Improved Sensitivity for the Selective Quantitation of LTB4 in Human Plasma and Sputum via UPLC-MS/MS

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Introduction

Leukotriene B4 (LTB4) is one of a family of eicosanoids that are synthesized in response to injury or inflammation, and are involved in the regulation of a variety of inflammatory responses. For this reason, LTB4 has been evaluated as a pharmacodynamics biomarker and a therapeutic target for the treatment of various inflammatory diseases. Leukotriene B4 (LTB4) is one of a family of eicosanoids that are synthesized in response to injury or inflammation, and are involved in the regulation of a variety of inflammatory responses. For this reason, LTB4 has been evaluated as a pharmacodynamics biomarker and a therapeutic target for the treatment of various inflammatory diseases.

Purpose

Development of a high-throughput method for the isolation and accurate determination of LTB4 from human plasma and sputum samples via UPLC-MS/MS.

Method Development

Sample Preparation

• Sample collection and preparation of standards and controls
• UPLC-MS/MS instrument parameters
• LTB4 extraction from human plasma/sputum samples by liquid-liquid extraction
• Calibration standard preparation

Results and Discussion

Unique method developed by scientists who at the time were affiliated with LabCorp Clinical Trials or Tandem Labs, now part of Covance.

• No matrix effects observed between biological and surrogate matrices
• Excellent accuracy and precision for human plasma and sputum
• LTB4 was chromatically resolved from its isomers in both human plasma and sputum samples (and other non-endogenous plasma samples). As shown in Figure 1, LTB4 was chromatically resolved from its isomers in both human plasma and sputum samples.

Method Qualification

• In the application matrix, multiple high-sensitivity calibrators were prepared in PBS buffer. The linearity of the matrix was determined by linear regression analysis. The results showed excellent linearity with a correlation coefficient r² = 0.9973 for the entire concentration range. The accuracy and precision of the method were determined by analysis of quality controls at four concentration levels. As shown in Figures 6 and 7, the 7 plasma lots had a mean ± SD of 99.2 ± 47.8 pg/mL (r² = 0.9973, weight 1/x²). The accuracy and precision of the method were determined by analysis of quality controls at four concentration levels. The results were excellent with a correlation coefficient r² = 0.9973 for the entire concentration range. The accuracy and precision of the method were determined by analysis of quality controls at four concentration levels. The results were excellent with a correlation coefficient r² = 0.9973 for the entire concentration range.

Conclusion

References


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