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Development and Validation of UV-Vis Spectrophotometric Method for estimation of Simvastatin in Bulk and Mucoadhesive Dosage Form

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ABSTRACT

Simvastatin (SIM) is an antihyperlipidemic drug (Statin) significantly used to lower the cholesterol level in the blood stream. The drug is derived synthetically from fermentation products of Aspergillus terreus and in higher doses can also reduce the triglycerides level. Therefore, the main purpose of the proposed methods was to develop simple, new and economic UV spectrophotometric methods for the estimation of simvastatin in bulk and in mucoadhesive buccal film dosage form and validated as per ICH guidelines. The reported method was validated for linearity, accuracy, precision, limit of detection (LOD) and limit of quantification (LOQ). The accuracy was determined to be considerable and within specification limitations. Recovery studies were carried out at three different levels i.e. 80 %, 100 % and 120 % (99.4 to 102.7%). The % recovery of the drug was found to be 99.32. The values are complying with the assay specifications for active drugs in the United States of Pharmacopoeia (90.0-110.0%) which are required to be met by most drug formulations.

Keywords:Simvastatin, UV spectrophotometry, Method development, Validation, Estimations.

INTRODUCTION

Simvastatin (SIM) is an Antihyperlipidemic drug (Statin) significantly used to lower the cholesterol level in the blood stream. Simvastatin is prodrug that limits the 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase enzyme, which is the rate limiting step needed for the conversion of HMG-CoA to mevalonate in the synthesis cholesterol in liver. The drug is derived synthetically from fermentation products of Aspergillus terreus and in higher doses can also reduce the triglycerides level. The drug is officially described in US pharmacopeia, British pharmacopeia and European pharmacopeia.[1]

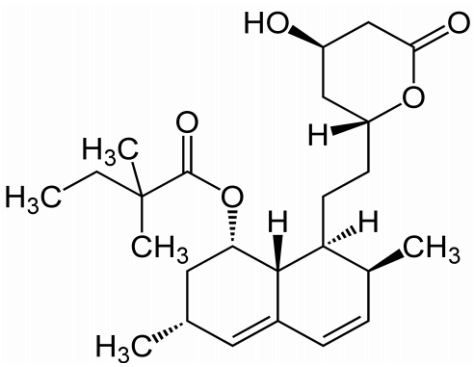

Figure-1- Structure of Simvastatin

Simvastatin can be estimated by UV visible spectrophotometry [2,3,4],RP-HPLC[5], Derivative Ratio spectrophotometry [6], Stability Indicating RP-UPLC, Stability Indicating RP-HPLC, RP-HPLC[7], Stability indicating HPTLC, HPTLC and LC-MS/MS alone or in combination with other drugs. Two official methods providing HPLC Gradient methodology are confirmed in European Pharmacopoeia (EP) United State Pharmacopoeia (USP). UV spectrophotometry is always favoured in small scale industries due to its low cost and minimal maintenance. A study of the literature finds that numerous UV spectrophotometric techniques have been published for estimating Simvastatin alone or in combination with other drugs[2]. But out of this only few methods included single estimation of simvastatin. Therefore, the main purpose of the developed methods was to develop simple, new and economic UV spectrophotometric methods for the estimation of Simvastatin in bulk and in mucoadhesive buccal film dosage form and validate as per ICH guidelines.

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MATERIALS AND METHODS

Chemicals and Reagents

The pure API sample of Simvastatin was obtained as gift sample from Micro labs Ltd (Mumbai, India) while solvent such as methanol and other solvent used were of spectroscopy grade.

Instrumentation

UV-Visible double beam spectrophotometer with matched quartz cells (1 cm, Model: (Shimadzu UV-1800) - Computer software UVProbe2.43.

Standard solutions

Stock of standard solutions for simvastatin were prepared separately in methanol. Stock solution of drug (1000 µg/mL) was prepared by dissolving 0.1 g ofsimvastatin in methanol to 100 mL volumetric flask. Further dilutions were prepared to make 10 µg/mL solution in methanol and the absorption spectrum was recorded within the range of 200-400 nm against a solvent blank and the λmax was found to be 238nm.

