Abstract

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Title of Diploma Thesis: Optimization of metabolomic workflow for a comparison of impurity profiles of levothyroxin tablets using UHPLC-HRMS

The aim of this diploma thesis was to compare 3 designs of measuring the impurity profiles of levothyroxine tablets and to evaluate the most suitable procedure. Analyses were performed by ultra-high performance liquid chromatography coupled with high resolution mass spectrometry.

Levothyroxine drug products are used to supplement reduced thyroid function. In this work, 23 batches of tablets from 2 different manufacturers were analysed.

The optimization of the tablet sample and internal standard preparation method and the compilation of 3 measurement designs using data from the preliminary screening was the first step. The designs were compiled as targeted metabolomics analyses. Then, a targeted analysis of 4 known impurities in designs 1 and 2 was performed, which was semi-quantitative (relative content of impurity to levothyroxine content). Differences in impurity content between designs were also evaluated. The next step was to compare individual designs in terms of variability, which was evaluated according to the change in the response of the internal standard between individual injections. The last step was to compare the designs based on a principal component analysis.

Based on the obtained data, design 3 was evaluated as the most suitable for profiling impurities. Design 3 was compiled as a metabolomics analysis in one batch.

Key words: levothyroxine; UHPLC-HRMS; impurity; lactose; mannitol; impurity profiling; targeted metabolomics analysis; optimization; ICH