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Estimation of Lovastatin in Pharmaceutical Formulation by Area under Curve Spectrophotometric Method

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ABSTRACT

Development of an accurate, simple and cost effective UV spectrophotometric method for estimation of Lovastatin was the aim of present study. This work was based upon an area under curve method i.e. "concentration of the component of interest is directly proportional to the area under two points on the mixture spectra". The UV spectrum between 238-258 nm was selected and the validation was carried out as per ICH guideline, Q2 (R1). This method obeyed Beer's Lamberts Law over the concentration range of 5-25µg /ml. The value of correlation coefficient was 0.9988. The method was precise due to the satisfactory value of percent relative standard deviation for the intraday and inter-day precision. Result of the recovery studies (99.8) showed accuracy of method. Hence, developed method can be used for routine estimation of Lovastatin in bulk and dosage form.

Key Words: - Lovastatin; AUC; Validation; UV-Spectroscopy.

INTRODUCTION-(1)(2)

Lovastatin, a specific and potent competitive inhibitor of 3-hydroxy- 3-methyl glutaryl coenzyme A (HMG-CoA) is a powerful serum cholesterol-lowering drug in humans and other species. It is formerly called as mevinolin; monacolin K, and mevacor® and it is a fungal secondary metabolite which inhibits HMG-CoA reductase (E.C 1.1.1.34), the first committed enzyme of cholesterol biosynthesis. The endogenous synthesis of cholesterol is carried out by the mevalonate pathway, in which the rate limiting reaction is the conversion of (S) HMG-CoA to (R) mevalonate, catalyzed by HMG-CoA reductase. The history of statin began in 1987 when the lovastatin received Food and Drug Administration (FDA) approval in the USA (Manzoni and Rollini 2002). Lovastatin have revolutionized the treatment of hypercholesterolemia and it is proven that lovastatin is also therapeutically and preventatively effective in the treatment of major kind of diseases like atherosclerosis, sepsis, peripheral arterial disease, peripheral vascular disease, cerebro vascular disease, ischemic disease, and bone fracture. Structure Lovastatin is [(1S,3R,7R,8aS)-8-[2-[(2R,4R)-4-hydroxy-6-oxooxan-2-yl]ethyl]-3,7-dimethyl-1,2,3,7,8,8a-hexahydronaphthalen-1- yl](2S)-2methylbutanoate (IUPAC name). The empirical formula of lovastatin is C24H36O5 and molecular weight is 404.55. Structure of Lovastatin is shown in Fig. 1.

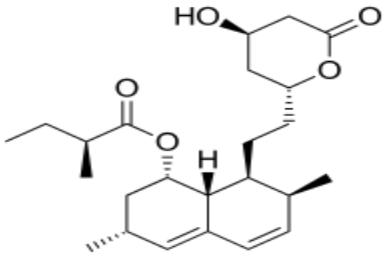

Fig. 1: Structure of Lovastatin

MATERIALS AND METHODS

Material:-

Lovastatin (API) was obtained as a gift sample from **Greenlands, Ameerpet Road, Leelanagar, Ameerpet, Hyderabad, Telangana.** A tablet formulation containing 10 mg of Lovastatin (LOSTATIN) was purchased from local market, (Pashwanath Medical, Narayangaon, Pune). Mfg. by Dr.Reddy Laboratories.

Instruments Used:-

A double beam UV-VIS spectrophotometer (UV-1800, Shimadzu) with spectra manager software UV Probe 2.21 was used. All weights were taken on electronic balance (Model Shimadzu AUX 120).

Method:-

Preparation of Standard Solution

Stock solution of 100 µg /ml of lovastatin was prepared by transferring an accurately weighed 10 mg of Lovastatin into 100 ml volumetric flask and diluted up to the mark with water.

Selection of Wavelength Range-

The standard solution of 10 µg /ml was scanned between 400 nm to 200 nm in UV spectrophotometer against water as a blank after baseline correction. The wavelength range was selected around wavelength maxima (248nm).