Preparation of calibration curve

From the above std. stock solution of Simvastatin (1000 µg/ml), pippete out 1 ml in 10 ml volumetric flask and dilute it 10ml (100 µg/ml). from that solution pippete out the aliquot of 0.2 to 1.2 ml of solution and transferred to series of 10 ml volumetric flasks and final volume made up to mark with methanol as diluent to form solutions of 2 to 12µg/ml of Simvastatin. The absorbance was recorded at the λmax of 238 nm against diluent as blank then calibration curve was plotted as absorbance vs concentration.

Absorbance maxima method

For the selection of analytical wavelength, standard solution of Simvastatin was scanned in the spectrum range from 200 nm to 400 nm separately. From the spectrum of the drug, λmax of simvastatin, 238 nm was selected for further analysis. The spectrum of the drug is shown in the figure 2.

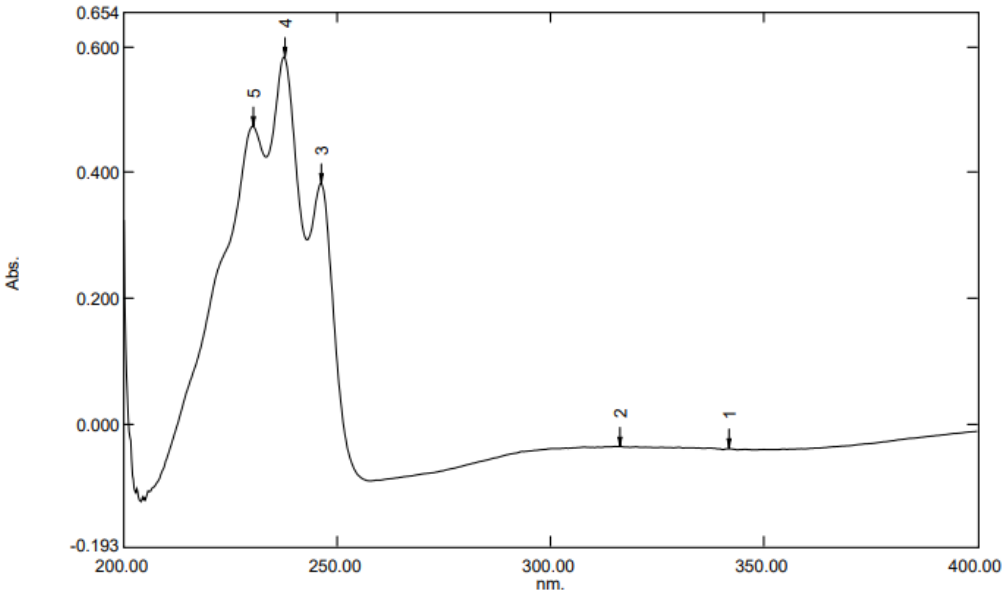

Figure -2- Absorbance maxima for Simvastatin

Validation
The present UV spectrophotometric methods were validated for linearity, accuracy, precision, LOD and LOQ as per ICH guidelines for the determination of Simvastatin in bulk and mucoadhesive buccal film dosage form.

Linearity
From standard stock solutions of Simvastatin (100 µg/ml), pippete out aliquots of 0.2 to 1.2 ml of Simvastatin transferred to series of 10 ml volumetric flasks and final volume made upto mark with methanol as solvent to form solutions of 2 to 12µg/ml of simvastatin. These solutions were scanned in the range of 200-400 nm against solvent blank at λmax of simvastatin and then calibration curve was plotted as absorbance vs concentration to check the linearity between absorbance and concentration of simvastatin.

Precision
Precision study expressed by performing Repeatability (intraday precision) and interday precision. The intraday (Repeatability) and interday precision analysis were carried out by evaluating corresponding responses three times on the same day and on the three different days for the three different concentrations for (8, 12 and 16µg/ml) for Simvastatin. The results of precision study were reported in terms of % relative standard deviation.

