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Simple spectrophotometric methods for the determination of lovastatin in pharmaceutical formulations

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ABSTRACT

Two new simple, sensitive selective, rapid economical spectrophotometric methods (A&B) were developed for the determination of Lovastatin in pharmaceutical formulations. Method A and B are based on the reaction of the drug giving an ion association complex formation with acidic dyes of the bromothymal blue (BTB) and methyl orange(MO) at pH 4.3 which are extractable into chloroform to form a colored product, with the maximum absorption at 430 and 520 nm . Beer's law is obeyed in the concentration range of 10-50 µg/ml and 1.0-5.0 µg/ml for Methods A and B, respectively. Both the methods (A&B) have been successfully applied for the assay of the drug in pharmaceutical formulations. 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

Spectrophotometric determination;
Lovastatin (LST);
Bromothymal blue (BTB);
Methyl orange (MO);
Ion-associatioon complex;
Pharmaceutical formulations.

INTRODUCTION

Lovastatin is [8-{2-[4-hydroxy–6-oxo-oxan-2-yl[ethyl{-3,7-dimethyl-1,2,3,7,8,8a, hexahydro-napthalene 1-yl] 2-methylbutanoate.Lovastatin is a member of the drug class of statins. 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 survey reveals that different analytical methods are used including Derivative Spectrophotometry[1], MS[2-4], GC[5], HPLC[6-8] and Polarography[9-12].

Extractive spectrophotometric procedures are popular for their sensitivity in the assay of drugs and, therefore, ion-pair extractive spectrophotometry has received considerable attention for the quantitative determination of many pharmaceutical compounds. Though few methods mentioned above have been reported in the literature, there are no simple spectrophotometric methods utilizing its hydroxyl group. This paper therefore describes the simple methods developed for the routine quality control analysis of pharmaceutical formulations containing Lovastatin exhibits basic character essentially due to the presence of a hydroxyl group. LST involves an ion association complex formation with acidic dyes Bromothymal Blue (BTB) which is extractable into chloroform, with absorbs at 420nm (method A) shown in Figure 1 and 2. and Methyl orange (MO) resulting in the formation of a yellow color solution

that exhibited absorption at 520 nm (Method B) as shown in Scheme 1 & 1(a) and Figure 3 and 4.