AREA UNDER CURVE-(3)

When there is no sharp peak or when broad spectra are obtained, The AUC (area under curve) method is usually applicable. This method consists of calculation of integrated value of absorbance with respect to the wavelength between the two selected wavelengths λ_1 and λ_2. Area calculation processing item calculates the area bound by the curve and the horizontal axis. The horizontal axis is selected by entering the wavelength range over which area has to be calculated. This wavelength range is selected on the basis of repeated observation so as to get the linearity between area under curve and concentration. The above mentioned spectrums were used to calculate AUC. Thus, the calibration curve can be constructed by plotting concentration versus AUC.

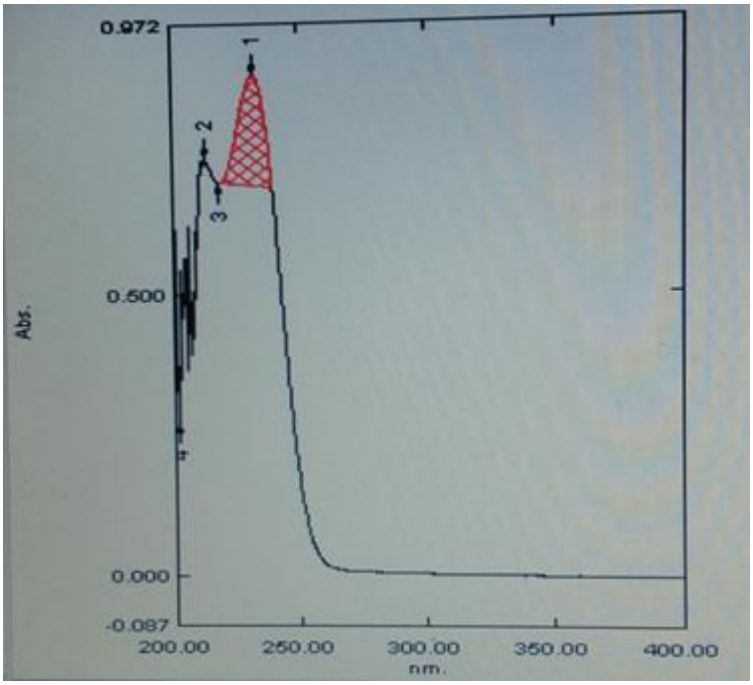

Fig.2 Spectrum of Lovastatin (10µg/ml)

PREPARATION OF CALIBRATION CURVE

Working solutions were prepared from standard stock solution by further dilution with water to obtain the concentration of 5,10,15,20 and 25µg /ml respectively. These solutions were scanned from 400 to 200nm and area under curve was integrated in the range of 238-258 nm. The calibration curve was plotted between areas under curve against concentration.

Table 1: Calibration data of Lovastatin for area under curve

Sr. No	Concentration	AUC
1	5	0.983
2	10	1.841
3	15	2.791
4	20	3.874
5	25	5.101

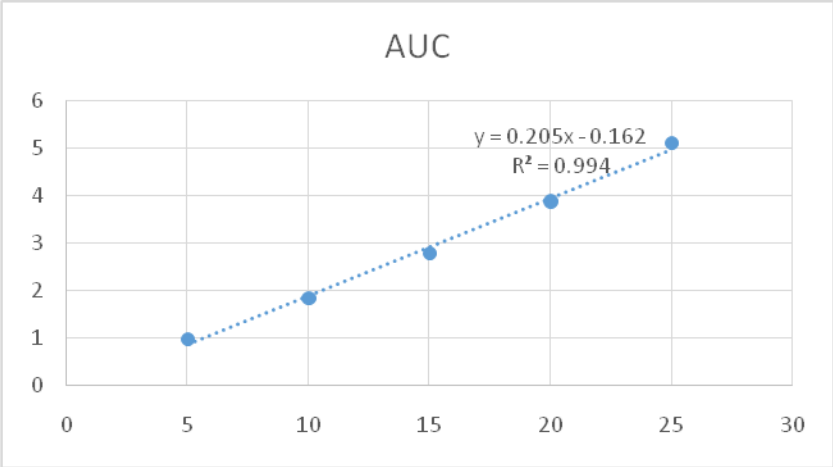

Fig.3 Calibration curve for AUC of Lovastatin.

