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NEW SPECTROPHOTOMETRIC METHODS FOR THE DETERMINATION OF LOVASTATIN IN PHARMACEUTICAL FORMULATIONS

Y. Suneetha [1], Dr. N.V.S.Naidu [2]
Research Scholar, Department of Chemistry, S.V. University, Tirupati-517 502.
Email: sunyphd@gmail.com

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Abstract:

Two simple, sensitive and economical spectrophotometric methods were developed for the determination of lovastatin in pharmaceutical formulations. Method A is based on the reaction of the hydroxyl group the drug involves an ion association complex formation with acidic dye of the solochrome black-T(SBT)which is extractable chloroform to form a violet colored product, which gives maximum absorption at 430 nm. Method B uses reaction of Lovastatin with ferric ion which is subsequently reduced to ferrous ion. The ferrous ion react potassium ferricyanide to produce an intense blue color chromogen at 680 nm. Beer's law is obeyed in the concentration range of 2-10 μgml^{-1} and 10-50 μgml^{-1} with methods A and B respectively. Both the methods have been successfully applied for the assay of the drug in pharmaceutical formulations. There is no interference was observed from common pharmaceutical adjuvants. The reliability and the performance of the proposed methods were established by point and interval hypothesis tests and through recovery studies.

Keywords: Lovastatin, Potassium Ferricyanide, Solochrome Black-T, Spectrophotometry, Bulk drugs and tablet formulations.

Introduction

Lovastatin is [8-{2-[4-hydroxy–6-oxo-oxan-2-yl [ethyl 3,7-dimethyl-1,2,3,7,8,8a, hexahydronapthalene 1-yl] 2-methylbutanoate. Lovastatin is a member of statin class of drugs. It is used for lowering cholesterol and so preventing cardiovascular diseases. This is an important fungal secondary metabolite inhibiting the enzyme which catalyses a rate limiting step in the biosynthesis of cholesterol. It is also an effective drug for the treatment of arthrosclerosis. Literature

review reveals that several methods have been reported for the determination of Lovastatin as such as Derivative Spectrophotometry [1], MS [2-4], GC [5] HPLC [6-8] and Polarography[9-13].

In the present Investigation the author have developed two simple and sensitive spectrophotometric methods for the determination of Lovastatin. It describes the facile methods developed for the routine quality control analysis of pharmaceutical formulations containing Lovastatin with ferric ion, which is subsequently reduced to ferrous ion. The ferrous ion so formed reacts with potassium ferricyanide to produce an intense blue colored chromogen in Method A. Lovastatin involves an ion association complex formation with acidic dye solochrome black-T, which is extracted into chloroform from the aqueous phase in Method B.

Experimental

Instrumentation*:* Spectral and absorbance measurements were made with Shimadzu UV-Visible double beam spectrophotometer (model 2450)

Reagents*:* - All the reagents used were of analytical reagent grade and all solutions were prepared afreshly. Ferric chloride (0.5%), Potassium ferricyanide (0.2%) were used for Method A. Solochrme Black-T (0.2%) is employed for Method B

Procedure

Standard stock solution:

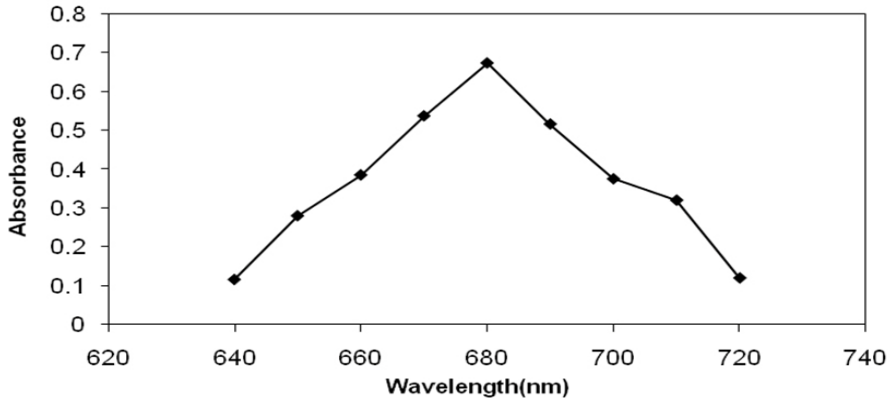
A standard stock solution containing 1mg/ml was prepared by dissolving accurately 100mg of Lovastatin in 100ml methanol. Working standard solutions were prepared by appropriate dilution of standard stock solution with methanol for Method A & B.