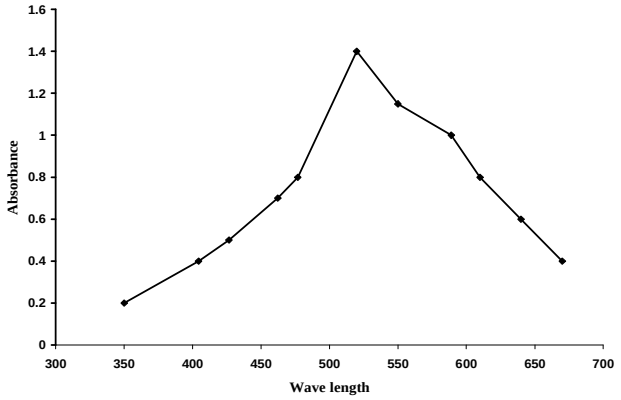


Figure 1 : Absorption spectrum of LST with BTB/$CHCl_3$ system

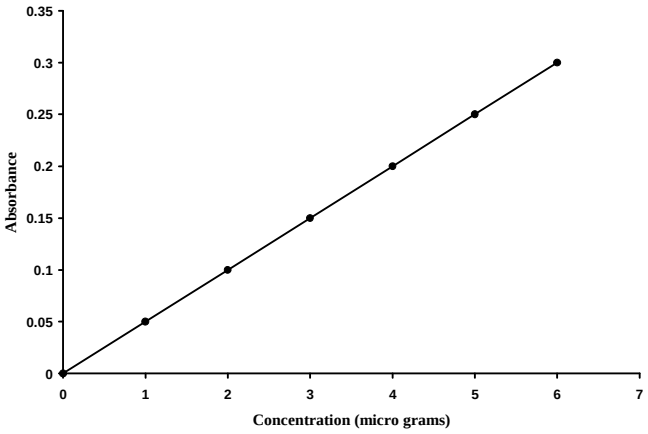


Figure 2 : Beer's law plot of LST with BTB/$CHCl_3$ system