Table 2: Analysis of Pure Drug

Sr.no.	Amount taken (µg/ml)	AUC	Amount of drug found	% amount found
1	10	2.141	9.632	96.32
2	10	2.099	9.428	94.28
3	10	2.119	9.525	95.25
4	10	2.171	9.778	97.78
5	10	2.176	9.803	98.03

Table 3: Statistical Evaluation of Pure Drug

% Mean	±SD	%RSD
96.33	1.4395	1.49

ASSAY OF TABLET

Twenty tablets (Lovastatin) containing 10 mg of Lovastatin weighed, average weight calculated and triturated to fine powder and then weight equivalent 10 mg of Lovastatin transferred into 100ml of volumetric flask and dissolved in water and diluted up to the mark with water to get a solution containing

of 100 µg /ml from the 2.5 ml was transferred to 25 ml volumetric flask and diluted up to the mark with water to get lovastatin solution containing 10 µg /ml of Lovastatin.

Table 4: Analysis of Marketed Tablet

Sr. No.	Amount Taken (µg/ml)	AUC	Amount of drug found	%amount found
1	10	1.543	10.39	103.9
2	10	1.539	10.35	103.5
3	10	1.534	10.31	103.1
4	10	1.544	10.40	104.0
5	10	1.599	10.89	108.9

Table 5: Statistical evaluation of marketed drug

% Mean	±SD	%RSD
104.68	2.1339	2.03

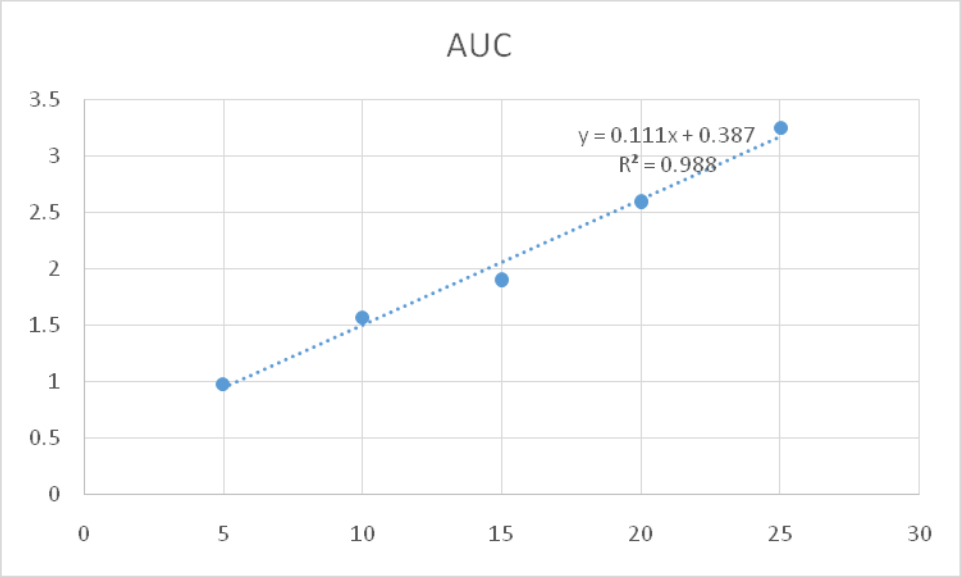

Fig.:4 Calibration Curve of Lovastatin tablet

Table 6: Calibration Data of marketed tablet

Sr. No.	Concentration	AUC
1	5	0.976
2	10	1.564
3	15	1.900
4	20	2.593
5	25	3.241

VALIDATION:-(4)

The developed method was validated as per ICH guidelines.

1. Linearity

The linearity was determined by using working standard solution between 5-25 µg/ml. The spectrums of thissolution were recorded and integrated at wavelength range 248 nm. Calibration curve of Conc. Vs AUC was plotted after suitable calculation and simple linear regression was performed.

2. Precision

The precision of the method was checked by repeatedly injecting 5-15 µg/ml. Absorbance of each of these solutions was measured at the 248 nm. Percent relative standard deviation (RSD) was calculated.

3. Accuracy

The accuracy for the analytical procedure was determined at 80%, 100% and 120% level of standard solution. Absorbance was measured at the range 248nm and result was expressed in term % recoveries. Three determinations at each level were performed and %RSD was calculated.

