concentration/ Theoretical Concentration].

Precision

Precision studies were carried out to ascertain the reproducibility of the proposed method. The precision of the assay method was determined by repeatability (intra-day) and intermediate precision (inter-day).The intraday precision was evaluated by analyzing six samples of 50µg/ml of the test concentration (n=6) at an interval of half an hour each.

Similarly interday precision was evaluated on two consecutive days (n = 12). Interday precision was evaluated by 3 samples at an interval of 1 hour on day 1 and3 samples at an interval of 1 hour on day 2.The concentration of the drug was determined and the value of relative standard deviation (%R.S.D) of the assay method was calculated. The precision result showed a Good repetability with percent relative standard deviation lessthan 2 (table 4 & 5).

Robustness

Robustness was determined by carrying out analysis by two different analyst and also by carrying out the analysis on two different instruments and the respective absorbance was noted and the results was indicated as SD. Four sample solutions each containing 50µg/ml were prepared and analyzed in two different U.V. visible spectrophotometers (Hewlett Packard 8453 and Shimadzu 160A) immediately after

preparation. (Table 6)

CONCLUSION

The linear calibration curve was obtained at concentration range 20 – 100 µg/ml. with a correlation coefficient (0.9992), Slope (0.0073) and Intercept (0.0081).

The proposed method was reproducible because results obtained with in inter-day and intra-day were in acceptable limit. The results of assay and % recovery were found to be satisfactory, indicating that the proposed method is precise and accurate and hence can be used for the routine analysis of La,motrigine in bulk and pharmaceutical formulation.

Table 1. Concentration and absorbance obtained for standard plot of Simavastatin in distilled ethanol`

Sr. No.	Concentration in µg/ml	Absorbance
1	10	0.677
2	20	1.552
3	30	1.722
4	40	2.240
5	50	2.827
6	60	3.466

Table 2. Optimum conditions, optical characteristics and statistical data of the regression equation for Simavastatin

PARAMETE	VALUE
Absorption maximum (nm)	238nm
Beer's Law limit (mcg/ml)	10-50
Correlation coefficient	0.9999
Regression equation	Y=Ax+b
Slope(A)	0.0565
Intercept (b)	0.0249

Table 3. Percentage recovery for Simavastatin according to the proposed method

S. No.	Initial Amount (mg)	Add of known qty of pure drug (to 100 ml of placebo formulation)	Total Theoretical drug concentration in µg/ ml	Mean Experimental drug concentration found in µg/ ml ± S.D.	% Recovery (±.S.D)
1	0 mg	3 mg	3	30 ± 0.03	100 ± 0.01
2	0 mg	4 mg	4	39 ± 0.10	98 ± 0.00
3	0 mg	5 mg	5	50 ± 0.00	100 ± 0.00

Table 4. Intraday Precision for Simavastatin

Time in mins	Absorbance N=3	Total Theoretical drug concentration in µg/m	Total Experimental drug concentration found in µg/ml
3	1.772,1.771,1.771	3	29.99± 0.011
9	1.770,1.772,1.771	3	30.00± 0.000
1	1.772,1.772,1.771	3	30.00± 0.000

Table 5. Interday Precision for Simavastatin

Time in mins	Absorbance N=3	Total Theoretical drug concentration in µg/ml	Total Experimental drug concentration found in µg/ml
3	1.770,1.772,1.771	3	29.98 ± 0.02
9	1.772,1.771,1.771	3	29.99± 0.01
15	1.772,1.771,1.771	3	29.98± 0.01

Table 6. Robustness data for Simavastatin

Sr.No.	Spectrophotometer 1 (Elico sl 210 double beam UV/VIS spectrometer)		Spectrophotometer 2 (Shimadzu 1600A)	
	A	Conc	Abs	Conc
1	1.8	30.88	1.729	30.47
2	1.8	30.80	1.731	30.47

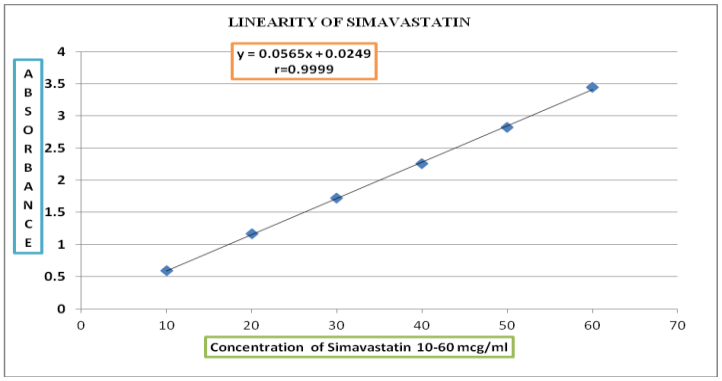

Figure 1.calibration curve for simavastatin at 238nm

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