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A Novel Stability-Indicating RP-HPLC Method For The Estimation Of Atorvastatin In Bulk And Pharmaceutical Dosage Forms

1Jyoti Chavan, 2Babita more

1asst.professor , 2Associate professor

1Mumbai University ,

2Mumbai University

Abstract: -

A simple, rapid, and precise stability-indicating reverse-phase high-performance liquid chromatography (RP-HPLC) method was developed and validated for the quantification of Atorvastatin. Chromatographic separation was achieved using a C18 column (250 mm × 4.6 mm, 5 µm particle size) with an isocratic mobile phase consisting of acetonitrile and 0.05 M phosphate buffer (pH 4.1, adjusted with orthophosphoric acid, in a ratio of 60:40 v/v. The flow rate was maintained at 1.0 mL/min. Detection was performed using a UV detector at 247 nm. The retention time for Atorvastatin was approximately 5.8 minutes. The method was validated according to ICH Q2(R1) guidelines. Linearity was observed in the concentration range of 5-50 µg/mL with a correlation coefficient (R^2) of 0.9997. Forced degradation studies showed significant degradation under acidic and oxidative conditions. The main drug peak was well-resolved from the degradation product peaks. The developed method is robust and suitable for routine quality control and stability analysis of Atorvastatin.

Keywords: - RP-HPLC, Atorvastatin, Method Validation, Stability-Indicating, Forced Degradation, Statins, ICH Guidelines.

1. Introduction: -

Atorvastatin is a synthetic compound that falls under the category of statins, a group of drugs known for lowering cholesterol. It works by inhibiting HMG-CoA reductase, which is the enzyme that limits the production of cholesterol. Clinically, Atorvastatin is used to reduce low-density lipoprotein (LDL) cholesterol and triglyceride levels, thus lowering the risk of cardiovascular issues such as heart attac k and stroke. Ensuring the quality, purity, and stability of Atorvastatin in its formulations is essential.

A review of previous literature shows that
there are various methods to analyze Atorvastatin, including spectrophotometry and high-performance liquid chromatography (HPLC) techniques.
However, many of the existing methods have long run times or are
not efficiency in indicating stability. A stability indicating method allows accurate measurement of the active pharmaceutical ingredient (API) without interference from its degradation products, which is crucial in determining the shelf-life and storage conditions of the drug.

The present research aims to develop and validate a simplified, reliable, and precise reversed-phase HPLC (RP-HPLC) method for measuring Atorvastatin in its bulk form and commercial tablets.
This method was systematically developed and validated under ICH guidelines to ensure it
is suitable for routine quality control.

2.Materials and Methods:

2.1.Chemicals and Reagents: A Atorvastatin calcium reference standard (99.8% pure) was obtained from [Supplier Name, e.g., Sigma-Aldrich]. Commercial tablets, such as Lipitor (20 mg), were purchased from a local pharmacy. Acetonitrile (HPLC grade), potassium dihydrogen phosphate (AR grade), and orthophosphoric acid (AR grade) were sourced from [Supplier Name, e.g., Merck]. High purity deionized water was used throughout the analysis.

2.2.Instrumentation: The analysis was conducted using an Agilent
1260 series HPLC system. The system includes a quaternary pump, an autosampler, a column oven, and a Diode Array Detector (DAD). Data acquisition and processing were handled using OpenLab CDS software.

2.3.Chromatographic Conditions:
Column: Agilent Zorbax Eclipse Plus C18 (250 mm × 4.6 mm, 5 µm)
Mobile Phase: Acetonitrile: 0.05 M Phosphate Buffer (pH 4.1) (60:40 v/v)
Flow Rate: 1.0 mL/min
Detection Wavelength: 247 nm
Injection Volume: 20 µL
Column Temperature: 30°C

2.4.Preparation of Solutions:
Standard Stock Solution (100 µg/mL): 10 mg of Atorvastatin was accurately weighed and dissolved in 100 mL of the mobile phase.

Sample Solution (20 µg/mL): Twenty tablets were weighed and crushed into a fine powder.
An amount equivalent to 10 mg of Atorvastatin was transferred to a
100 mL volumetric flask, sonicated with 70 mL of mobile phase for 15 minutes, and then diluted to the mark. This solution was filtered through a 0.45 µm nylon syringe filter. 2 mL of this filtrate was further diluted to 10 mL with the mobile phase.

2.5.Method Validation: Validation was conducted according to the ICH Q2(R1) guidelines.

Specificity: Was assessed by subjecting Atorvastatin
to forced degradation under various conditions including acidic (0.1 N HCl), basic (0.1 N NaOH), oxidative (30% H2O2), thermal (80°C), and photolytic (UV light) conditions.

Linearity: Was tested by analyzing six concentrations, ranging from 5 to 50 µg/mL.

Accuracy (% Recovery): Was determined using the standard addition method at 80%, 100%, and 120% of the test concentration.
Precision: Was evaluated as repeatability (intra-day) and intermediate precision (inter-day)
by analyzing six replicate samples.

Limit of Detection (LOD) and Limit of Quantification (LOQ): Was calculated based on the standard deviation of the response and the slope of the calibration curve.

Robustness: Was checked by introducing small, intentional variations in the mobile phase composition (±2%) and flow rate (±0.1 mL/min).

3. Results and Discussion: -

3.1 MethodDevelopment: Chromatographic conditions were optimized to produce a sharp, symmetric peak for Atorvastatin with a reasonable run time. A mobile phase consisting of Acetonitrile:Phosphate Buffer (60:40) at pH 4.1 was found to be optimal, providing a retention time of approximately 5.8 minutes and a detection wavelength of 247 nm, corresponding to the absorption maximum of Atorvastatin.

3.2.Method Validation:-Linearity: A good linear relationship was observed within the range of 5–50 µg/mL, with a regression equation of y = 45872x + 1254 and a high correlation coefficient (R^2 = 0.9997, indicating excellent linearity.

Accuracy: The mean percentage recovery was found to be between 99.2% and 101.5%, confirming the method's accuracy.

Precision: The percentage RSD (repeatability and intermediate precision) was below 2%, indicating high precision.

Limit of detection (LOD, 0.12 µg/mL and limit of quantitation (LOQ, 0.38 µg/mL and high sensitivity is achieved in the method.
Specificity: Forced degradation studies confirmed the method's specificity, with good resolution of the method.
Degradation Studies:- Degradation under acidic and oxidative conditions were studied, where significant degradation was observed in Atorvastatin due to the formation of a lactone degradant.

Peak purity analysis confirmed no co-elution of degradants with the main drug.

3.3.Analysis of Marketed Formulation:
The developed method was applied to a commercial tablet formulation.

The amount of Atorvastatin found was 19.95 mg per tablet, corresponding to 99.75% of the label claim, demonstrating the method's suitability for routine analysis.

4. Conclusion: -

A straightforward, fast, accurate, and precise stability-indicating RP-HPLC method was created and tested for measuring Atorvastatin in both raw material and tablet forms. This method follows ICH guidelines and clearly separates the drug from any broken-down products. Because it is dependable and consistent, it works well in quality control labs for regular testing and studying how the drug changes over time.

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