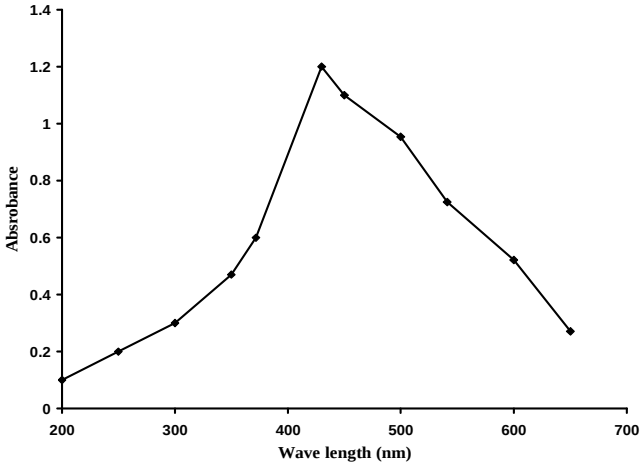


Figure 3 : Absorption spectrum of LST with MO/$CHCl_3$ system

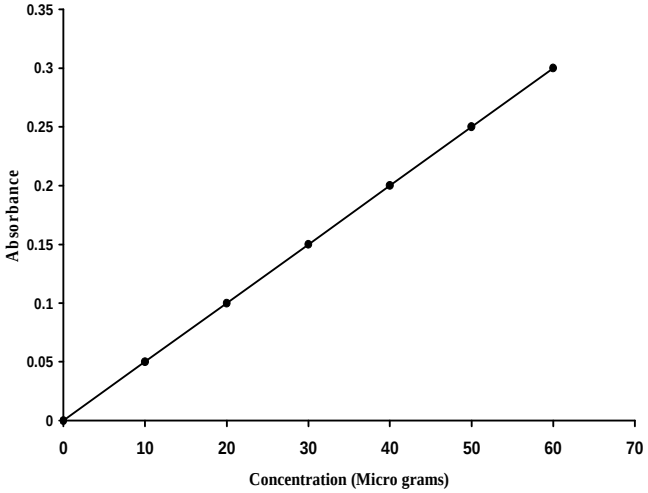
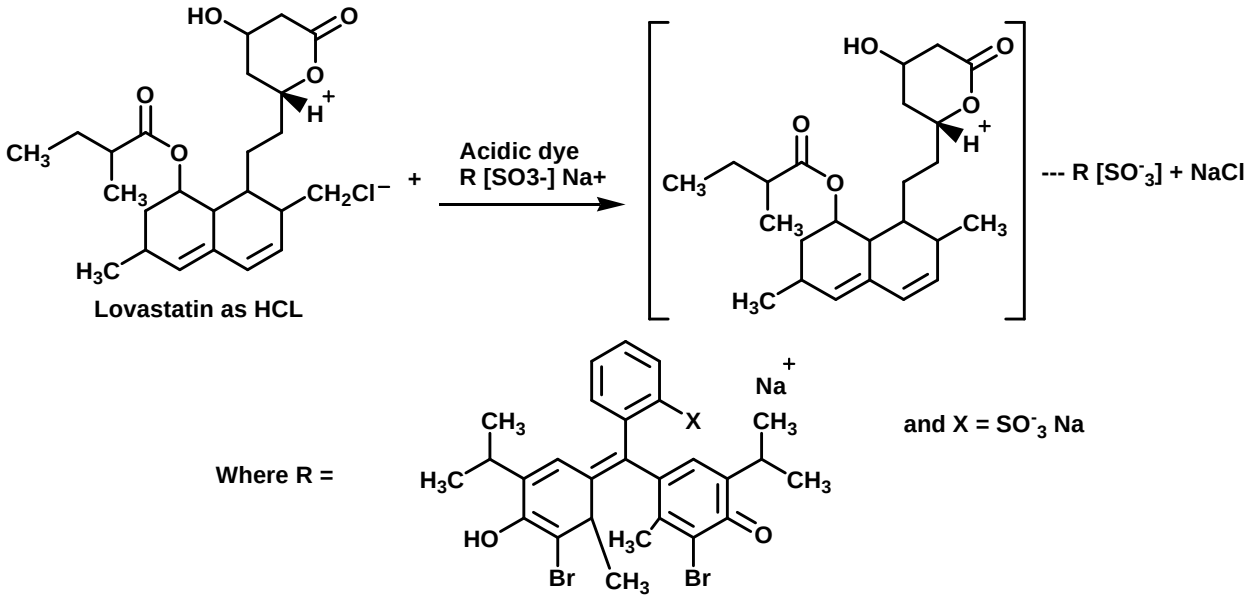
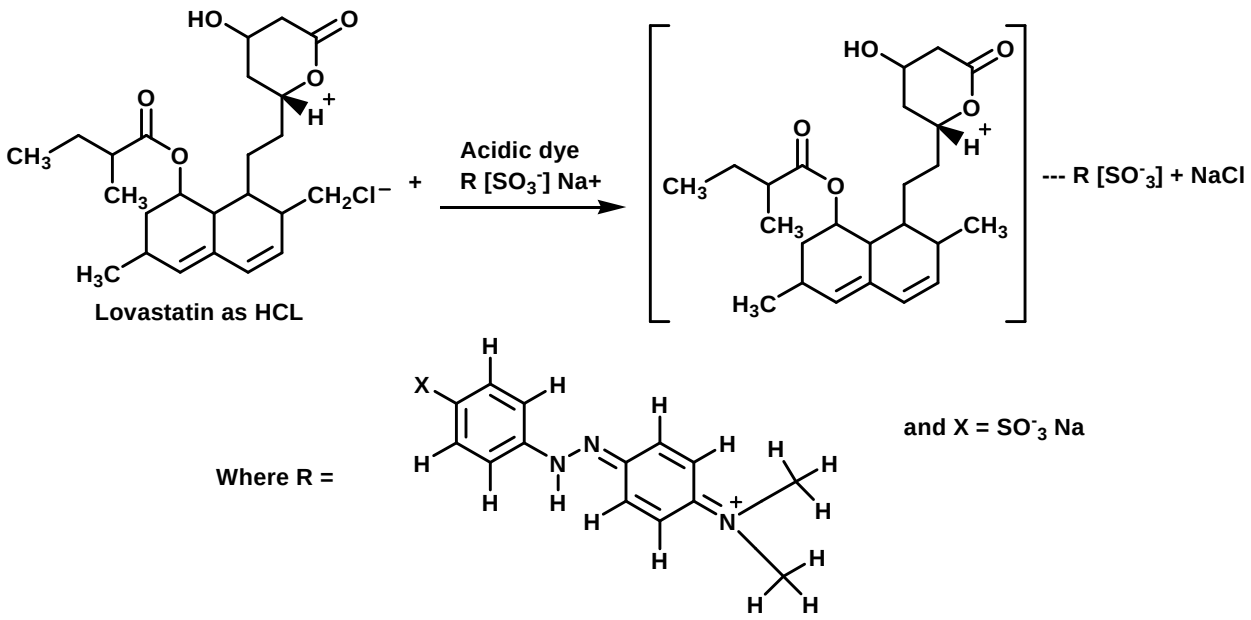