Method-*A*

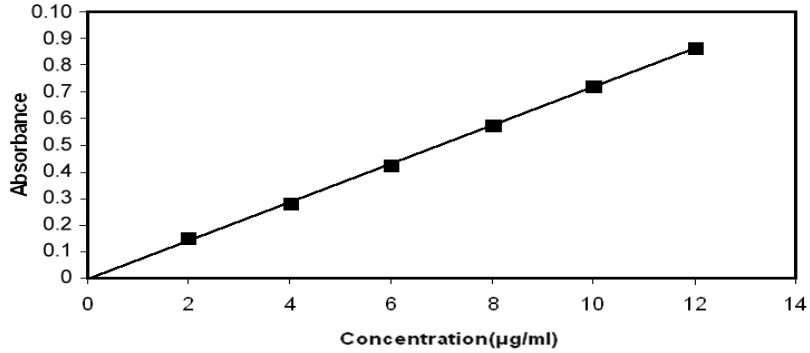
Aliquots of standard lovastatin (1ml=100µg/ml) solution ranging from 0.5-2.5 ml were transferred into a series of 250 ml separating funnels. To this funnel, 2ml of Solochrome black-T (0.2%) was added and the total volume of the aqueous phase made up to 10 ml with distilled water. About 10 ml of chloroform was added to each funnel and the contents were shaken for 2 min. The two phases were allowed to separate and the absorbance of the chloroform layer was measured 430 nm against the corresponding reagent blank. The amount of Lovastatin present in the sample solution was computed from its calibration curve.

Method-*B*

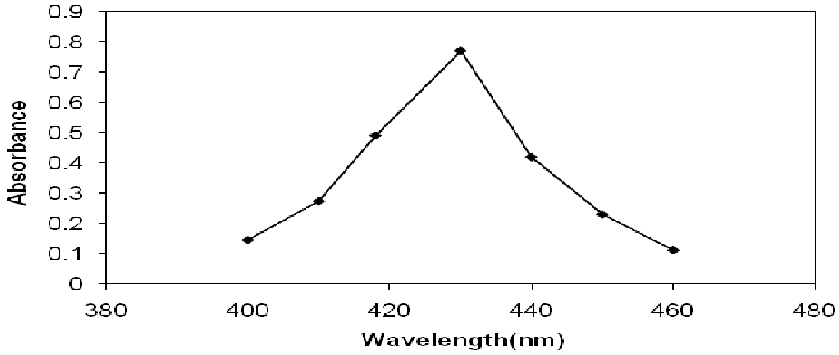
A series of 10 ml graduated tubes filled with lovastatin solution ranging from 0.1 to 0.5ml (1ml=100µg/ml) were taken. Ferric chloride (0.5%, 1ml), potassium ferricyanide (0.2%, 2ml) were added to them. (HCl 1N, 1ml) was added to each one of them and kept aside for 10 minutes. The absorbance of the bluish green colored chromogen was recorded at 680nm the corresponding reagents absorbance was measured to use as reference. The amount of Lovostatin present in the sample solution was computed from its calibration curve.



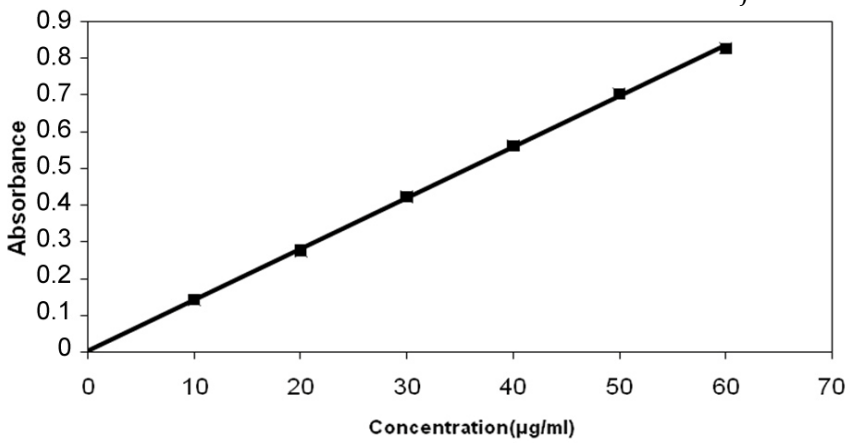
Absorption spectrum of LST with $K_3Fe(CN)_6/FeCl_3$ system