4. Sensitivity

The International Conference on Harmonization (ICH) [16] guidelines on determination of limit of detection (LOD) and limit of quantitation (LOQ) define LOD as 3 s/δ while LOQ as 10 s/δ, where s is the standard deviation of replicate determination values under the same conditions as for the sample analysis in the absence of the analytes and δ is the sensitivity, the slope of the calibration curve.

RESULT AND DISCUSSION

The calibration curve of Lovastatin was performed and graph plotted concentration versus area under curve.

Table 7: Interday and Intraday precision

Sr. No.	Parameter	Result
1	**Intra- day Precision**	
	Added (µg/ml)	10
	%RSD	3.17
	SD	0.017
	Accuracy(% recovery)	98.73
2	**Interday Precision**	
	Added (µg/ml)	10
	%RSD	3.30
	SD	0.012
	Accuracy(% recovery)	108

Table 8: RESULT OF RECOVERY STUDIES

Sr. No.	Concentration Taken (µg/ml)	Concentration Added	% Concentration added	Absorbance	% Recovery
1	10	0.8	80	0.778	77.8
2	10	0.8	80	0.784	78.4
3	10	0.8	80	0.798	79.8
4	10	1.0	100	0.978	97.8
5	10	1.0	100	0.986	98.6
6	10	1.0	100	0.998	99.8
7	10	1.2	120	1.17	117
8	10	1.2	120	1.18	118
9	10	1.2	120	1.19	119

ANALYSIS OF PURE DRUG

The standard solution of 10µg/ml was scanned between 400-200nm in UV spectrophotometer against methanol as a blank after baseline correction. The area Under Curve of Solution was measured.

1. Statistical Evaluation of Pure Drug :-

Statistical Evaluation of Pure Drug is shown in Table No.3.

ANALYSIS OF MARKETED FORMULATION

Twenty Tablets (lostatin) containing 10mg of lovastatin weighed, average weight calculated and Triturated to fine powder, then weighed equivalent to 10mg of lovastatin and transferred to the 100ml of volumetric flask and dissolved into methanol. Diluted up to the mark with methanol to get solution containing 100µg/ml. From this, 2.5ml was transferred to the 25ml volumetric flask and diluted up to the mark with methanol to get Lovastatin solution containing 10µg/ml of Lovastatin and results were obtained.

2. Statistical Evaluation of Marketed Formulation

Table 5 shows statistical evaluation of marketed formulation.

VALIDATION

1. Linearity

Calibration curve of area under curve versus concentration was plotted after suitable calculation and simple linear regression was performed and results were shown in Table 1 and Fig.2.The regression equation obtained is y=0.2054x-0.1624. and R^2=0.9949.

2. Precision

Percent relative standard deviation (RSD) was calculated and results are shown in Table 7.

The %RSD for the Intraday and Interday was found to be 3.17 and 3.30 respectively.

3. Accuracy

The % recovery was obtained between the 98.73 to108 as shown in table no.8.

Table No.9: Summary Data Of the Validation Parameter

Sr. No.	Parameter	Observation
1	Linearity Range	5-25
2	Regression Equation	Y=0.2054-0.1624
3	Correlation coefficient	R^2=0.9949
4	Precision - Intraday - Interday	 3.17 3.30
5	% Recovery	98.73-108

DISCUSSION

An attempt was made to develop a simple and specific AUC spectrophotometric method for the determination of Lovastatin in tablet dosage form. The generated regression equation was y=0.2054x-0.1624(R^2=0.9949).The AUC between 238-258nm, x is the concentration and R is correlation Coefficient. The R^2 value 0.9949, indicates that developed method was linear.

The proposed method was found to be precise, % RSD value for interday and intraday precision were satisfactory. The drug has good recoveries (99.8%). Hence, it can be said that this method is accurate.

The result of analysis of formulation by developed method was consistent with labeled claim, highly reproducible and reliable.The method can be used for routine analysis of Lovastatin. The validation parameters are summarized in table no.9.

CONCLUSION

No any spectrophotometric methods have been described for AUC estimation of Lovastatin. Therefore, simple, fast and reliable area under curve spectrophotometric method was developed for routine analysis of Lovastatin. The developed method can be concluded as accurate, sensitive and precise and be easily applied to the pharmaceutical formulation.

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