Accuracy
The accuracy of developed method was carried out by determining the % recovery of the drug by standard addition method at three different levels i.e. 80 %, 100 % and 120 %. Known amount of standard solutions of simvastatin were added to pre-determined sample solutions of simvastatin.

LOD and LOQ
Limit of detection (LOD) is described as lowest concentration of analyte that can be detected while limit of quantitation is described as lowest concentration of analyte that can be quantitated. With suitable precision and linearity, LOD and LOQ can be calculated from the following formulas.
LOD = 3.3* r / S and LOQ = 10 * r/ S

Where r is the Standard deviation of y-intercept of the regression line and S is slope of the calibration curve.

RESULTS AND DISCUSSION

Method development
The current study illustrates development and validation of UV spectrophotometric methods for the quantification of simvastatin in bulk and mucoadhesive buccal film dosage form. The Solubility studies confirmed that a simvastatin expresses the better solubility in methanol as compared to solubility in distilled water and the λmax of was found to be 238 nm. Because of lowest cost and minimal maintenance requirement, the present UV spectrophotometric methods can be favoured at small scale companies as compared to other reported methods.

Validation

Linearity
Linearity was determined by analysis of standard solution of simvastatin at six different concentrations. The drug was found to be linear within conc. range of 2-12µg/ml with regression coefficient of 0.9997. The results of regression analysis are reported in (Table 1). A result shows that within the concentration range reported above, there was an excellent correlation between peak area and concentration.

Table 1- Statistical data of calibration curves of simvastatin using UV spectrophotometry

Parameter	Simvastatin
λmax	238nm
Linearity	2-12µg/mL
Regression equation	y = 0.0289x + 0.0118
Standard Deviation	0.006
%RSD	0.98
Correlation coefficient	0.9997

Accuracy and Precision

Table 2- Recovery studies of simvastatin

Drug	Concentration of Drug added µg/mL	%Level	% Recovery ±SD	Intraday Precision	% Recovery ±SD	Interday Precision
Simvastatin	8	80	99.4± 0.035	0.539	101.3± 0.33	0.525
	10	100	101.5± 0.26	0.535	101.6± 0.26	0.516
	12	120	102.7± 0.21	0.537	101.2± 0.21	0.522

From the precision studies, it was reported that the percent relative standard deviation (% RSD) is less the 2% which indicates that the method has good repeatability. Also, the results of recovery studies was found between80to120%(99.4to102.7%),This has mentioned that the method is accurate and that regularly used excipients and additives used in formulations did not interfere with the suggested procedure. Recovery experiments verified the method's accuracy, which was determined to be considerable and within specification limitations.(i.e. within the acceptablerange98-120%recovery).

LOD and LOQ

The limit of detection was found to be 2.07µg/ml. The limit of quantification was found to be 6.35µg/ml for simvastatin.

Assay

Analysis of mucoadhesive buccal film containing 25 mg simvastatin was carried out and the amounts recovered were noted as a % amount of the label claims. The % recovery of simvastatin were 99.32 for simvastatin mucoadhesive buccal film and values are complying with the assay specifications for active drug Simvastatin in the United States of Pharmacopoeia (90.0–110.0%) which are required to be met by most drug formulations. Results of film assay are reported in table 3.

Table 3- Result of Assay of mucoadhesive buccal film

Simvastatin	Label claim(mg/film)	Amount of Drug* Estimated (mg/film)	Assay
Formulation A	25mg	24.7	98.8
Formulation B	25mg	24.8	99.2

CONCLUSION

Simple UV spectrophotometric methods have been produced and validated for the quantification of Simvastatin in bulk and buccal film dosage form. The results of the validation parameters show that the UV spectrophotometric methods were found to be accurate, precise and sensitive. Because of cost-effective and minimal maintenance, the present UV spectrophotometric methods can be preferred at small scale industries and successfully applied and suggested for the quantitative analysis of simvastatin in formulations for QC, where economy and time are essential and to assure therapeutic efficacy.

ACKNOWLEDGEMENT

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Conflict of Interest

The authors report no conflicts of interest.

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