Beer's law plot of LST with $K_3Fe(CN)_6/FeCl_3$ system



Absorption spectrum of LST with $SBT/CHCl_3$ system



Beer's law plot of LST with SBT/$CHCl_3$ system

Preparation of sample solution

Tablets containing Lovastatin were successfully analyzed by the proposed methods. Twenty tablets of commercial samples of Lovastatin were accurately weighed and powdered. Tablet powder equivalent to 100 mg of Lovastatin was dissolved in 20 ml of methanol and filtered, the filtrate was diluted with methanol up to 100 ml and the final volume of the solution was used for the assay of Lovastatin in bulk samples.

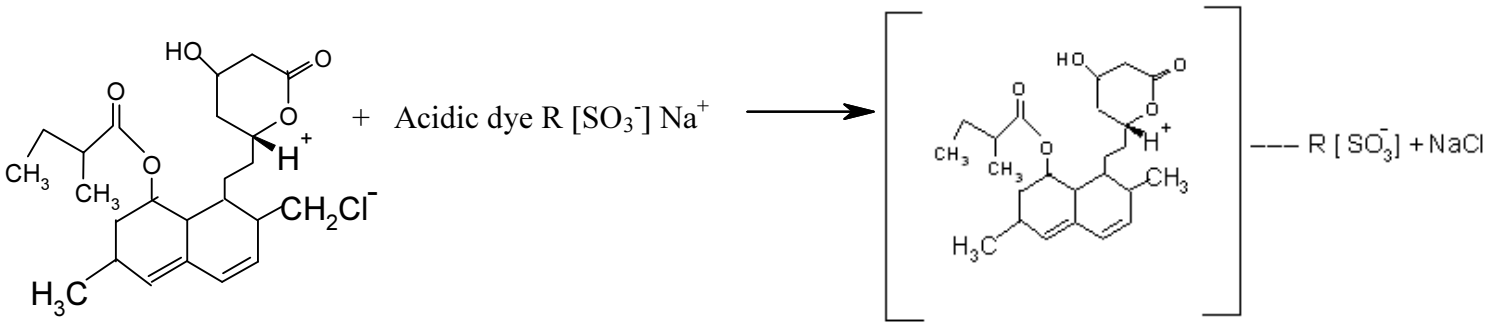
Result and Discussion

Lovastatin involves an ion association complex formation with acidic dye (SBT) which is extractable with chloroform the absorption maximum is 430nm in methodA. Lovastatin exhibits basic character essentially due to the presence of hydroxyl group. Lovastatin react with ferric chloride due to redox reaction followed by complex formation between the drug ferric chloride and potassium ferricyanide to form a bluish green colored solution that exhibited maximum absorption at 680nm in methodB. Method A&B Beer'slaw obeyed the concentration range 10-50µg/ml, 2-10µg/ml respectively.

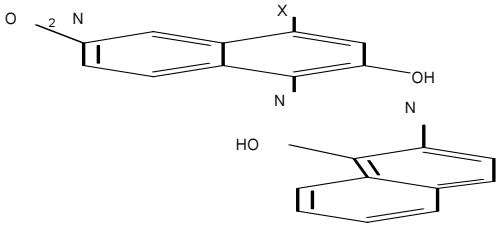
The optical characterstics such as Beer's law limits absorption maxima, molar absorptivity, sandell's sensitivity, percent relative standard deviation and percent range of errors (0.05 level and 0.01 confidence limits were calculated for the two methods and the results are summarized in Table1. The optimum conditions for colour development for method A&B have been established by varying the paramaters one at a time keeping the other paramaters fixed and observing the effect of product on the absorbance of the colored species and incorporated in the procedures. The values obtained for the determination of LOVASTATIN brand samples. To evaluate the validity and reproducibility of the methods, known

amounts of pure drug were added to the previously analyzed by the proposed methods. The percent recoveries are given Table.2.

