Macedonian Pharmaceutical Bulletin, 72 (Suppl 1) 255 - 256 (2026)
Online ISSN: 1857-8969
DOI: 10.33320/maced.pharm.bull.2026.72.03.122
Short communication

Lifecycle-based optimization of an HPLC method for the determination of related and degradation products in Lamotrigine tablets

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Introduction

Analytical Lifecycle Management (LCM) represents a systematic approach for continuous monitoring, evaluation, and improvement of analytical procedures throughout their lifecycle, from method development and validation to routine application. According to ICH Q12 and ICH Q14 guidelines, LCM enhances method understanding, robustness, and long-term analytical performance while reducing the occurrence of out-of-specification (OOS) results.

The internal HPLC method for determination of related and degradation products in Lamotrigine tablets has been continuously monitored through routine quality control and stability testing. During lifecycle evaluation, recurring chromatographic issues related to peak fronting were observed, potentially affecting method robustness and reliability.

The aim of this study was to perform a lifecycle-based assessment of the analytical method, identify the root cause of chromatographic inconsistencies, optimize the method conditions, and confirm improved analytical performance through validation and routine application.

Materials and methods

Lifecycle assessment of the analytical method

A retrospective evaluation over five years was performed using data from routine and stability analyses. Monitored parameters included retention time, peak asymmetry, theoretical plates, and RSD of the Lamotrigine peak, together with impurity profiles.

Occurrences of OOS and OOE results were also reviewed to assess method reliability. Comparison with pharmacopoeial methods was performed to identify critical chromatographic factors affecting peak shape.

Present method

The in-house HPLC method used methanol as a diluent. The test solution concentration was 2.0 mg/mL Lamotrigine, prepared in methanol. Standard and resolution solutions were prepared in the same solvent system.

Newly optimized method

The optimized method uses a mixture of methanol and water (80:20, *v/v*) as the diluent. The test solution concentration was reduced to 0.75 mg/mL of Lamotrigine. Standard and resolution solutions were prepared using the same diluent with adjusted concentrations to improve impurity detection and chromatographic performance.

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Results and discussion

Chromatographic performance of the original method

Lifecycle assessment of the original method demonstrated stable retention times and acceptable column efficiency. However, peak asymmetry values ranging from 0.66 to 0.85 confirmed significant peak fronting during both release and stability analysis, indicating limited method robustness despite acceptable impurity levels.

Method optimization and validation results

Minor modifications to the analytical method, including addition of 20% water to the diluent and a reduction in sample concentration, effectively resolved the peak fronting issue and improved impurity identification and quantification. Validation confirmed compliance with all predefined criteria for specificity, accuracy, precision, linearity, robustness, filter recovery, and solution stability.

Performance of the optimized method

Following implementation, the optimized method demonstrated improved chromatographic performance, with peak asymmetry values of 0.97–1.03 and increased theoretical plate counts (10,549–18,209), confirming enhanced robustness, stability-indicating capability, and long-term reliability**.**

Conclusion

Lifecycle-based assesment of the internal HPLC method for determination of related and degradation products of Lamotrigine successfully identified peak fronting as a recurring chromatographic issue affecting analytical performance.

Minor targeted modifications of the analytical method were sufficient to significantly improve chromatography, resulting in enhanced peak symmetry, increased efficiency, improved impurity quantification, and greater method robustness.

Application of the optimized method during routine quality control and stability testing confirmed sustained improvement in analytical performance.

This study highlights the importance of analytical lifecycle management as an effective tool for continuous method improvement and long-term assurance of reliable analytical performance throughout the product lifecycle.

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