Figure 4 : Beer's law plot of LST with MO/$CHCl_3$ system



Scheme 1 : Reaction mechanism of lovastatin with BTB



Scheme 1(a) : Reaction with methyl orange (MO)

EXPERIMENTAL

Instrumentation

Spectral and absorbance measurements were made with Shimadzu UV/Visible double beam spectrophotometer (model 2450)

Reagents

All the chemicals used were of analytical reagent grade only. All the solutions were freshly prepared with double distilled water. 0.2% solution of Bromothymol blue and 0.1% solution of Methyl orange were used.

Standard and sample solutions of lovastatin

The stock solution (1mg/ml) of Lovastatin (mevinolin) was prepared by dissolving 100 mg of drug in 20 ml of methanol and made up to 100 ml with methanol to get a clear solution. A portion of this stock solution diluted stepwise to get the working standard solutions of concentration 100 µg/ml.

Assay procedures

Methods A&B

Aliquots of standard Lovastatin ranging from 0.1-0.5 ml were transferred into a series of 250 ml separating funnels. To this 2 ml of 0.2 % Bromothymol blue (BTB) and 0.2 % of Methyl orange was added and the total volume of the aqueous phase was made up to 10 ml with distilled water in two separate separating funnels. 10 ml of chloroform was added in three initial amounts 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 at 430 nm/520 nm against the corresponding reagent blank. The amount of LST present in the formulation solution was computed from its calibration curve.

RESULTS AND DISCUSSION

Anionic dyes like BTB, MO form ion-association complex with the positively charged drug. The drug-dye stoichiometric ratio as calculated by the continuous variation and mole- ratio method is found to be 1:1 with BTB, MO. The drug dye complex, with two positively charged ions, behaves as a single unit held together by an electrostatic force of attraction.

Optimization of variables

Optimum conditions necessary for rapid and quantitative formation of colored ion-pair complexes with maximum stability and sensitivity were established preliminary experiments. Chloroform was preferred as better solvents (Carbon tetrachloride, Dichloromethane and ether) for these methods for its selective and quantitative extraction. Optimum con-

Full Paper

ditions were fixed by varying one parameter at a time while keeping other parameters constant and observing its effect on the absorbance at 430nm for BTB and 520nm for MO. The effect of pH was studied was observed at the pH 4.3 and using 2ml of buffer The optical characteristics such as molar absorptivity, Beer's law range, sandell's sensitivity are presented in TABLE 1. The regression analysis using the method of least squares was made for the slope (a), intercept (b) and correlation coefficient (r) obtained from different concentrations and the results are summarized in TABLE 1. The relative standard deviations and percent range of error (0.05 and 0.01) level, confidence limits calculated for the eight measurements are given in TABLE 1.

TABLE 1 : Optical characteristics, precision and accuracy of the proposed methods

Parameter	Method A	Method B
λ_{max}(nm)	430	520
Beer's law limit (µg/ml)	10 - 50	1 - 5
sandell'ssensitivity(µg/cm^2/0.001 absorbance unit)	0.0069	0.0076
Molar absorbitivity (Litre mole^{-1}cm^{-1})	6.83×10^5	5.62×10^4
Correlation coefficient®	0.9985	0.9949
Slope (a)	0.0139	0.013
Intercept (b)	0.0696	0.0427
Standard deviation	0.0041	0.0059
% Relative standard deviation	0.84	1.4
% Range of error		
0.05 level confidence	±0.6921	±1.343
0.01 level confidence	±1.0147	±1.982

***Y = a +bX, where x is concentration in µg/mL and y is the absorbance.**

**** Replication of six samples**

From their values it is indicated that method B is more sensitive than method A.

Assay procedures

Aliquots of standard Lovastatin ranging from 0.1-0.5 ml were transferred into a series of 250 ml separating funnels. To that 2 ml of BTB (0.2%) and Methyl orange (0.2%) was added and the total volume of the aqueous phase was made up to 10 ml with distilled water. 10 ml of chloroform was added in three initial amounts 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 at 430 nm/520nm against the reagent blank.

Satisfacctory results were obtained for drug analysis in pharmaceutical formlutions and the results were reproducible with low R.S.D.values. The average percent recoveries obtained were quantitative, indicating good accuracy of these methods. The results of analysis of the commercial tablets and the recovery studies of drug suggested that there is no interfere from any excipients (such as Strarch, Lactose, Titaniumdioxide, and Magnesium stearate) which are present in TABLE 2.

TABLE 2 : Estimation of lovastatin in pharmaceutical formulations

Formulations (Tablets)	Labelled Amount (mg)	Amount found by proposed methods*		Amount found by reference method	% Recovery**	
		Method A	Method B		Method A	Method B
1	20	19.96 ±0.21	19.89 ±0.18	19.94 ±0.19	99.8 ±0.31	100.2 ±0.64
2	20	19.97 ±0.21	19.92 ±0.19	19.98 ±0.20	100.2 ±0.64	100.4 ±0.62

CONCLUSIONS

This paper therefore describes the simple methods developed for the routine quality control analysis of pharmaceutical formulations containing Lovastatin exhibits basic character essentially due to the presence of a hydroxyl group. The proposed methods are economical, simple and sensitive for the determination of LST in pharmaceutical preparations and free from interference due to common excipients of tablets like Talc, Starch, Magnesium stearate and Lactose with agreeable recoveries.

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