The proposed visible spectrophotometric methods are simple, sensitive, selective accuarate , precise, and economical and can be used for the routine estimation of Lovastatin in bulk drug and its pharmaceutical preparations.

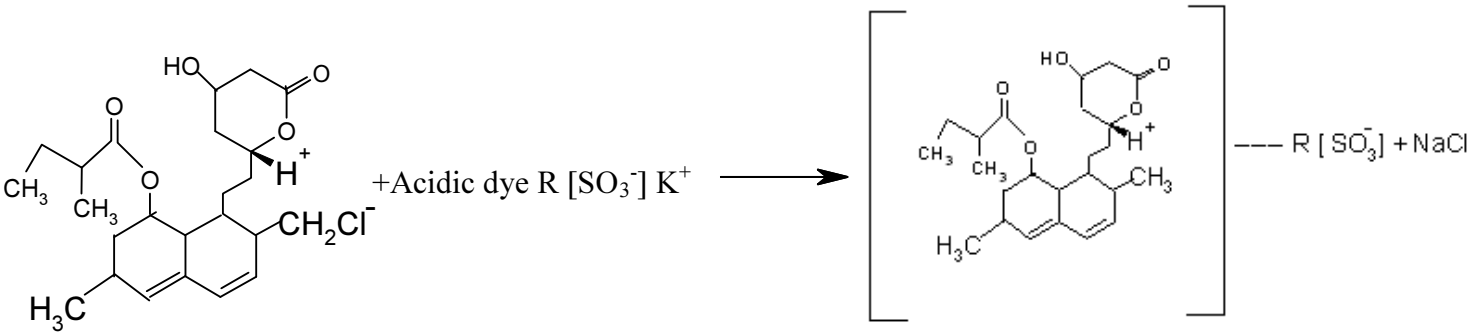


LOVASTATIN as HCL



Where R= and X = SO_3^-Na

Reaction of Lovastatin with SBT



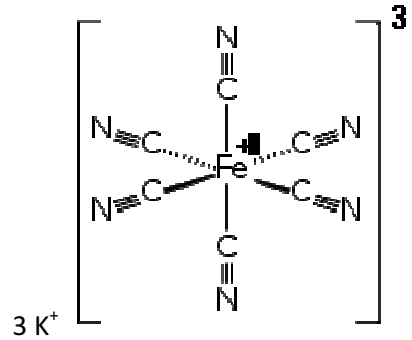


Table-1: Optical Characteristics, Precision and accuracy of the proposed method for Lovastratin.

Parameter	Method-A	Method-B
λmax (nm)	440	680
Beer's law Limits (μg/ml)	1-10	1-10
Molar absorptivity(1 $mole^{-1}$ cm^{-1})	4.23 x 10^3	6.73 x 10^3
Sandell'ssensitivity ($\mu g/cm^2$/0.001 absorbance unit)	0.015	0.010
Slope (b)	0.0058	0.0046
Intercept(a)	0.079	0.102
Correlation coefficient(r)	0.9976	0.9949
Standard deviation	0.0045	0.0113
%Relative standard deviation		
%Range of Error (Confidence limits)		
0.05 level	0.2406	0.7025
0.01 level	0.3714	1.1542

Assay and Recovery of Lovastatin in dosage forms.

S.NO	**Pharmaceuti cal Formulation**	**Labelled amount (mg)**	**Proposed method**			**Found by reference method ±S.D**	***% recovery by proposed methods ±S.D***
			Amount found (mg)	**t (Value)**	**F (Value)**		
1	MEVACOR	5	5.04±0.056	0.164	1.942	5.06±0.053	*100.2±0.36*
	MEVACOR	5	4.69±0.045	1.012	1.465	4.94±0.018	*99.81±0.12*
	MEVACOR	5	4.92±0.075	0.998	2.383	4.96±0.029	*99.86±0.84*
2	**Altoprev**	10	10.02±0.022	0.933	2.045	9.32±0.068	*99.89±0.28*
	Altoprev	10	9.97±0.022	0.641	2.321	10.07±0.024	*99.8±0.44*
	Altoprev	10	9.96±0.036	1.323	2.581	10.07±0.068	*99.98±0.17*

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Corresponding Author:

Y. Suneetha*,

Email: *sunyphd@gmail.com*