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Development and validation of RP-HPLC method for the estimation of lovastatin in bulk and tablet dosage form

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ABSTRACT

A simple, rapid, sensitive and precise High Performance Liquid Chromatographic (HPLC) method has been developed for the estimation of lovastatin in pure and tablet dosage form. In this method RP-C_{18} column (250mm×4.6mm I.D., 5µm particle size) with mobile phase consisting of acetonitrile, methanol and water in the ratio of 79:12:9 v/v/v in isocratic mode was used. The detection wavelength is 230nm and the flow rate 1.2ml/min. The linearity was found in the range of 10-100µg/ml and shows a correlation coefficient of 0.9997. The proposed method was validated by determining sensitivity, accuracy, precision and linearity. The proposed method is simple, fast, accurate, precise and reproducible hence can be applied for routine quality control analysis of lovastatin in pure and tablet dosage form.

Key words: Lovastatin, HPLC, Validation.

Lovastatin is a HMG-COA reductase inhibitor[1] used in the treatment of hypercholesterolaemia. It is chemically, [1*S*-[1α(*R**),3α,7β,8β(2*S**,4*S**), 8aβ]]-1,2,3,7, 8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2*H*-pyran-2-yl)ethyl]-1-naphthalenyl 2-methylbutanoate. Literature survey reveals that various HPLC methods[2-7] have been reported for the determination of lovastatin in pure and tablet dosage form. In this study a simple, rapid, accurate, sensitive and precise HPLC method was developed for the estimation of lovastatin in tablet dosage form.

Instrumentation

The separation was carried out on isocratic HPLC system (Shimadzu) with Shimadzu Binary HPLC pump, Shimadzu LC- 10AT UV-Visible Detector, Spinchrom software and RP-C_{18} column (250mmx4.6mm I.D; particle size 5µm).

Chemicals and Reagents

Lovastatin was a gift sample by Krebs Biochemicals & Industries Ltd., Mumbai. Methanol and acetonitrile of HPLC grade were purchased from E.Merck (India) Ltd., Mumbai.

HPLC conditions

The mobile phase consisting of acetonitrile (HPLC grade), methanol (HPLC grade) and water (HPLC grade) were filtered through 0.45µ membrane filter before use, degassed and were pumped from the solvent reservoir in the ratio of 79:12:9v/v/v was pumped into the column at a flow rate of 1.2ml/min. The detection was monitored at 230nm and the run time was 8min. The volume of injection loop was 20µl prior to injection of the drug solution the column was equilibrated for at least 30 min. with the mobile phase flowing through the system.

Procedure

Stock solution of lovastatin was prepared by dissolving 25mg of lovastatin in 25ml standard volumetric flask containing 25ml of methanol and the solution was sonicated for 15 min. 5ml of the above solution was transferred to 50ml volumetric flask and the volume was made up to the mark with mobile phase. Subsequent dilutions of this solution were made with mobile phase to get concentration of 10-100µg/ml. The solutions were injected into the 20µl loop and the chromatogram was recorded in Fig. 1. The calibration curve was constructed by plotting concentration vs peak area ratio. The linearity experiment was carried out in triplicate to ascertain accuracy and precision of the method.

Assay

Two commercial brands of tablets were chosen for testing suitability of the proposed method to estimate lovastatin in tablet dosage form. Twenty tablets were weighed accurately and powdered. A quantity equivalent to 50mg of lovastatin was weighed accurately and transferred to 50ml volumetric flask. About 30ml of methanol was added and kept in ultrasonic bath for 15min. This solution is filtered through a membrane filter and the volume was made up to the mark to get 1mg/ml concentration. From the above solution 5ml was transferred to 100ml volumetric flask and the volume was made up to 100ml with mobile phase. Sample solution was injected under the chromatographic conditions and the chromatogram was recorded. The amount of lovastatin present in tablet formulation was determined by comparing the peak area from the standard. The results are furnished in Table 1.

Validation of proposed method

Selectivity of the method was assessed on the basis of elution of lovastatin using the above mentioned chromatographic conditions. To study the accuracy, reproducibility, precision of the proposed method, recovery studies were carried out in triplicate by adding a known quantity of drug to pre analysed sample and the percentage recovery. The results are furnished in Table 2.

By applying the proposed method, the retention time of lovastatin was found to be 4.5min (Fig.1). Linearity range was observed in concentration range of 10-100µg/ml. The regression equation of lovastatin concentration over its peak area ratio was found to be Y=-27.292X-9.4599 (r=0.9997) where Y is the peak area ratio and X is the concentration of lovastatin(µg/ml). The asymmetry factor was found to be 1.000, which indicated asymmetric nature of peak. The number of theoretical plates was found to be 7860, which indicates efficient performance of the column. The limit of detection and limit of quantification was found to be 0.034µg/ml and 0.083µg/ml, indicates the sensitivity of the method. The high percentage of recovery indicates that the proposed method is highly accurate.

Table 1: Validation summary

System Suitability	Results
Linearity range (µg/ml)	10-100
Correlation Coefficient	0.9997
Asymmetry factor	1.00
Theoretical Plates (N)	7860
LOD (µg/ml)	0.034
LOQ (µg/ml)	0.083
Percentage recovery (Accuracy)	99.49

Table 2: **Assay and Recovery studies**

Formu-lation	Label claim (mg)	Amount found (mg)	% of Amt found*	% Recovery
Brand-1	100	99.621	99.54	98.23
Brand-2	100	99.782	99.82	100.45

CONCLUSION

The proposed HPLC method was found to be highly accurate, sensitive and precise. Therefore this method can be applied for the routine quality control analysis of lovastatin in pure and its tablet dosage form.

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